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**PARTICIPANT INFORMATION AND CONSENT FORM**

**TITLE:** An Open-Label, Multi-Site Phase 2 Study of the Safety and Effect of Manualized MDMA-Assisted Psychotherapy for the Treatment of Severe Posttraumatic Stress Disorder

Canada

**PROTOCOL NO.:** MP17  
WIRB® Protocol #20171866

**SPONSOR:** Multidisciplinary Association for Psychedelic Studies (MAPS)

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**For emergencies only:** Call the centre nearest you and ask for your study doctor or, if he or she is not available, ask for your usual doctor or the doctor on-call.

Names and Numbers for local hospitals: McGill University Health Centre, the Montreal General Hospital at 514-934-8090

**For non-emergency contact numbers:** Sabrina Adams at 438-818-9918 (24 Hours)

You should keep a copy of this form. If you have any questions or problems during the study, call the phone number(s) above.

**PURPOSE OF THE PARTICIPANT INFORMATION AND CONSENT FORM**

This consent form describes a research study and your role as a 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 therapy team anything about the information provided.

The purpose of this form is to give you information about the study and, if signed, the form gives us your permission to participate. The form describes the purpose, procedures, benefits, risks, discomforts and precautions of the study. You should participate 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. Signing this form will not result in you losing any of your rights. The main purpose of this form is to make sure that we are doing our job explaining to you what the study is about.

You may take home an unsigned copy of this consent form to think about or discuss with family or friends before deciding to participate.

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.

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

Your therapy team will be paid for their time to conduct this research study.

This document uses words such as treatment, drug, medication, and participant. Please remember this is a research study and the use of these terms does not mean the use of the drug has been found to be safe or effective for your condition.

Before you decide whether to participate, you should think about how the tests and study visits will affect your time away from work and your schedule.

## **BACKGROUND**

You are being asked to participate because you have been diagnosed with posttraumatic stress disorder (PTSD) with symptoms lasting for at least six months.

This multi-center study is designed to provide information on whether the drug MDMA combined with psychotherapy is safe and helpful for people who have PTSD.

MDMA is an experimental drug, which means that it has not been approved by Health Canada for sale for medical use in Canada or the Food and Drug Administration (FDA) in the United States (U.S.). MDMA is also a controlled drug (illegal to use outside of research) and is sometimes known as "Ecstasy" or "Molly" (which is supposed to contain MDMA, but often contains other drugs instead of or in addition to MDMA). MDMA is a chemical that is structurally similar to some stimulant chemicals, like methamphetamine, which is a major drug of abuse, and to some psychedelic (hallucinogenic) chemicals, like mescaline, which is found in peyote cactus. MDMA has already been used legally in research and illegally in uncontrolled environments, such

as nightclubs. While much is known about MDMA and its risks, much remains unknown about this drug.

The study is sponsored by a U.S.-based non-profit organization, the Multidisciplinary Association for Psychedelic Studies (MAPS, [www.maps.org](http://www.maps.org)). MAPS has completed six studies of MDMA-assisted psychotherapy in the U.S., Canada, and Israel.

The Principal Investigator Dr. Emma Hapke and Dr. Simon Amar, Inc., has received financial compensation from the sponsor MAPS for the work required in doing this clinical research and/or for providing advice on the design of the study/travel expenses/etc. Financial compensation to researchers for conducting the research is associated with obligations defined in a signed contractual agreement between the researchers and the sponsor. Researchers must serve the interests of the participant and also abide by their contractual obligations. For some, the payment of financial compensation to the researchers can raise the possibility of a conflict of interest. You are entitled to request any details concerning this compensation from the Principal Investigator.

Before MDMA became illegal in 1985, some psychologists and psychiatrists combined it with psychotherapy to help people with psychological problems or challenges, including PTSD and couples therapy. Though we do not know exactly why it may help people with PTSD, we know that MDMA may increase positive mood and changes the way we see and think about the world around us, making it easier to think about and recall things that happened to us that are upsetting. People say they feel caring and forgiving toward themselves and others during the MDMA experience. It is possible that these drug effects, when combined with psychotherapy, help people work through thoughts, memories and emotions related to PTSD and other past experiences.

This study will test the safety of MDMA-assisted psychotherapy, as well as whether it works. During MDMA-assisted psychotherapy sessions, you will receive a dose of MDMA and possibly a second dose equal to half the size of the first dose about two hours later. You will have either the same dose or a slightly higher dose for the second and third sessions, which will happen roughly one month apart.

### **TYPE OF STUDY**

This study is open-label, meaning that you will definitely receive MDMA, and both you and the study researchers will know. There is no chance that you will receive placebo in this study. There will be a total of up to 5 people in this study across multiple locations.

### **LENGTH OF STUDY**

The length of active participation in the study will be about 19 to 38 weeks, depending on the length of screening and the time in between your study visits. Participation in the study requires a large time commitment from you over the active study period. To confirm that you are eligible for the study, there will be multiple in-person visits to the study location, lab, and doctor's office, at least one online meeting with an evaluator,

and phone calls from the study team. Then, there will be three preparatory visits, three day-long visits with overnight stays, and nine integrative (talk-therapy) visits for you in a 13 to 26-week period (depending on visit scheduling). There will be two evaluation days where you complete many questionnaires. There will also be three online meetings with an evaluator who will ask you questions about your PTSD symptoms, and meetings with the staff and therapy team about two months after your last Overnight Test Session.

The timeline for starting treatment after enrollment is variable depending on availability of open appointments. You may start therapy as soon as two weeks, or as long as six weeks after your first visit. Overnight Test Sessions last all day and require an overnight stay at the clinic afterwards. After these overnight stays, you will have four brief phone calls with the therapy team during the seven days after the visit.

You will be invited to enroll in a 12-month follow-up study at the end of your participation. This will be explained in another informed consent form.

#### **TYPES OF VISITS AND DURATION:**

**Screening Visits:** Multiple visits at the study location, lab, and/or doctor's office, and phone calls from the study team.

**Preparatory Visits:** (~90 minutes each): three introductory sessions at the start of participation in the study, spaced about one week apart.

**Integration Sessions:** (~90 minutes each): three sessions after each Overnight Test Session. These are approximately one to three weeks apart and will involve you talking to your therapists about your thoughts and feelings.

**Overnight Test Sessions:** (~8 hours long plus an overnight stay): three visits about a month apart. You will be given MDMA during these visits along with psychotherapy.

**Online Meetings:** (60-90 minutes each): four online video meetings

**Evaluation and Testing Visits:** (90 to 120 minutes): Testing and completing questionnaires two 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.

#### **PROCEDURES/WHAT WILL HAPPEN**

##### **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. If you are taking certain medications, you may need to stop taking them before you are enrolled in the study. Only stop medications if the study doctor

gives you specific instructions for how to stop. 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. Medications will only be stopped after consultation with your prescribing doctor.

Before you can be in the study, the study doctor must first make sure that you qualify for the study and that you are generally physically healthy. This screening process can take up to six weeks, and there will be one or more office visits and online meetings during this time. The study doctor may ask you 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 you can be in the study or not.

You may need additional testing by a cardiologist if you have hypertension. If this occurs, you will sign an additional consent form at the cardiologist's office. If there are other medical concerns during screening, you may be asked to do additional testing. The study doctors will explain any tests they are asking you to do.

During online meetings with researchers, you must be in a quiet place with stable internet connection. Your device can be a phone, computer, or tablet. Your device must have a camera and you must be in a location in which you feel comfortable to discuss personal information. If needed, we can arrange for these online visits to occur in our offices.

Psychological and medical screening will be done by staff, doctors, or your therapy team. The tests will include the following:

- 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.
- An interview about any psychological or psychiatric issues you may be experiencing, or that you have experienced in the past.
- A brief interview about thoughts you might have about hurting or killing yourself.
- Psychological questionnaires you fill out yourself.
- A physical examination that will include measures of your blood pressure, pulse, temperature, and body weight. This information will also be used to calculate your Body Mass Index (BMI).
- An ECG (electrocardiogram) and rhythm strip will also be taken, which are recordings of the electrical activity of your heart.
- A sample of your blood (about 30 mL [about 2 tablespoons]) and a urine sample for routine laboratory testing, including tests of metabolism, liver function, and alcohol use. We will also test for the human immunodeficiency virus (HIV) and Hepatitis C virus (HCV).

- If you have positive test results for HIV or Hepatitis C, we will notify you. We are required to notify provincial health authorities of positive results. If the HIV test is positive you cannot take part in this research study. If you test positive for Hepatitis C you will only be able to participate if you currently don't have symptoms of Hepatitis C (asymptomatic) and have been previously treated for it. If you do not want to be tested you should not take part in this research study.

Your personal information or information that could identify you will not be revealed without your express consent unless required by law. If facts become known to the researchers which must be reported by law to public health authorities or legal authorities, then your personal information will be provided to the appropriate agency or authority.

- A urine test for drugs of abuse. Urine drug screen will be reviewed in order for you to take part in the study. We will not report findings of drugs to any authorities.
- A urine pregnancy test if you are able to get pregnant. Your urine pregnancy test must be negative for you to take part in the study.

If you pass the initial screening and choose to participate, you will be enrolled in the study. However, the screening process continues until Visit 3, when you will have additional psychological testing by an online video meeting. You will not know for sure whether you will get treatment until that time.

### **Beginning of Study**

Once you are in the study, we will schedule your first preparatory psychotherapy session with the therapy team. 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 therapy team 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 therapy team 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, should you become at risk of hurting yourself or someone else, or if the study team cannot get in touch with you, so they can reach that person to let them know what is going on or find out if you are okay.

## **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 in-person visits and online sessions you will have. All visits and sessions will be recorded to video so that the therapy team will have accurate records of the sessions, and so that they can gather more information about these sessions.

**Table 1: Schedule of Events**

	Screening (2-6 weeks)	Screening, Intro, Preparation (1-11 weeks)				Treatment 1 (about 4 weeks)				Treatment 2 (about 4 weeks)				Treatment 3 (about 4 weeks)				Evaluation	Study Termination		
		(about 6 weeks)																			
Visit #		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Informed Consent	✓																				
Medical Screening	✓																				
Bloodwork, ECG, rhythm strip	✓																				
Drug and Pregnancy Test	✓					✓					✓						✓				
Measure PTSD Symptoms				✓				✓						✓					✓		
Other Psychological Testing	✓				✓				✓						✓			✓			✓
Psychotherapy		✓	✓		✓		✓	✓		✓		✓	✓		✓		✓	✓	✓		
Overnight Test Session					✓						✓						✓				
Phone Calls over 1 week							✓					✓									
Overnight Stay					✓					✓							✓	✓			

### **Preparatory Sessions**

The first two preparatory sessions will last approximately 90 minutes and the last preparatory session will last about 2 and a half hours. During each preparatory session, you will talk about the traumatic incidents that led to your PTSD, the ways PTSD symptoms are affecting your life, and what you would like to achieve during the study. You will be asked questions about thoughts or feelings you might have about hurting or killing yourself and complete psychological questionnaires in the 3<sup>rd</sup> preparatory session. There will be four visits total during this period: three therapy visits and an online meeting with a researcher who will ask you questions about your PTSD symptoms. This information will be used to learn how you are doing after the study treatment. After the online video meeting, the staff will let you know whether you will continue on to the treatment part of the study.

### **Overnight Test Sessions**

There will be three day-long Overnight Test Sessions. These visits will happen three to five weeks apart. The first Overnight Test Session will occur after you have had three preparatory sessions. During the Overnight Test Session, you will receive a dose of MDMA followed 1.5 to 2 hours later by a dose of half the first dose of MDMA. During the second and third Overnight Test Sessions, you and your therapy team can decide if you would like to take the same dose you took in your first Overnight Test Session, or if you would like to try a higher dose. Your therapy team will discuss the optimal dose of MDMA with you for the second Overnight Test Session. The goal will be to decide on the optimal dose for you.

You must not eat any food or drink any alcohol after midnight on the night before each visit, 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 Overnight Test Session (or longer depending on the specific drug – this should be discussed with the therapy team). You cannot use caffeine or nicotine for two hours before and six hours after you take the first dose during the Overnight Test Session. For one week before each Overnight Test Session, you cannot take any herbal supplements, nonprescription medications, or prescription medications that have not been discussed and approved with the therapy team and study doctor.

If you are taking certain opioid medications for pain management, you can stay on these medications during treatment, although we will ask you to reduce the dose before each Overnight Test Session and stop taking them for 12 hours before and at least 24 hours after the first dose in each Overnight Test Session. If your pain becomes too severe to handle during this period, you will be allowed to take your medication.

First, you and the therapy team will discuss your goals for the Overnight Test Sessions and the therapy team will answer any other questions you may have.

Before an Overnight Test Session:

- Your urine will be tested for drugs of abuse, including stimulants, sedatives, opioids and cannabis.
- If you can become pregnant, you will take a urine pregnancy test.
- Answer questions about thoughts you might have about hurting or killing yourself.

After urine testing, you will receive a capsule containing MDMA. After taking the capsule, you 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 Overnight Test Session, either through headphones or room speakers. During the session there will be times when you will be asked to talk to the therapy team. If you are wearing headphones, you may remove them yourself if you want to talk to the therapy team 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 past traumatic experiences. The therapy team will remain with you, 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 therapy team 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 juices or 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 two hours after you take the first capsule, you may take a second capsule, after discussion with the study doctor. The second dose will contain half the amount of the first capsule. The thought behind taking the second capsule is that it is supposed to make the session last longer. If you or the therapy team notice you have problems after the first capsule, then you will not get the second capsule.

The therapy team will watch for any side effects (unwanted effects or health problems), which will be treated if necessary. If this happens, the therapy team will keep you fully informed about any concerns or treatment. Your blood pressure, temperature, and pulse will be measured before taking the first and second capsules and at the end of the session. If you have any symptoms including confusion, light-headedness, dizziness, chest pain, shortness of breath, tell your therapy team. More frequent measurements may be needed if this happens.

If you are confused or upset eight or more hours after the start of an Overnight Test Session, the therapy team will stay with you until you have fully recovered. If the therapy team thinks 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. The therapy team will ask you how you feel at the beginning and end of the Overnight Test Session and on several occasions during the phone follow-up period.

You will be spending the night in a room at the office of the therapy team 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 therapy team or you are having other problems and need to contact the therapy team, the attendant will contact them immediately.

The next day, you will have a non-drug therapy session with the therapy team. You will need to have someone drive you to wherever you are staying (home, hotel or another location) from the non-drug therapy session on the day after the Overnight Test 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 do not have anyone to take you home, the therapy team will find someone to drive you.

After you return home from the therapy session, the therapy team will talk to you by phone four days out of the following week to ask how you are feeling and see whether you should see the therapy team before your next scheduled non-drug psychotherapy session. You and your therapy team can decide which days would be best to speak on the phone. The phone calls will take approximately 5 to 15 minutes, though they can be as long as you need them to be. The therapy team will ask you about thoughts about killing or harming yourself during the second and seventh day of phone contact. You can call the therapy team at any time; except for a few times when they may be out of town. At those times the study doctor will be on call and can be called at the 24-hour number provided on this consent form.

The therapy team will give you a card with phone numbers for calling your therapy team and the REB (Research Ethics Board), 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 therapy team if you need to.

If there are delays in following the usual study schedule, the therapy team 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 the following 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
- you start or stop taking a prescription medicine or an over-the-counter medicine that you have not previously cleared with the therapy team
- you go to the hospital for any reason

If you have very high blood pressure, get sick, or have an uncomfortable and strong lasting negative reaction (unwanted effect or health problem) during or after an Overnight Test Session, you or the therapy team may decide that you should not have

the next Overnight Test Session. You may make this decision to stop treatment in the study for any reason.

If the therapy team decides to take you out of the study, they will let you know that they are doing this and their reason for doing it. They will help you find a therapist who can continue to help you with your PTSD, if needed. 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 Overnight Test Session, you will still have to stay in the office until the therapy team thinks that you are stable 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.

### **Integration Visits**

The day after each Overnight Test Session, and 2-4 weeks afterward, you will have therapy visits 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 the Overnight Test Session. There will be three of these visits after every Overnight Test Session visit. These visits will last about 90 minutes. The therapy team will ask you questions about thoughts about killing or harming yourself at these sessions. At the last integration therapy visit you will also complete a psychological questionnaire.

### **Measuring PTSD After Sessions**

Within one month after the first two Overnight Test Sessions, you will meet with the study researcher online again, which may be recorded. The researcher will ask about your PTSD symptoms. You will also meet with your therapy team and the study researcher about two months after your last Overnight Test Session to fill out the same questionnaires from the start of the study, and to complete the same online interview about your PTSD symptoms. You will also be asked if you have had any thoughts about hurting or killing yourself. The researchers will measure your blood pressure, weight, and BMI. The tests will help the therapy team tell if your symptoms have changed or stayed the same over time.

At this visit you will also be invited to participate in a long-term follow-up study for an additional visit 12 months from the last time you had an Overnight Test session to see if the changes in people's PTSD symptoms continue to improve, stay the same, or worsen over time after the study. There will be a separate consent form for this study.

### **POSSIBLE RISKS OR DISCOMFORTS**

MDMA has not been widely tested in humans, but as of October 2016, more than 1,260 people have been given MDMA in clinical research settings, without any serious unexpected problems happening. Some of the effects that have been observed are listed below.

Side effects that are typically not severe but are frequently reported include:

- Teeth grinding or tight jaw muscles (64%)
- Lack of appetite (50%)
- Dizziness (45%)
- Sensitivity to cold (40%)
- Muscle tension (35%)
- Difficulty balancing or walking (26%)
- Dry mouth (24%)

Between 40% and 70% of subjects in previous studies reported these side effects. Between 15% and 40% of participants reported (from most to least common) feeling either hot or cold, feeling that their heart was racing, sweating, dizziness, drowsiness, upset stomach, diarrhea, anxiety, tenseness, thirst, weakness, fatigue, shaking, headache, irritability, or feeling faint. When these side effects occur, they usually last less than four hours. However, some effects have been reported to last for more than 24 hours and (rarely) for as long as four days.

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 research 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 research grade MDMA in a controlled setting with a trained therapy team who will be closely monitoring your physical and psychological reactions, these problems are not expected to occur either during or after the Overnight Test 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:** In previous studies in which MDMA was given to volunteers, most participants 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 two to three hours. People also reported unusual feelings in their bodies, such as tingling or numbness (between 12% and 33%).

**Blood pressure and heart rate:** The effects of MDMA usually last six to eight hours with the first and second dose. 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 11.3 mmHg (measurement unit for blood pressure) and average diastolic blood pressure increase is 13.1 mmHg. Heart rate may increase by approximately 30 beats per minute (bpm) on average.

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 pre-existing 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 with an anxiety disorder who received MDMA (70.1%) reported feeling over-stimulated or anxious at a similar rate. 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 therapy team 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 therapy team 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.

The way MDMA affects the brain has the potential to cause mania in some people, although mania has not been reported in individuals receiving MDMA or ecstasy.

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 1.4% and 62% of participants have reported insomnia (difficulty sleeping) or feeling tired, irritable, or drowsy for as long as 3 days after taking MDMA. If needed, the study doctor may prescribe medication for sleep. **You should not drive or use machinery immediately after Overnight Test 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 two or three days later. While some participants feel that their mood is better, 20% to 33% feel that it is worse.

**Immune System:** You may have a less active immune system for two or three 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 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.

### **RISKS OF BEING IN THE STUDY**

If you are tested for drugs of abuse within three days of each Overnight Test Session, you may test positive. The therapy team 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 therapy team to verify that you are in this study. This card may not protect you from discipline at work or loss of employment. The study doctors 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 so you should not operate machinery or drive a car until you feel normal again.

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 therapy team. If you have to start taking medicine again, then the study doctors will have to take you out of the study.

### **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 Overnight Test 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. You will be asked to remain in the study for follow up but treatment will be stopped.

Those who are able to become pregnant and are engaging in penile-vaginal intercourse 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 being of childbearing potential is defined as permanent sterilization or postmenopausal or assigned male at birth. The therapy team 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 of childbearing potential, you will be tested at the start of the study and again before each Overnight Test 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 therapy team 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. If you become pregnant, you will discontinue treatment but remain in the study for follow-up purposes.

## **NEW FINDINGS**

If any new information becomes available about MDMA while you are in this study, the therapy team will tell you about it as soon as possible. You may be asked to sign a new consent form if this occurs. Your willingness to remain in the study upon learning new information will be discussed with you. You may contact the therapy team at any time after your participation ends to find out if any new information about this study has become available.

## **POSSIBLE BENEFITS**

Your symptoms of PTSD 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.

## **PAYMENT FOR PARTICIPATION**

There will be no payment for taking part in this study. There are no plans to offer you payment for such things as lost wages.

The results from this study may lead to new commercial products or tests. If this happens you will not receive any compensation.

## **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 provincial 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.

## **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 approved medicines that may help treat your symptoms of PTSD (such as paroxetine) 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 therapy team can discuss the alternatives and their potential risks and benefits with you.

## **CONFIDENTIALITY**

Your confidentiality will be respected. However, research records and health or other source records identifying you may be inspected in the presence of the Investigator or his or her designate by representatives of MAPS, Health Canada, FDA and Western Institutional Review Board® (WIRB®) for the purpose of monitoring the research. No information or records that disclose your identity will be published without your consent, nor will any information or records that disclose your identity be removed or released without your consent unless required by law. The information collected from you will be kept for 25 years as required by law.

You will be assigned a unique study number as a participant in this study. This number will not include any personal information that could identify you (e.g., it will not include your Personal Health Number, SIN, or your initials, etc.). Only this number will be used on any research-related information collected about you during the course of this study, so that your identity will be kept confidential. Information that contains your identity will remain only with the Principal Investigator and/or designate. The list that matches your name to the unique study number that is used on your research-related information will not be removed or released without your consent unless required by law. Your initials and birth date will also be provided if requested by the sponsor or responsible regulatory agency.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected. You also have the legal right of access to the information about you that has been provided to the sponsor and, if need be, an opportunity to correct any errors in this information. Further details about these laws are available on request to your study doctor.

To ensure confidentiality, your information will be stored in secure electronic systems or in a locked office. Absolute confidentiality and security cannot be guaranteed, but every effort will be made to maintain your confidentiality.

People outside of your therapy team will need access to your information to monitor the study and conduct further research and training. Any paperwork copied will have any information that could be used to identify you removed first, except for videos, which will still show your face. If records are copied, only your participant number and initials will identify you to the study Sponsor unless you give specific permission, for example at a time when you sign a media release.

Medical records, including video, which identify you, and the consent form signed by you will be looked at and/or copied for research or regulatory purposes. These records may be looked at by:

- The Sponsor, MAPS and the people they hire.
- Researchers who cooperate with MAPS to conduct further research, and people who conduct therapy trainings on behalf of MAPS.
- The FDA and similar agencies in other countries.
- Health Canada
- Governmental agencies in other countries.
- Western Institutional Review Board (Research Ethics Board/REB). The REB is a group of scientists and non-scientists who review the ethics of research. The goal of the REB is to protect the rights and welfare of study subjects.

All records are subject to subpoena by a court of law.

Any study related data, sent outside of Canadian borders may increase the risk of disclosure of information because the laws in those countries, (for e.g.) the Patriot Act in the United States dealing with protection of information may not be as strict as in Canada. However, all study related data, that might be transferred outside of Canada will be coded (this means it will not contain your name or personal identifying information) before leaving the study site. By signing this consent form, you are consenting to the transfer of your information, to the study sponsor, MAPS located outside of Canada.

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

**Video recordings:** The therapy team will video record each visit. The purposes for this recording that you are agreeing to by signing this informed consent are:

- So the therapy team will have accurate records of the session.
- So that trained raters working for the Sponsor can verify that the therapy is being carried out properly
- For further research on the therapy and how it is performed.

- For training other therapy teams and scientists to develop and work on additional research.

For the above purposes the adherence raters, researchers and therapy team 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.

Information contained in recordings that could be used to identify you may include:

- Your physical appearance
- Your voice
- Your name (if it is spoken on the recording)
- Situations from your life that might be discussed

With your permission only, the investigators and/or sponsor may 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. You are not required to agree to use of your video in these settings in order to participate in the study. Signing this consent form does not mean you have given permission for your videos to be used in this way. You will have the opportunity to sign an additional release for these situations if they arise and if you choose to allow this use. At the end of the study (Visit 20) 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 hard drives stored in a locked and secure location when not in use. No personally identifying information will be used to label the video recordings. A copy will be transferred to the Sponsor for secure electronic storage on the web to allow for viewing purposes described above. Electronic systems used will include measures to protect confidentiality of your identity and protection of this video data. Total security cannot be guaranteed, but the Sponsor is consistently working to maintain and improve the security of its data systems.

During your study sessions you may ask to stop the recording at any time, but your therapy team 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.

There is no expiration for your permission. You may take away your permission to collect, use and share information about you at any time by providing reasonable notice to the study doctor. If you do this, you will not be able to stay in this study. No new information about you will be gathered after that date. However, the information about you that has already been gathered may still be used and given to others as described in this form.

## **TREATMENT AND COMPENSATION FOR INJURY**

By signing this form, you do not give up any of your legal rights and you do not release the study doctor, participating institutions, or anyone else from their legal and professional duties. If you become ill or physically injured as a result of participation in this study, call your study doctor at the number on the first page. Medical treatment will be provided at no additional cost to you. The costs of your medical treatment will be paid by your provincial medical plan and/or by the study sponsor, MAPS. Neither the Sponsor nor the therapy team 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.

## **LEGAL RIGHTS**

The above section does not restrict your right to seek legal assistance. You have not waived any of your rights to legal recourse, including if you are harmed as a result of the research, by participating in this research.

## **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 or loss of benefits 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.

## **WITHDRAWAL**

Your therapy team, the Sponsor, or the medicine agency in your country 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 or follow study procedures,
- if you do not take the study drug as instructed,
- if you become pregnant, or
- if the study is canceled by Health Canada, the FDA, REB, or the Sponsor.

The Sponsor, Health Canada, the FDA, or the REB may decide to stop the study at any time.

## **CONTACT FOR QUESTIONS**

If you have any questions, concerns, or complaints about your participation in this study or if you feel that you have experienced a study-related injury or reaction to the study drug, or have a complaint about the research study, contact the study doctor using the information found on page 1 of this form.

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

This research is being overseen by a Research Ethics Board (REB). You may talk to Western Institutional Review Board® (WIRB®) at 1-800-562-4789 or 360-252-2500 or Help@wirb.com or write to them at 1019 39<sup>th</sup> Avenue SE Suite 120, Puyallup, Washington 98374-2115 if:

- You have questions, concerns, or complaints about the research that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

WIRB is a group of people who perform independent review of research.

WIRB will not be able to answer some study-specific questions, such as questions about appointment times.

**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

*An Open-Label, Multi-Site Phase 2 Study of the Safety and Effect of Manualized MDMA-Assisted Psychotherapy for the Treatment of Severe Posttraumatic Stress Disorder - Canada*

- I understand that my participation in this study is voluntary.
- I understand that I am completely free at any time to refuse to participate or to withdraw from this study at any time, and that this will not change the quality of care that I receive. I will call the researchers if I decide to do this.
- The staff 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 their instructions.
- I agree to have my sessions video-recorded during this study.
- I have read and understood the information in this consent form.
- I have been given sufficient opportunity to consider whether to participate.
- I have been able to ask questions and have had satisfactory responses to my questions.
- I freely consent to take part in this research study.
- I authorize access to my health records and samples as described in this consent form.
- I understand that I am not waiving any of my legal rights as a result of signing this consent form.

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 will receive a signed copy of this consent form for my own records.

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Signature of Participant

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Date

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Printed Name of Participant

I certify that the information provided was given in language that was understandable to the participant. I attest to adhering to informed consent procedures.

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Signature of Person Obtaining Consent

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Date

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Printed Name of Person Obtaining Consent