Participant Information and Consent Form and HIPAA Authorization

Study Title: *A Phase 2 Open Label Treatment Development Study of MDMA-Assisted Cognitive-Behavioral Conjoint Therapy (CBCT) in Dyads in which 1 Member has Chronic Posttraumatic Stress Disorder (PTSD)*

Protocol #:	MPVA-1
Study Sponsor:	Multidisciplinary Association for Psychedelic Studies (MAPS) 1115 Mission Street Santa Cruz, CA 95060
Clinical Investigator Name:	[redacted]
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1.0 Purpose of the PTSD+ Participant Information and Consent Form

This consent form describes a research study and your role as a study participant. This consent form may have words in it you do not clearly understand. Please read this form carefully before you decide to be in this study. You may ask the study therapists anything about the information provided.

The purpose of this form is to give you information about the research study and, if signed, gives your permission to be in the study. The form describes the purpose, procedures, benefits, risks, discomforts and precautions of the research study. You should be in the study only if you want to. You may refuse to take part or withdraw from this study at any time without penalty or loss of benefits to which you are otherwise entitled. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision. You should not sign this form if you have any questions that have not been answered to your satisfaction.

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 website will include a summary of the results. You can search this website at any time.

If you would like to review the information for this study, or a summary of the results, ask the study team doctor for the ClinicalTrials.gov study registration number.

Your study therapists will be paid for their time to conduct this research study

2.0 Length of Study

The length of the study will be about 6 to 7 months. Participation in the study requires a big time commitment from you and your partner for 1 month. There will be 4 in person visits, 2 over night visits and 10 videoconferencing visits for you and your partner in a 30-day period. After that you will have videoconferencing visits 3 and 6 months after your last video CBCT therapy visit.

The timeline for starting treatment after enrollment is variable depending on availability of open appointments. You may start therapy as soon as one week or as long as two months after your first visit. Experimental sessions last all day and require an overnight stay for you and your partner. After these overnight stays, you will each have a brief daily phone call with the therapists for 7 days. Of the visits listed above, 4-5 of them will be longer interviews.

Types of visits and duration:

Psychotherapy sessions (90-minutes each): Two introductory sessions at the start of participation and 5 sessions after each Experimental Session. These are approximately two days apart; most of these visits will be over videoconference.

Experimental sessions (8-hours long plus an overnight stay): Two sessions for you and your partner together. These are about 2 weeks apart.

Evaluation and Testing Visits (Up to 4 hours): Testing and completing questionnaires 5 times, starting with the beginning of the study.

You will need to be flexible about taking the appointments offered most of the time because there is a limited time frame for each type of visit.

3.0 Type of Study

This study is open label, meaning you and the study researchers will know what dose of MDMA you and your partner will get. There will be up to 10 pairs/20 people total in this study at this location, which is the only location in which this study is being done.

4.0 Procedures/What Will Happen

4.1 Screening/Evaluation and Beginning of Study

If you agree to be in this study, you will first sign this form before any study-related procedures are done. You need to stay on any current medications until you are confirmed to be enrolled in the study. Only stop medications if you are officially enrolled under the care of the study doctor. Some PTSD medications can cause thoughts about wanting to kill yourself if you stop taking them too quickly and without the care of a doctor. This is very important.

Before you can be in the study, the study doctor must first make sure that you and your partner qualify for the study and that you are generally physically healthy. This screening process can take up to one month, and there will be one or more office visits or videoconferencing visits during this time. The study doctor may ask you and your partner for written permission to contact your doctors or psychotherapists to get information about your medical history. They may need to do this so that they will know whether or not you both can be in the study.

Psychological and medical screening will be done by a study researcher and a physician other than your study therapists. The tests will include the following:

- An interview about your PTSD symptoms and how you deal with them in your everyday life. Your score on this interview will be used to decide if you can be in the study. This session may be recorded to video.
- Questions about your medical history, including questions about your emotional and psychiatric history. This may include any previous medical or psychiatric problems or treatment and may include questions about difficult experiences you may have had during childhood or at other times of your life. The study doctor will rate how well you are doing in general.
- A questionnaire that you fill out yourself about your PTSD symptoms.
- A questionnaire about feelings of depression or other symptoms or feelings you might experience.
- Answer questions about thoughts you might have about hurting or killing yourself.
- A questionnaire about your quality of sleep.
- A questionnaire about any dissociation symptoms (level of detachment from immediate surroundings or from what you feel).
- A visual scale of chronic body pain and tinnitus (ringing in the ears) levels if you have

these symptoms.

- Questionnaires about how you handle your emotions.
- A questionnaire about your compassion and empathy.
- A questionnaire about any positive/negative change resulting from the struggle with trauma.
- A questionnaire about your beliefs about trauma.
- Questionnaires about your relationship with your partner including satisfaction, accommodation, conflict, closeness, relations to others, disclosure and intimacy.
- A physical examination that will include measures of your blood pressure, pulse, temperature, and body weight.
- 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 and liver function. Laboratory tests will also include testing for the human immunodeficiency virus (HIV) and Hepatitis C (HCV).
- A urine test for drugs of abuse. Your urine drug screen must be negative to take part in the study.
- A urine pregnancy test if you are a woman and are able to get pregnant. Your urine pregnancy test must be negative for you to take part in the study.

If you test positive for HCV, we will tell you. If you test positive for HIV, we will tell you, then the study doctors will have to tell the [redacted] within seven days, as stated by law. If you live outside [redacted], the study doctors may need to report the results according to the laws of the state you live in. If you do not want to be tested, you should not be in this research study.

4.2 Beginning of Study

Once you are in the study, we will schedule your first preparatory psychotherapy session with the study therapists. You will need to be enrolled in the study before receiving psychotherapy. If you were taking psychiatric medicines before enrolling in the study, you will have to stop taking them after you are enrolled in the study. The study doctors and your physician will help you do this. You must let the study therapists know about any change in medicines or medical conditions or procedures, like surgery, within 48 hours of it happening.

You will need to give the study therapists the name and contact information (telephone number, cell phone number or email) of a relative, spouse or close friend to contact in case of medical emergency, as when you might be at risk of hurting yourself, or someone else, so they can reach that person to let them know what is going on.

4.3 Schedule of Events

Time is counted from the first study visit after you are selected to be in the study. The tables below show the type of visits you will have.

Table 1: Schedule of Events

What will happen in the study	Screening	Preparing for MDMA sessions		MDMA Session 1, Talk Therapy Sessions with CBCT						Midpoint Assess	MDMA Session 2, Talk Therapy Sessions with CBCT						Primary Assess	3 Mo Follow-up	6 Mo Follow-up
Visit #	Pre-Study	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	Visit 10	Visit 11	Visit 12	Visit 13	Visit 14	Visit 15	Visit 16	Visit 17	Visit 18
Type of Visit	Screening	Prep	Prep	MDMA	Therapy	Therapy	Therapy	Therapy	Therapy	Assess/Prep	MDMA	Therapy	Therapy	Therapy	Therapy	Therapy	Outcome	Assess	Assess
	Telemedicine or In-person Visit	Telemedicine	Visit	Visit (overnight)	Visit	Telemedicine	Telemedicine	Telemedicine	Telemedicine	Visit	Visit (overnight)	Visit	Telemedicine	Telemedicine	Telemedicine	Telemedicine	Telemedicine	Telemedicine	Telemedicine
Visit Timing or Study day or Window	During month prior to Visit 1	Less than 4weeks before V2[J]	Day 0	Day 1	Day2	Day 4	Day 6	Day 10	Day 12	Day 14	Day 15	Day 16	Day 18	Day 20	Day 24	Day 26	30 days after V15	3 Mo after V15	6 Mo after V15
Target Day			Fri	Sat	Sun	Tues	Thurs	Mon	Wed	Fri	Sat	Sun	Tues	Thurs	Mon	Wed			
CBCT Manual Session #			1,2	3,4,5	Review	Review	6	Review	7	Review	8,9,10,11	Review	12	13	14	15			
Initial Phone Screen	✓																		
Informed Consent	✓																		
Medical/Psychiatric History & General Phys Exam & EKG	✓																		
Clinical Lab Tests, w/ HIV, HCV test	✓																		
Collect Medications	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Study Enrollment		✓	✓																
Drug Screen/Pregnancy Test	✓			✓							✓								
MDMA Session + Therapy/CBCT				✓							✓								
Talk Therapy/CBCT					✓	✓	✓	✓	✓			✓	✓	✓	✓	✓			
Homework				✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓				
7 days of Telephone Contact					✓	✓	✓					✓	✓	✓					
PTSD Interview	✓																✓	✓	✓
Study Questionnaires	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Changes in Tinnitus and/or Chronic Pain	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Serious Medical Problems/Hospitalizations/Psychiatric changes		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Illnesses Needing Medical Attention				✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
All medical problems/Illnesses				✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓			

4.4 Preparatory Psychotherapy Sessions

You will meet with the study therapists on two separate occasions before the first Experimental Session. One of these meetings will be by videoconference. These visits will last 90 minutes. During each introductory session, you and your partner will talk about the traumatic incidents that led to your PTSD, the ways PTSD symptoms are affecting your life together and what you would like to achieve during these sessions. You will be asked the same questions about thoughts or feelings you might have about hurting or killing yourself during one of these Preparatory Sessions. You will also both learn more about what to expect during Experimental Sessions. The introductory sessions will be recorded to audio and video so that the study therapists will have accurate records of the sessions and so that they can gather more information about drug-assisted psychotherapy sessions. You can ask the study therapists to let you hear or see these recordings if you wish.

4.5 Experimental Sessions

There will be two day-long MDMA (experimental) sessions, when you and your partner will have an active dose of MDMA and talk therapy including CBCT therapy. These visits will happen two weeks apart. The first Experimental Session will occur after you have had two introductory sessions. Your therapists will discuss the optimal dose of MDMA with you and your partner for the second Experimental Session.

One week before each of the Experimental Sessions, you and your partner will need to avoid taking:

- Any herbal supplement (except with prior permission).
- Any non-prescription medications, unless you have permission from the study therapists (with the exception of non-steroidal anti-inflammatory drugs or acetaminophen [Tylenol]).
- Any prescription medications, unless you have permission from the study therapists (with the exception of birth control pills, thyroid hormones or other medications approved by the study therapists).

You must not eat any food or drink any alcohol after midnight on the night before each session, though you can drink non-alcoholic liquids during this time, such as water or juice. You cannot use any psychoactive drug, with the exception of caffeine or nicotine, within 24 hours of each Experimental Session (or longer depending on the specific drug – this should be discussed with the study therapists). You cannot use nicotine or caffeine for two hours before and six hours after drug administration.

If you are taking opiate medications for pain management, you can stay on these medications, although we may ask you to reduce the dose or stop taking them for at least 24 hours before the Experimental Sessions, because these medications may reduce the effectiveness of MDMA. If your pain becomes too severe to handle during this period, you will be allowed to take your medication.

First, you, your partner and the study therapists will discuss your goals for the Experimental Session and the study therapists will answer any other questions you may have.

Before an Experimental Session:

- Your urine will be tested for drugs of abuse, including stimulants, sedatives, opiates and cannabis.
- If you are a woman who can become pregnant, you will take a urine pregnancy test.

During the Experimental Session:

- Your blood pressure, temperature, and pulse will be measured before taking the first and second capsules of MDMA and at the end of the session. If you have any symptoms including confusion, light-headedness, dizziness, chest pain, shortness of breath, tell your study therapists. More frequent measurements may be needed if this happens.
- You will also complete a very brief, simple test of how comfortable or distressed you feel by picking a number that best matches the level of any distress you may feel. You will complete it every 60 to 90 minutes during the Experimental Sessions.
- About an hour before receiving the drug and about six hours afterward, you will answer questions about thoughts you might have about hurting or killing yourself.
- The study therapists will talk to you at least every hour or so to see how you and your partner are doing.
- If you had tinnitus or chronic pain before the study and mention any changes in these symptoms, the therapists will note the changes.

The Experimental Session will be recorded to audio and video so that the study therapists will have accurate records of the session and so that they can gather more information about drug-assisted psychotherapy sessions. You can ask to see or hear these recordings if you would like.

After urine testing, you will receive a capsule containing an active dose of MDMA. After taking the capsule, you and your partner will then sit or lie down in a comfortable position. You can ask for an eyeshade if you wish. You will listen to music during much of each Experimental Session, either through headphones or room speakers. During the session there will be times when you will be asked to talk to the study therapists. If you are wearing headphones, you may remove them yourself if you want to talk to the study therapists or have times of silence. Lying or sitting in a comfortable position and listening to music are meant to bring out thoughts and feelings, including thoughts and feelings about the trauma. Both study therapists will remain with you, and your partner and they will help you if you need them to. They will speak with you and ask you to talk to them at least once an hour, but you can talk to them whenever you wish. There may be times when the study therapists will suggest that you stop talking for a while in order to pay attention to your thoughts and feelings. There will be beverages available, including water, juices and Gatorade® or similar sports drinks, and you will be encouraged to drink an adequate amount of fluid. You can drink it whenever you wish to do so, within the limits of the amount that is safe for your body. Later on, food will also be provided.

Approximately one and a half to two and a half hours after you take the first capsule, you and your partner will take a second capsule. The second dose will contain half the amount of the first capsule. The thought behind taking the second capsule is that it is not supposed to make the MDMA stronger, just make it last longer. If you or the study therapists notice problems after the first capsule, then you or your partner will not get the second capsule.

The study therapists will watch for any side effects (unwanted effects or health problems), which will be treated if necessary. If this happens, the study therapists will keep you fully informed about any concerns or treatment.

If you are confused or upset eight or more hours after the start of an Experimental Session, the therapists will stay with you until you have fully recovered. If the therapists think you are at risk of hurting yourself or others, they will either remain with you all night or have you admitted to a hospital until you are no longer at risk of hurting yourself or others. The therapists will ask you about thoughts of killing or harming yourself before and after drug administration and on several occasions during the phone follow-up period. You will also be asked to complete homework assignments during the study. These should be completed and returned at 11 out of 19 visits.

You and your partner will be spending the night in a room at the office of the therapist with an attendant who will be staying in another room nearby. You can use the kitchen or walk around outside if you want. If you find you need to talk with the therapists or you are having other problems and need to contact the therapists, the attendant will contact them immediately.

On the next day, you and your partner will have a non-drug talk therapy session with the study therapists. You will need to have someone drive you and your partner to wherever you are staying (home, hotel or another location) from the non-drug therapy session on the day after the Experimental Session because we do not know how MDMA will affect your ability to drive, and because some people report feeling tired, less alert or having trouble concentrating a day after having taken MDMA. If you cannot find anyone to take you home, the therapists will find someone to drive you.

After you return back home from the talk therapy session, the therapists will talk to you and your partner either by phone or videoconferencing every day for a week to ask how you are feeling and see whether you should see the study therapists before your next scheduled non-drug psychotherapy session. The phone calls will take approximately 5 to 15 minutes, though they can be as long as you need them to be. The therapists will ask you about thoughts about killing or harming yourself during the second and seventh day of phone contact. You can call the study therapists at any time. The study therapists may be called 24 hours a day during the research study; except for a few times they may be out of town. At those times the study doctor will be on call and can be called at a number that will be given to you.

The therapists will give you and your partner a card with phone numbers for calling your study therapist and the Copernicus Group Independent Review Board (IRB), which is an independent committee that protects the rights and welfare of study participants. You can keep this card in your wallet to make it easier for you to contact the therapists if you need to.

If there are delays in following the usual study schedule, the study therapists will call you at least once a week to talk about how you're doing. These calls will take about 15 minutes. You need to agree to call the study doctors if any of these things happen: you have an increase in symptoms that you have taken medication for in the past, you need to contact your outside therapist other than for the usual appointments, and/or you start or stop taking a prescription medicine or an over-the-counter medicine that you have not previously cleared with the study therapists.

If you have very high blood pressure, get sick, or have an important and strong lasting reaction (unwanted effect or health problem) during or after an Experimental Session, you or the study therapists may decide that you should not have the next Experimental Session. You may make this decision to stop treatment in the study for any reason. If either you or your partner needs to quit the study, you will both need to quit the study at the same time.

If the study therapists decide to take you or your partner out of the study, they will let you both know that they are doing this and their reason for doing it. If you are taken out of the study or decide you do not want to receive treatment in the study, the study researchers will ask you to

complete some final questionnaires about your PTSD symptoms. If you decide you do not want to continue in the study during an Experimental Session, you will still have to stay in the office until the study therapists think that you are well enough to leave and that all the acute effects of the drug have worn off. If this happens, you will also be asked to take part in some of the same interviews and questionnaires you completed at the beginning of the study. You will also be expected to take part in the 6-month long-term follow-up.

4.6 Psychotherapy (Talk Therapy) After Experimental Sessions

You will have regular psychotherapy to help you express, understand, bring together and connect any thoughts or feelings you may be having about your symptoms and their causes, and to think and talk about your experience during Experimental Sessions. You and your partner will have psychotherapy with the study therapists the morning after each Experimental Session. These sessions will last 60 to 90 minutes. You and your partner will have 2 longer videoconference calls about 2 days apart during the week after the MDMA session for CBCT/ talk therapy. You and your partner will have 2 additional videoconference calls about 2 days apart during the second week for CBCT therapy. You may schedule more meetings with the study therapists besides those that are scheduled as part of the study if you, your partner and/or the therapists think they are needed. You and the study therapists will also talk about ways to use what you learned to help work on treating your PTSD, face and solve difficulties you may have faced during the Experimental Sessions and with your partner and gain maximum benefit and understanding from Experimental Sessions. Each regular psychotherapy session will be recorded to audio and video, just like the preparatory and Experimental Sessions, and you can hear or see these recordings if you wish.

If you had tinnitus or chronic pain before the study and mention any changes in these symptoms, the visual analog scale will be used to collect the changes.

The therapists will ask you about thoughts about killing or harming yourself at these visits. Questions about your PTSD symptoms and the way you connect with others will also be asked during each of these visits.

4.7 Measuring PTSD After Experimental Sessions

Approximately two weeks after each Experimental Session you will meet with the study researcher again, which may be recorded. The researcher will ask about your PTSD symptoms. You will also meet with your study therapists two weeks after each Experimental Session to fill out the same questionnaires from the start of the study. You will also be asked if you have had any thoughts about hurting or killing yourself. You will also complete the scale of pain and tinnitus levels if you had these problems before the study. The tests will help the study therapists tell if your symptoms have changed or stayed the same over time.

You will complete a questionnaire about your experience as a research participant 2 weeks after your second Experimental Session. The study therapists will give you and your partner a memory aid card. This card is to help you to remember any new problems or medical conditions, or changes in medication during the months between this visit and your last visit, the 6-month follow-up videoconference visit. On this card you will record any new important health problems, changes to your mental health, hospitalizations and medications to treat these problems.

Three and 6 months after your second Experimental Session, you will meet with the study researcher by video conference again, which may be recorded. The researcher will ask about your

PTSD symptoms. The questionnaires will be given to you or mailed for you to fill out for your 3-month and 6-month follow-up videoconference visit. If mailed to you, it will come with an envelope that is already stamped and have only the researcher's address on it. Do not put your name on the questionnaire.

The researchers will use your answers to these questionnaires to see if there are any long-lasting effects of being in the study, such as changes in PTSD symptoms or other life events.

5.0 Possible Risks or Discomforts

MDMA has not been widely tested in humans, but as of December 2015 more than 1185 people have been given MDMA in clinical research settings, without any serious unexpected problems happening.

Side effects during the MDMA experience that are less severe but more frequently reported, are:

- Lack of appetite (68%)
- Dry mouth (64%)
- Teeth grinding or tight jaw muscles (60%)
- Decreased concentration (53%)
- Thirst (48%)
- Restlessness (46%)

In two studies of MDMA in a total of 37 people with PTSD, these reactions were commonly reported after a 125 mg active dose of MDMA:

- Fatigue (77%)
- Anxiety (74%)
- Muscular tightness/tight jaw (62%)
- Insomnia (61%)
- Headache (51%)
- Lack of appetite (48%)

In previous studies and in a placebo-controlled study of MDMA-assisted psychotherapy in people with PTSD, 48% to 77% of participants reported:

- Nausea
- Low mood
- Feeling cold
- Dizziness
- Impaired balance
- Disturbance in attention
- Restlessness
- Perspiration
- Thirst
- Feeling weak
- Need for more sleep (listed from most to least commonly reported)

When any of these side effects occur, they usually last less than four hours, though some people report that some of these side effects can last for more than twenty-four hours, and rarely longer.

There may be unknown side effects or risks from the use of MDMA.

Other possible risks of MDMA may include the following:

Serious problems: There have been some serious problems, and even deaths, associated with the use of ecstasy outside of controlled clinical or laboratory settings. These problems have included high fever, brain swelling associated with drinking too much liquid, convulsions, and liver damage. Some recreational users of ecstasy have become severely anxious, depressed or paranoid (thinking that other people are out to get them). Since you will be receiving moderate amounts of uncontaminated MDMA in a controlled setting with trained therapists who will be closely monitoring your physical and psychological reactions, these problems are not expected to occur either during or after the Experimental Session. While this does not guarantee that they will not occur, it does mean that if they do occur, the study doctors are prepared to respond in a safe and professional manner.

Changes in vision, hearing or other senses: Most participants that took part in past MDMA studies reported experiencing temporary and minor changes in vision and hearing, such as sounds seeming closer or farther away than usual or objects seeming brighter than usual. These changes typically lasted 2 to 3 hours. Between 12% and 33% of people who took MDMA also reported unusual feelings in their bodies, such as tingling or numbness.

Blood pressure and heart rate: The effects of MDMA usually last 4 to 6 hours. At the dose in this experiment, the increases in blood pressure and heart rate are likely to be moderate. Average increase in systolic blood pressure is 35 mmHg (measurement unit for blood pressure) and average diastolic blood pressure increase is 20 mmHg. Heart rate may increase by about 30 beats per minute (BPM), sometimes more.

In past studies supported by MAPS and published studies, blood pressure rose well above normal levels in a few participants (a little less than 5%) after taking MDMA, but these participants did not report any discomfort and did not require any treatment. Although these increases in blood pressure are similar to what happens after heavy exercise, they could cause serious problems in individuals with pre-existing heart or blood vessel conditions. These serious problems could include an irregular heartbeat, heart attack or stroke. We will screen all potential participants for preexisting heart problems before they are allowed to be in this study. While this doesn't guarantee that no heart problems will occur, it does reduce the risk of this happening.

Anxious or jittery feeling: Some participants in past studies (16%) reported feeling over-stimulated or anxious. These feelings usually lasted less than 30 minutes. Letting yourself accept and feel these emotions deeply can be part of the psychotherapy. If you are not able to deal with these experiences in a way that helps you, the study doctors will work with you to deal with these feelings. It is possible that if such periods of heightened emotion do not clear up or grow weaker during the session, you could be at increased risk for suicide or other self-harm afterwards. You will be encouraged to ask the attendant to call the study therapists immediately if you have any thoughts about hurting or killing yourself so they can safely help you. If needed, they may prescribe anti-anxiety medication or medication for sleep.

If you are in immediate danger of hurting or killing yourself or hurting someone else, then the researchers may require you to be admitted to a hospital.

Insomnia & drowsiness: In previous studies, between 17% and 23% of participants have reported insomnia (difficulty sleeping) or feeling tired, irritable, or drowsy for as long as 3 days after taking MDMA. **You should not drive or use machinery immediately after Experimental Sessions (up to 24 hours afterwards)**. This is because the study drug may cause drowsiness, lack of coordination or slower reaction time.

Mood: Some after-effects of MDMA may be noticed up to 2 or 3 days later. While some participants feel that their mood is better, 14% feel that it is worse.

Immune System: You may have a less active immune system for 2 or 3 days after taking MDMA. This may make you more likely to become sick with a cold or other infection during this time. The study describing this finding did not report how many people in the study showed these changes.

Addiction: There is a small chance that you will become dependent on (addicted to) MDMA. One study found that up to 6% of people using ecstasy for recreational purposes were dependent on it. However, a study of people who had received MDMA for the first time in a legal laboratory setting found that they did not want to try MDMA again outside of the laboratory.

People who have recently (in the last 2 months) had problems with drug abuse should not be in this study.

Possible Brain Damage: Experiments in rats and monkeys show that high and repeated doses of MDMA can change certain brain cells that release a chemical called serotonin; in mice (though not in humans), the affected cells release dopamine. The changes include loss of the parts of the cell (called "axons") that connect different brain areas. Rodents given repeated, high doses of MDMA are less sensitive to a later dose of MDMA, are more likely to become overheated when placed in a warm room, and some studies find they perform worse in difficult memory tests. Recent studies in monkeys and rodents suggest that the doses used in these studies are far higher than those typically taken by humans in either recreational or laboratory settings.

Many studies found that people who had used ecstasy many times in recreational contexts were not able to recall words, pictures or patterns as well as people who did not use ecstasy, and performed less well on tests of planning and impulse control. These differences are not great, but they have lasted for at least a year after people had stopped taking ecstasy. Not all studies have found ecstasy users to have difficulty recalling words or pictures or to have impulse control problems. When compared with people who do not use ecstasy, studies found Ecstasy users were more likely to report feeling generally anxious or depressed. Many of these studies found that using alcohol or other drugs was also associated with feeling anxious or depressed. At least two studies found that people who are anxious, depressed or have psychological problems before taking any drugs are more likely to take ecstasy than people without these problems, but there is no proof that MDMA might not cause these problems in some people.

Only one study has looked at brain scans of people before they got MDMA and then again after they have received one or two moderate doses of MDMA. This study did not show any changes in the brain following MDMA, though it is possible that there were changes that were too small to notice. Other studies looked at people before and after they decided to take a few tablets of ecstasy in a recreational setting, and found one small change in the amount of blood flow in a specific part of the brain, but did not show signs of brain injury. The decrease in blood volume might be from temporary lowering of a type of brain receptor, or it might be a sign of reduced function in this area. Findings from these studies suggest that the amount of MDMA you will receive in this study will not produce any lasting changes in your brain, though this is not

guaranteed.

Studies of people receiving one or two doses of MDMA in a laboratory setting have not found any lasting changes in memory or planning. Studies comparing people before and after they decided to take a few tablets of ecstasy in a recreational setting with people who did not take them found less improvement in memory in the people who took ecstasy, and no other changes in thinking or planning. It is believed that the amount of MDMA you will receive will not produce any lasting changes in memory or planning, though this cannot be guaranteed.

6.0 Risks of Being in the Study

If you are tested for drugs of abuse within three days of each Experimental Session, you may test positive. The study therapists will provide you with an information card in case you are tested for drugs of abuse, and if you are tested for drugs of abuse while you are in this study, you can have the person(s) testing you call your study therapist to verify that you are in this study.

The interviews you have during the study involve no specific risks or discomforts beyond those of a standard clinical interview situation. You may feel upset at 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.

The medical evaluation involves some blood tests. The risks of blood drawing include temporary discomfort from the needle stick, bruising and, rarely, infection at the site of the needle stick. Fainting could also happen.

It is possible that after you stop taking psychiatric medicine (as for depression or anxiety) as part of the study, you may start to have symptoms again. There is also a risk that you may have thoughts of hurting or killing yourself when you stop taking medicine, especially if you have had these thoughts before. If this happens, you should talk with your outside therapist and your study therapist. If you have to start taking medicine again, then the study doctors will have to take you out of the study.

7.0 Reproductive Risks

Effects of MDMA on the growth and development of an unborn baby are not known; therefore, you will not be allowed to be in the study if you are pregnant. If you get pregnant after you have had at least one Experimental Session, the study doctors and the sponsor, MAPS, will ask you about and keep track of your pregnancy and will need to know about the outcome of your pregnancy.

Women who are able to become pregnant must use one of the allowed birth control methods, intrauterine device (IUD), injected or implanted hormonal methods, abstinence, oral hormones plus a barrier contraception or double barrier contraception. Two forms of contraception are required with any barrier method or oral hormones (i.e. condom + diaphragm, condom or diaphragm + spermicide, oral hormonal contraceptives + spermicide or condom). Not of childbearing potential is defined as permanent sterilization or postmenopausal females until 10 days after the second Experimental Session. The study therapists will explain these methods to you and will help you decide which might be best for you, and they can suggest to you where you can get more information and advice.

If you are a woman of childbearing potential, you will be tested at the start of the study and again before each Experimental Session to see if you are pregnant. If, at any time during the study, you think that you may be pregnant or are worried that you may become pregnant, you must tell your study therapist immediately. If you should become pregnant during the study, the study doctors will help you get proper advice and help you and your unborn baby get proper care while you are pregnant.

8.0 New Findings

If any new information becomes available about MDMA while you are in this study, the study therapists will tell you about it as soon as possible. You may contact the study therapist at any time after your participation ends to find out if any new information about this study has become available.

9.0 Possible Benefits

Your symptoms of PTSD and relationships may improve while taking part in this study. There is no guarantee that you will benefit from taking part in this research study. Information obtained from this study may help doctors and researchers to improve treatment for PTSD and relationships in the future.

10.0 Payment for Participation

There will be no payment for taking part in this study.

11.0 Costs

The sponsor of this study, MAPS, will cover the costs that are directly related to the research. This includes the costs for all psychotherapy sessions that are a part of this study, for the psychological and laboratory testing, for 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), or 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 not included in the study.

If you live over 165 miles away from the research site (which assumes a 3-hour car ride), you will be reimbursed for up to two nights in a hotel room at a hotel close to the study site that will be comfortable for you and your partner for each visit you attend in person per study protocol.

12.0 Alternatives

One alternative to being in this study is to decide not to take part. You may decide to try other treatments for PTSD. There are other medicines, such as Paxil (paroxetine) or Zoloft (sertraline) and anti-anxiety medications such as Xanax (alprazolam) and other forms of psychotherapy that you could try. If you are currently having psychotherapy and/or taking medicine, you could continue with those for a longer period of time. The study therapist can discuss the alternatives and their potential risks and benefits with you.

13.0 Confidentiality

To ensure confidentiality, only participant numbers will be provided to the study sponsor unless you give specific permission, for example at a time when you sign a media release. When not in use, your information will be stored in a locked office. Absolute confidentiality cannot be guaranteed, but every effort will be made to maintain your confidentiality.

Some people need access to your 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. Medical records may be looked at by:

- The sponsor, MAPS and the people they hire to over-see the study.
- The FDA and similar agencies in other countries.
- The Department of Health and Human Services (DHHS) agencies.
- Governmental agencies in other countries.
- The Copernicus Group Independent Review Board (IRB).

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

The results of this research study may be presented in meetings, presentations, or in publications, where your identity will not be disclosed. Videotapes of your sessions may be used in training sessions for research therapists or other researchers only in controlled settings as described below

Audio and video recordings: The study therapists will audio and video record each visit after enrollment. The purposes for this recording that you are agreeing to by signing this informed consent are:

1. So that you will have access to review your own therapy sessions.
2. So the study therapists will have accurate records of the session.
3. So that trained raters working for the sponsor can verify that the therapy is being carried out according to the protocol and the methods described in the Treatment Manual. The raters watch randomly selected video sessions through an online portal that requires strictly controlled, time-limited password access.
4. For further research on the therapy and how it is performed.
5. For training other therapists and scientists to develop and work on additional research. For this purpose, your videos may be viewed in online trainings, requiring strictly controlled time-limited password access, or in in-person trainings.

For the above purposes the adherence raters, researchers and therapists who may be viewing these recordings will be selected by the sponsor, and will sign confidentiality agreements to ensure they do not share the identifying information they may receive.

You may listen to or watch the recordings if you wish, but you do not have to. Due to processing time required, they will not be available immediately after your visit. Once the recordings are processed you may request a unique password to allow you to access your own recordings, which will be identified only by your study participant number. No identifying information will be written or otherwise attached to the video recordings.

It is also possible that the investigators and/or Sponsor may wish to use portions of your videos to

educate a broader audience at medical conferences or other settings. In these settings the audience will not be specifically screened and selected, and confidentiality agreements will not be obtained from the audiences. By signing this consent, you are not agreeing to the use of your video in these kinds of settings where confidentiality cannot be carefully guarded, and you are not required to agree to use of your video in these settings in order to participate in the study. At the end of the CBCT therapy (Visit 16) when you have completed all of the questionnaires and measures, you can make a decision about whether or not you wish to grant this additional consent.

These recordings will be stored on encrypted back-up hard-drives stored in a locked and secure location when not in use. A copy will be transferred to electronic secure storage on the web to allow for viewing purposes described above. Electronic systems used will include measures to protect confidentiality of your identity and video data. Your videos may be viewed in online trainings or in in-person trainings with pre-screened therapists. People viewing these videos will be asked to sign a confidentiality agreement. No identifying information will be written or otherwise attached to the video recordings.

During your study sessions you may ask to stop the recording at any time, but your therapists will ask your permission to turn it back on when you are ready.

By signing this consent form, you consent to the collection, access, use and sharing of your information as described above. You have the right to check your study records.

14.0 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 therapist 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 will pay for any study-related procedure that your insurance will not cover.

15.0 Legal Rights

The above section does not restrict your right to seek legal assistance. You do not waive any legal rights by signing this form.

16.0 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.

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 study. Before withdrawing from this study, 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 office for tests.

17.0 Withdrawal

Your study therapist, the sponsor company, or the FDA 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 effect from the study drugs, if you need a treatment not allowed in this study, such as restarting medication for depression or anxiety, if you do not keep appointments, if you do not take the study drug as instructed, if you become pregnant, or if the study is canceled by the FDA or the sponsor company.

18.0 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:
Daytime telephone number:
24-hour contact number:

If you have any questions or concerns about your rights as a research participant 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 participant's rights and welfare in mind. Copernicus Group IRB has reviewed and approved the research study described in this 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 participant, 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 Copernicus Group 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.

Participant's Statement of Consent

"A Phase 2 Open Label Treatment Development Study of MDMA-Assisted Cognitive-Behavioral Conjoint Therapy (CBCT) in Dyads in which 1 Member has Chronic 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 agree to have my sessions audio- and video-recorded during this study.

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 take part in this study. All of my questions so far about the study and my participation in it have been answered. I freely consent to take part 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 participant in a research study. I have been told that I will be given a copy of this consent form after it has been signed and dated.

_____ _____
Signature of Participant Date

_____
Printed Name of Participant

I certify that the information provided was given in language that was understandable to the participant.

_____ _____
Signature of Person Obtaining Consent Date

_____
Printed Name of Person Obtaining Consent

HIPAA Authorization

The United States government has issued a privacy rule to protect the privacy rights of patients. This rule was issued under a law called the Health Insurance Portability and Accountability Act of 1996 (HIPAA). The Privacy Rule is designed to protect the confidentiality of your personal health information. The document you are reading, called an "Authorization," describes your rights and explains how your health information will be used and disclosed (shared).

In working with the sponsor, the study doctor, [redacted], will use and share personal health information about you. This is information about your health that also includes your name, address, telephone number or other facts that could identify the health information as yours. This includes information in your medical record and information created or collected during the study. This information may include your medical history, physical exam and laboratory test results. Some of these tests may have been done as part of your regular care. The study doctor will use this information about you to complete this research.

In most cases, the study doctor will use your initials and assign a code number to your information that is shared with the sponsor. The sponsor and its representatives may review or copy your personal health information at the study site. Regulatory authorities and the Copernicus Group Independent Review Board may also review or copy your information to make sure that the study is done properly or for other purposes required by law.

By signing this Authorization, you allow the study doctor to use your personal health information to carry out and evaluate this study. You also allow the study doctor to share your personal health information with:

- The sponsor and its representatives
- The Copernicus Group Independent Review Board
- The U.S. Food and Drug Administration (FDA)
- Other regulatory agencies

Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the Privacy Rule. However, these groups are committed to keeping your personal health information confidential.

You have the right to see and get a copy of your records related to the study for as long as the study doctor has this information. However, by signing this Authorization, you agree that you might not be able to review or receive some of your records related to the study until after the study has been completed.

You may choose to withdraw this Authorization at any time, but you must notify the study doctor in writing. Send your written withdrawal notice to the address below:

If you withdraw from the study and withdraw your Authorization, no new information will be collected for study purposes unless the information concerns an adverse event (a bad effect) related to the study. If an adverse event occurs, your entire medical record may be reviewed.

All information that has already been collected for study purposes, and any new information about an adverse event related to the study, will be sent to the study sponsor.

If you withdraw from the study but do not withdraw your Authorization, new personal health information may be collected until this study ends.

This Authorization does not have an expiration date. If you do not withdraw this Authorization in writing, it will remain in effect indefinitely. Your study doctor will keep this Authorization for at least 6 years.

If you do not sign this Authorization, you cannot participate in this research study. If you withdraw this Authorization in the future, you will no longer be able to participate in this study. 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.

19.0 Authorization

I authorize the release of my medical records and personal health information related to this study to the sponsor and its representatives, the Copernicus Group Independent Review Board, the FDA, and other regulatory agencies as described above. I have been told that I will receive a signed and dated copy of this Authorization for my records.

_____ _____

Signature of Participant Date

_____

Printed Name of Participant

_____ _____

Signature of Person Obtaining Consent Date

_____

Printed Name of Person Obtaining Consent