SUBJECT INFORMATION AND CONSENT FORM AND AUTHORIZATION TO USE AND DISCLOSE PERSONAL HEALTH INFORMATION FOR RESEARCH

Study Title: A Randomized, Triple-Blind Phase 2 Pilot Study Comparing 3 Different Doses of MDMA in conjunction with manualized psychotherapy in 24 Veterans, Firefighters, and Police Officers with Chronic, Treatment-resistant Posttraumatic Stress Disorder (PTSD)

Protocol #: MP8 Amendment 5

Study Sponsor: Multidisciplinary Association for Psychedelic Studies (MAPS)
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PURPOSE OF THE SUBJECT INFORMATION AND CONSENT FORM

This consent form describes a research study and your role as a participant. Please read this form carefully before you decide to take part in this study. You may ask the study doctors anything about the information provided. You are being asked to participate in this research study because you are a military veteran, firefighter or police officer and you have been diagnosed with posttraumatic stress disorder (PTSD) related to your service, and because your symptoms have not gone away after psychotherapy, medicines, or both, or you stopped your treatment because you could not tolerate it.

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

PURPOSE AND BACKGROUND

This small ("pilot") study is designed to provide information on whether psychotherapy ("talk therapy") combined with the drug MDMA is safe and helpful for subjects with posttraumatic stress disorder (PTSD). The researchers plan to use the results of this study to design further studies.

MDMA is an experimental drug, which means that it has not been approved by the United States Food and Drug Administration (FDA) for medical use except in research studies. MDMA is also a controlled drug (illegal to use outside of research) and is sometimes known as "Ecstasy" (which is supposed to contain MDMA but often contains other drugs instead of or in addition to MDMA). 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 US-based non-profit organization, the Multidisciplinary Association for Psychedelic Studies (MAPS, www.maps.org). MAPS' first small study of MDMA-assisted psychotherapy in 21 people with PTSD is finished in the US, with promising results. MAPS has other MDMA/PTSD pilot studies in Switzerland and is planning new studies in the US, Canada, and Israel.

Before it became illegal in 1985, some psychologists and psychiatrists combined MDMA with psychotherapy to help people with psychological problems, including PTSD. Though we do not know why it may help people with PTSD, we know that MDMA increases 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.

This study will compare three doses of MDMA: 30, 75 and 125 mg, possibly followed one and a half to two and a half hours later by a second dose half the size of the first dose.

LENGTH OF STUDY

This study can take up to 1.5 years or 20 visits if you receive 125 mg MDMA in "Stage 1." It can last for an additional three months or 15 more visits if you receive 30 or 75 mg MDMA in "Stage 1," and decide to go on to have an active dose of MDMA in the second part of the study, "Stage 2." This time period includes a long-term follow-up visit 12 months after the last experimental or open-label session.

TYPE OF STUDY

This study is double blind, meaning that neither you nor the study researchers will know what dose of MDMA you get. The dose of MDMA you get will be decided at random, as if by tossing a coin. Each person in this study has a 50% chance of getting 125 mg, a 25% chance of getting 30 mg and a 25% chance of getting 75 mg. You will find out what dose of MDMA you received approximately 1 month after your second experimental session. There will be approximately 24 subjects in this study.

PROCEDURES/WHAT WILL HAPPEN TO YOU

SCREENING/EVALUATION AND BEGINNING OF STUDY

If you agree to take part in this study, you will first sign this Subject Information and Consent Form before any study-related procedures are performed. You will not be asked to stop taking any of your current medications until you are enrolled in the study. If you are taking psychiatric medications when you are enrolled you will be required to slowly stop taking them under the supervision of your prescribing physician or the study doctor. It is possible that stopping some medications could lead to recurrent or new symptoms, including thoughts of wanting to kill yourself

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. The screening process can take up to 4 months, and there will be one or more office visits during this time. The study therapists may ask your permission to contact your doctor or psychotherapist to get information about your medical history. They may need to do this so that they will know if you can be in the study or not.

The tests will include the following:

- A questionnaire about your PTSD symptoms and how you deal with them in your everyday life. Your score on this questionnaire will be used to decide if you can be in the study. The person asking you these questions will be a different person from the therapists. 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 about feelings of depression or other symptoms or feelings you might experience.
- A questionnaire about thoughts or feelings you might have about hurting or killing yourself.
- A questionnaire about your personality.
- A questionnaire about your quality of sleep.
- Another questionnaire about your PTSD and its effects on your life
- A questionnaire about any dissociation symptoms.
- A visual scale of pain and tinnitus (ringing in the ears) levels if you have these symptoms.
- 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 virus (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.

You may have to have extra medical tests to make sure you can be in the study. People who control their high blood pressure with medication may have to see a cardiologist (heart doctor) for more tests, and people with a liver disease called hepatitis C may have to visit a liver specialist. If you have hepatitis C, you will have to complete treatment the liver specialist or your physician (your doctor) prescribes for HCV. If the tests find out that you test positive for HCV or HIV, then the study doctors will have to tell the South Carolina department of Health and Environmental Control within seven days, as stated by law. If you live outside South Carolina, the study doctors may need to report the results according to the laws of the state you live in.

You may be asked if you want to participate in another study while you are in this study. If you are interested in learning more about this study, you will receive information about it separately and it will involve additional tests.

BEGINNING OF STUDY

Once you are in the study, you will schedule your first introductory (preparatory) psychotherapy session with the study therapists. It may happen that the first preparatory session will be done at the Screening visit, after you have signed this consent form. You will need to be enrolled in the study before the second psychotherapy session. If you were taking psychiatric medicines before enrolling in the study, you will have to stop taking them after you are enrolled. The study doctors and your physician will help you do this. If it takes over a month between when you stop taking your medication and your first MDMA session, then you may have to answer questions about your PTSD symptoms again. You must let the study therapists know about any medical conditions or procedures, like surgery, within 48 hours of their occurrence.

You will have to give the study therapists the name and contact information (as 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.

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 in Stage 1 and Stage 2 (if you are in the low or medium dose groups).

Stage 1	Screening	Start study	Intro and Preparation	MDMA and Non-Drug Therapy 1	MDMA and Non-Drug Therapy 2	Evaluation	MDMA and Non-Drug Therapy 3	Evaluation	Long Term Evaluation
For All Groups							**For full dose group only**		

Study Visit #		1 Enroll	2*	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	

Screening	X																		
Measure symptoms	X												X					X	X
Psycho therapy			X	X	X		X	X	X		X	X	X		X	X	X		
Psycho therapy With MDMA						X				X				X					
Medical Exam	X																		
Learn dose you received													X						

* Visit 2 may happen at the time of screening, before Visit 1.

Stage 2	Preparation	MDMA and Non-Drug Therapy 1			MDMA and Non-Drug Therapy 2				Evaluation	MDMA and Non-Drug Therapy 3				Evaluation	Long Term Evaluation
For Low and Medium Dose Groups Only															
Study Visit #	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	
Measure symptoms	X*									X					X	X
Psychotherapy	X		X	X	X		X	X	X			X	X	X		
Psychotherapy With MDMA		X				X					X					

* Symptoms may be measured again if more than a month passes between Stage 1 and Stage 2.

INTRODUCTORY PSYCHOTHERAPY SESSIONS:

You will meet with the study therapists on three separate occasions before the first experimental session. These visits will last 90 minutes. During each introductory 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 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 learn more about what to expect during experimental sessions. The introductory sessions will be recorded to audio and video, so that the study doctors 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 have a copy, hear or see these recordings if you wish. In addition, you will be asked to read a brief script that does not contain any information related to the study for a computer program that will allow converting audio recordings to text from these sessions.

EXPERIMENTAL SESSIONS:

There will be two day-long experimental sessions, when you will have MDMA (30, 75 or 125 mg) and psychotherapy, each happening three to five weeks apart. The first experimental session will occur after you have had three introductory sessions. If you are in the 125mg or Full Dose Group, you will have a third day-long experimental session with 125 mg MDMA. If you received 30 or 75 mg (low or medium dose MDMA), you will be offered one of two active doses of MDMA sessions during the Stage 2 experimental sessions. Your therapists will discuss the optimal dose of MDMA with you for the second and third experimental sessions.

One week before each of the MDMA sessions you will need to avoid taking:

- any herbal supplement (except with prior permission);
- any nonprescription medications, unless you have permission (with the exception of non-steroidal anti-inflammatory drugs or acetaminophen (Tylenol);
- any prescription medications, unless you have permission (with the exception of birth control pills, thyroid hormones or other medications).

You must not eat 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 MDMA session. You cannot use nicotine or caffeine for two hours before and six hours after MDMA treatments.

First, you 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.

Throughout an experimental session:

- Your blood pressure and pulse will be measured periodically (every 15 to 30 minutes).
- Your temperature will be measured every hour.
- You will also complete a very brief, simple test of how comfortable or distressed you feel by marking a number on a sheet of paper that matches the way you feel at that moment. You will complete it every 60 to 90 minutes throughout each experimental session.
- About an hour before receiving the drug and about six hours afterward, you will complete the questionnaire about thoughts you might have about hurting or killing yourself.
- The study therapists will check in on you every hour or so to see how you are doing.

The experimental session will be audiotaped and videotaped, 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. The study therapists can give you copies of these recordings for you to keep and watch if you want them.

After urine test results come back, you will receive a capsule containing MDMA mixed with some lactose to make all capsules appear and weigh the same. The capsule can contain either 30, 75, or 125 mg MDMA. After taking the capsule, you will then sit or lie down in a comfortable position. You can ask for an eye shade if you wish. You will listen to music during much of each experimental session, either through headphones or room speakers. Periodically 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 periods 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 they will help you if you need them to do so. 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 took the first capsule, you and the study therapists will talk about taking a second dose of MDMA. The second dose will contain half the amount MDMA of the first dose. If you and the study therapists agree, you will take the second dose. If you or the study therapists notice problems after the first dose of MDMA, then you will not get the second dose of MDMA.

The study therapists will keep measuring blood pressure, pulse and temperature, and the study therapists will watch for any side effects (unwanted effects or health problems), which will be treated if they see them. If this happens, the study therapists will let you know what they are doing.

If you are confused or upset eight or more hours after the start of an experimental session, the researchers will stay with you until you have fully recovered. If the researchers 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 researchers will ask you about thoughts of killing or harming yourself before and after MDMA administration and throughout the follow-up period. You will also be asked to complete a questionnaire about thoughts, feelings or other things you might have experienced during the experimental session. You can complete this questionnaire at any time between the end of the experimental session and you leave the study site the next day.

If you request it and the study therapists agree to it, you can have a person of your choosing stay with you during some or all of the experimental session, starting at an agreed-upon time, or when you stay at the office of the study doctors after the session. When he or she arrives, this person will stay in the waiting room until there is a good time for them to come into the session.

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

On the next day, you will have a non-drug (integrative) therapy session with the study therapists. 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 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 researchers will find someone to drive you.

After you return from the non-drug therapy session, the researchers will telephone you every day for a week to inquire about how you are feeling and determine whether you should see the study doctors before your next scheduled non-drug psychotherapy session. These telephone calls will take approximately 5 to 15 minutes, though they can be as long as you need them to be. You may schedule additional meetings with the study therapists besides those that are scheduled as part of the study. You can contact the study therapists at any time. The study therapists will be reachable by telephone 24 hours a day throughout the research study, except on occasions when he is out of town. At those times another psychiatrist familiar with the study will be on call and can be reached through his phone number which will be given to you as well.

The researchers will give you a card with telephone numbers for reaching [redacted] 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 researchers if you need to do so.

If there are delays in following the usual study schedule, the study therapists will telephone you at least once a week to talk about how you're doing. These telephone calls will take approximately 15 minutes, and you agree to call the investigators if any of these things happen: you have an increase in symptoms for which you previously took medicine, you need to contact your outside therapist other than for the usual appointments, and/or you start or stop taking prescribed medicine.

If you have very high blood pressure, get sick, or have an important and strong lasting negative reaction (unwanted effect or health problem) after the first experimental session, you or the study therapists may decide that you should not participate in the second experimental session. You may make this decision to stop being in the study for any reason. If the study therapists decide to take you out of the study, they will let you know that they are doing this and their reason for doing this. If you are taken out of the study or decide you do not want to be in the study, the study doctor 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 effects of the drug have worn off.

The experimental sessions will occur three (3) to five (5) weeks apart. All experimental sessions will be carried out in an identical manner to the first session.

PSYCHOTHERAPY 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 will have psychotherapy with the study therapists the morning of the day after each experimental session and then two more visits during the next three to five weeks after each experimental session. These sessions will last 60 to 90 minutes. 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 gain maximum benefit and understanding from experimental sessions. Each regular psychotherapy session will be recorded to audio and video, just like the introductory and experimental sessions, and you can hear, see, or have a copy of these recordings.

Before starting psychotherapy on the day after each experimental session, you will be asked to guess whether you got 30, 75 or 125 mg MDMA. You will not be told if your guess is correct. The researchers will ask you about thoughts about killing or harming yourself during each follow-up session, and during the second and seventh day of telephone contact with the study doctors.

MEASURING PTSD AFTER EXPERIMENTAL SESSIONS

Approximately four months after the start of the study (one month after the second experimental session), you will meet with a study researcher who is not one of the study therapists. You will be asked not to tell this researcher what your guess is about what dose of MDMA you think you received. The study researcher will ask you questions about your PTSD symptoms, (which may be videotaped with your permission). You will also complete a questionnaire on feelings of depression, dissociation symptoms, a questionnaire on your sleep quality, a personality questionnaire, and one more questionnaire related to your PTSD. This visit should last up to two hours. The researchers will ask you about thoughts about killing or harming yourself. You will also complete the scale of pain and tinnitus levels if you had these problems before the study.

After you complete these tests, you will meet with the study therapists and all of you will find out if you received 30, 75 or 125 mg MDMA. The study researcher who measured your PTSD symptoms will not find out.

If you learn that you had the low (30 mg) or medium (75 mg) dose of MDMA, you can then enroll in "open label" study sessions, or "Stage 2," described below. If you decide not to participate in Stage 2, then you will complete a questionnaire about your experience as a research subject before you leave the first part of the study.

If you are in the full dose group (125 mg), you will be asked about your thoughts on having a third experimental session.

Full Dose (125 mg) Group Only – Approximately six months after the start of the study (two months after the third experimental session), you will meet with the study researcher again. The researcher will ask about your PTSD symptoms (which may be videotaped, with your permission), and you will fill out a questionnaire on feelings of depression, another questionnaire

on PTSD, a dissociation symptoms questionnaire, and a sleep quality questionnaire. You will also be asked if you have had any thoughts about hurting or killing yourself. This visit should last about 2.5 and 3.5 hours.

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 subject before you leave the first part of the study. You will be asked about your thoughts on having a third experimental session. The study therapists will give you 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 12-month follow-up visit. On this card you will record any new important health problems, changes to your mental health, hospitalizations and medications to treat these problems.

OPEN-LABEL MDMA SESSIONS FOR PEOPLE WHO RECEIVED 30 OR 75 MG MDMA (STAGE 2)

If you are one of the twelve subjects who received 30 or 75 mg MDMA, you can take part in three open-label MDMA-assisted sessions scheduled 3 to 5 weeks apart as part of Stage 2. In this study segment, you will receive an active dose of MDMA (either 100 mg possibly followed by 50mg or 125 mg possibly followed by 62.5 mg) , with the 125 and 62.5 doses possible during the second and third sessions. . Stage 2 can start any time after you learn what dose of MDMA you received but not later than five months after that point. Signing this consent form means you agree to take part in the second part of the study though you can change your mind at any time and still take part in the 12 month follow up without participating in Stage 2. **The twelve people who receive a full dose of MDMA during the first stage of the study cannot take part in Stage 2.**

If more than 8 weeks pass between Stage 1 and Stage 2, you will need answer questions about your PTSD symptoms, and the questionnaires about depression, dissociation, and sleep quality again before you start Stage 2. If you take part in Stage 2, you will have 15 more visits. These sessions will be like the experimental ones you had during the first part of the study, except that you will know you are getting an active dose of MDMA and will have 3 experimental sessions instead of only two. You will also only have one review and introductory session instead of three. Otherwise, you will have three experimental sessions scheduled three weeks apart followed by an overnight stay and non-drug integrative therapy afterwards. You will complete the scale of pain and tinnitus levels if you notice changes in your symptoms that you had before the study. You will have tests of your PTSD symptoms and complete a questionnaire on symptoms of depression, dissociation symptoms, and sleep quality one and two months after the third open-label session, and a personality questionnaire two months after the third session. You will also be asked if you had any thoughts about hurting or killing yourself during that time. You will be asked about your thoughts on the experimental sessions before and after your third session. At the 2-month follow-up, you will complete a questionnaire about your experience as a research subject. The study therapists will give you 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 12-month follow-up visit. On this card you will record any new important health problems, changes to your mental health, hospitalizations and medications to treat these problems

LONG-TERM FOLLOW-UP 12 MONTHS AFTER LAST EXPERIMENTAL SESSION FOR ALL PARTICIPANTS
Approximately 12 months after your last MDMA-assisted session, you will answer questions about your PTSD symptoms, dissociation symptoms, feelings of depression and sleep quality, and a personality questionnaire, and you will fill out a questionnaire on the positive and negative effects of being in the study. You will complete the scale of pain and tinnitus levels if you had them before the study. If you were only in Stage 1, then this will happen 12 months after your third experimental session, and if you were in Stage 2, then this will happen 12 months after the third open-label session.

The same study researcher who asked you about your PTSD symptoms will do so again, either in person or over the telephone. The study therapists will ask you about any changes in medications or your psychiatric health, including any benefits or harms, during the follow-up period between your last visit and the 12-month follow-up visit.

You will also answer the questionnaire about feelings of depression, your personality, your sleep quality and another PTSD-related questionnaire. The questionnaires will include questions about any thoughts, feelings or events that happened after being in the study. You will also answer a questionnaire about your attitudes and feelings about being in the study, any thoughts you have about the good and bad points of MDMA-assisted therapy, and your thoughts about taking MDMA. There are no right or wrong answers to these questions.

A researcher who is a part of the study team will ask you about any changes in medication or your psychiatric health, including any benefits or harms, during the follow-up period between your last visit and the 12-month follow-up visit.

The questionnaires will be mailed to you for you to fill out. It will come with an envelope that is already stamped and has 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. They may be able to learn what happens to people who started out receiving full dose MDMA versus people who received lower doses of MDMA first, and then received full dose MDMA.

POSSIBLE RISKS OR DISCOMFORTS

MDMA has not been widely tested in humans, but as of May 2013 approximately 845 people have received MDMA in clinical research settings, without any serious problems happening.

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

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 full 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 subjects reported

- Nausea,
- Low mood,
- Feeling cold,
- Dizziness,
- Impaired balance,
- Disturbance in attention,
- Restlessness,
- Perspiration,
- Thirst,
- Feeling weak, and
- 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, but no more than 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 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 subjects that participated in previous 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 approximately 30 beats per minute (BPM).

In previous studies, blood pressure rose well above normal levels in a few subjects (a little less than 5%) after receiving MDMA, but these subjects 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 vessel conditions. These serious problems could include heart attack or stroke. We will screen all potential subjects 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 subjects in previous 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 help you resolve them safely. If necessary, 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 subjects have reported insomnia (difficulty sleeping) or feeling tired, irritable, or drowsy for as long as 3 days after receiving MDMA. **You should not drive or use machinery immediately after each experimental session (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 noticeable up to 2 or 3 days later. While some subjects 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 receiving 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 take part 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.

If you are in immediate danger of hurting or killing yourself or hurting someone else, then the study therapists may require you to stay in a hospital.

Other 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 [redacted] 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 and are in psychotherapy, especially if you have had these thoughts before. If this happens, you should talk with your outside therapist and [redacted] 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. Birth defects could include physical deformities, mental retardation and premature birth; therefore you will not be allowed to enter the study if you are pregnant. If you become 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 the 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, such as birth-control pills or shots, IUDs, and diaphragms used along with spermicide and with partner use of condoms, or sexual abstinence while they are in the study and for at least one month afterward. 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 MDMA 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 contact [redacted] 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.

NEW FINDINGS

If any new information becomes available about MDMA while you are taking part in this study, the study therapists will tell you about it as soon as possible. You may contact the study doctor 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 participating in this study. There is no guarantee that you will benefit from taking part in this research study, however, information obtained from this study may help doctors and researchers to improve treatment for PTSD in the future.

COSTS

The sponsor of this study, Multidisciplinary Association for Psychedelic Studies (MAPS), will cover the costs that are directly related to this study. This includes the costs for all 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), and the public health insurance plan will not be charged for any procedures done solely for the purpose of the study. You or your insurance company will remain responsible for on-going treatment unrelated to the study.

PAYMENT FOR PARTICIPATION

The Sponsor, MAPS, will reimburse you for travel related expenses as follows:

Subjects who drive to the study site:
If you must drive more than 50 miles round trip for visits, you will be reimbursed at a rate of $0.25 per mile. If you live far enough away that it is not practical or desirable to make the round trip in one day, MAPS will pay up to $150.00 a night for all motel bills and up to $50.00 per day for meals.

Subjects who fly to the study site:
MAPS will pay for all travel expenses submitted by you for reimbursement. MAPS will pay up to $150.00 a night for all motel bills and up to $50.00 per day for meals.

If you must pay for travel or parking, the researchers will pay you back the costs of travel or parking.

ALTERNATIVES

One alternative to being in this study is to decide not to participate. 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 doctor can discuss the alternatives and their potential risks and benefits with you.

CONFIDENTIALITY

To ensure confidentiality, only subject numbers will be provided to the study sponsor. When not in use, subject information will be stored in a locked office. **Absolute confidentiality cannot be guaranteed**.

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

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

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

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

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

Audiotapes and videotapes: The study therapists will listen to or watch these recordings, as well MAPS staff and other researchers seeking to better understand the principles of MDMA-assisted psychotherapy. No identifying information will be written or otherwise attached to the tape recordings. You may listen to or watch the recording if you wish, but you do not have to. You will not automatically receive a copy of the recordings of your experimental session, but if you wish, you may receive a copy of the recording.

You have the right to check your study records and ask for changes if the information is not correct.

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

TREATMENT AND COMPENSATION FOR INJURY

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

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

LEGAL RIGHTS

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

VOLUNTARY PARTICIPATION

Your decision to take part in this research study is completely voluntary. There will not be any penalty or loss of benefits to you if you decide not to take part.

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 clinic for tests.

WITHDRAWAL

Your doctor, 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.

CONTACT FOR QUESTIONS

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

Investigator Name: [redacted]

Daytime telephone number(s): [redacted]

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

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

The researchers will give you a wallet card containing contact information for the researchers, the sponsor and the IRB.

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

SUBJECT'S STATEMENT OF CONSENT

"A Randomized, Triple-Blind Phase 2 Pilot Study Comparing 3 Different Doses of MDMA in conjunction with manualized psychotherapy in 24 Veterans, Firefighters, and Police Officers with Chronic, Treatment-resistant Posttraumatic Stress Disorder (PTSD)"

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 taped 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 participate in this study. All of my questions so far about the study and my participation in it have been answered. I freely consent to participate in this research study.

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

	SUBJECT	**INVESTIGATOR**
Printed Name		
Signature		
Date		

AUTHORIZATION TO USE AND DISCLOSE PERSONAL HEALTH INFORMATION FOR RESEARCH

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:

[redacted]

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 or receive study drug. 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.

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.

	SUBJECT	**INVESTIGATOR**
Printed Name		
Signature		
Date		