LOS ANGELES BIOMEDICAL RESEARCH INSTITUTE AT HARBOR-UCLA MEDICAL CENTER

Human Subjects Research Consent Form

This form describes a research study. Please discuss the content of this form with the study doctor or a member of his study team before you agree to take part.

Subject's Name:_____Date:_____.

Study Title: *A Placebo-Controlled, Randomized, Blinded, Dose Finding Phase 2 Pilot Safety Study of MDMA-Assisted Therapy for Social Anxiety in Autistic Adults*

Who is conducting this study?

[redacted]

Why am I invited to take part in this research study?

We are asking you to take part in this study because you are on the autism spectrum and have symptoms of social anxiety or social phobia. Social anxiety (or social phobia) is an anxiety disorder in which a person has an excessive and unreasonable fear of social situations.

What should I know about a research study?

- Someone will explain this research study to you.
- Research studies only include people who choose to take part.
- Whether or not you take part is up to you.
- You can choose not to take part in the research study.
- You can agree to take part now and later change your mind.
- Whatever you decide will not be held against you.
- Feel free to ask all the questions you want before you decide.

Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have questions, you can ask your study doctor to explain the study more.

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A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website any time.

Why is this study being done?

This small ("pilot") study is designed to provide information on whether therapy combined with the drug 3,4-methylenedioxymethamphetamine (MDMA) is safe and helpful for autistic adults with social anxiety symptoms. 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 U.S. 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" or "Molly" (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.

This study is sponsored by a US-based non-profit organization, the Multidisciplinary Association for Psychedelic Studies (MAPS). Before it became illegal in 1985, some psychologists and psychiatrists combined MDMA with psychotherapy (therapy involving talking with others and counseling) to help people with psychological problems, including posttraumatic stress disorder (PTSD). Though we do not know why MDMA therapy may help people with anxiety disorders like 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 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 therapy, could help people work through thoughts, memories and emotions related to anxiety.

This study will compare the effects of therapy combined with MDMA to just therapy alone.

Are there potential conflicts of interest?

The study doctor conducting this research does not have any financial interest in the sponsor or in the study; this means that the study doctor will not be financially affected by the results of the study (good or bad). However, the study doctor and his staff will be reimbursed by the sponsor for the work that he and the study staff have to do as part of this study and for the use of the site's facilities.

The person inviting you to take part in this research study may also be your treating doctor. In such cases, the doctor has an interest in both your care and promoting the successful conduct of this research. Sometimes these two interests may cause conflict. You can choose not to take part in the study and still receive treatment from your doctor. If you wish, you may also request to speak to another doctor who is not a member of the study team about your options.

How many people will take part in the study?

A total of 12 people will take part in this study. At this time LA BioMed is the only site that is conducting this study.

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What will happen if I take part in this research study?

You must be aware of the following:

- We may video record all office visits and therapy sessions for research purposes which include developing a treatment manual and to possibly train future therapists in this type of therapy. We will also use the video recordings to make sure all procedures are being done consistently. You can ask to view these recordings at any time while you are taking part in this study. We will post the video recordings on a secure (password is needed) website and only select researchers, but also including yourself if you ask, can view them. When we video record you, we will include your face. We will not label the video with your name, address or any other identifying information.

  We may also audio record (record only voices – no images) all office visits and therapy sessions. We will not label this recording with your name, address or any other identifying information. This recording will be used as a back-up for the video recordings for training and manual development. You may ask to hear these recordings as well.

  Video and audio recordings will be destroyed after 20 years from the end of the study.

- You will have to avoid taking any medicines for psychological problems from the beginning of the study up until you complete the last integrative session unless the study doctor makes a specific exception, such as giving you medicine for sleep or anxiety temporarily and if needed. If you are taking this type of medicine, you will need to give the study doctor or a member of his study team permission to talk with your own doctor about how best to stop taking your medicine. We will help you do this. You may return to taking your medications during the follow-up period.

- You must let us know about any medical conditions or procedures, like surgery, within 48 hours of their occurrence.

- You will need to bring a relative, spouse or close friend with you to visits to be your support partner during the study. This person (called a Support Partner) will also take part in this study by providing you with transportation during the study. We will not allow you to drive after each experimental session in which you receive the study drug (MDMA or placebo). We will ask your support partner to also provide you with emotional support during the study. We may ask this person to take part in the study sessions and provide information about you.

- If you are currently seeing a psychotherapist, you may not begin any new psychotherapy or change the type, frequency or length of visits with your psychotherapist until after your final session/visit. This is so any change in your social anxiety symptoms are more likely to be from the experimental treatment rather than from any new psychotherapy treatments.

- For your safety, it is very important to tell us about all medicines you are taking, including herbal or "natural" remedies or supplements, and to check with us before you begin taking a new medicine while in this study.

- You will also need to tell us if you become pregnant anytime during the study. If you are a woman that can have children you must not get pregnant while you are taking part in this research study. You must agree to practice two effective and acceptable forms of birth control (described later in this form).

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- If you have an increase in symptoms for which you previously took medicine, if you need to contact your outside therapist other than for the usual appointments, and/or if you start or stop taking prescribed medicine, you should contact us before doing this.

- You should not be a part of any other clinical trial (research study) or take MDMA or Ecstasy outside of the study during the whole time you are in this study.

- If you must go the hospital or are in a life-threatening situation at any time during the study even if it doesn't have anything to do with the study, you will need to call us as soon as you can to let us know the details.

Screening

You will need to have the following exams, tests or procedures to find out if you can be in the study. This is called screening and this process can take up to 2 months. You may see the study doctor ([redacted]) or a member of his study team on two or more occasions during this time. We may ask your permission to contact your doctor or psychotherapist to get information about your medical and psychiatric history. We may need to do this so that we will know if you can be in the study or not. If you feel that these evaluations are too much to deal with during a given office visit, please tell us so we can schedule a different office visit for you to complete them.

The screening tests and procedures include the following:

- We will ask you questions about your medical history, including questions about your emotional and psychiatric history and medications you have taken in the past. 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 during your life.
- We will interview you and ask about your social anxiety symptoms and how you deal with them in your everyday life. We will use your score on this interview to decide if you can be in the study.
- We will ask you questions about the features of autism you experience.
- We will ask you questions about thoughts or feelings you might have about hurting or killing yourself.
- You will undergo a physical and neurological examination that will include measuring your blood pressure, pulse, temperature, and body weight. The neurological examination will check your reflexes and senses.
- You will have an ECG (electrocardiogram) taken. This is a recording of the electrical activity of your heart. For the ECG, you will have sticky patches placed on your chest, abdomen and sides. We will connect the wires (electrodes) from the ECG to these patches. Once the recording is complete, we will remove the sticky patches. This will take about 5-10 minutes.
- We will take a sample of your blood (about 1.5 tablespoons) from a vein in your arm and collect a sample of your urine for routine laboratory testing, including tests to check your metabolism and liver function. Once it looks like you can enroll in the study, a second sample of your blood (about 2 tablespoons) will be taken from a vein in your arm to measure the amount of hormones in your body.
- We will also use the first blood sample for a test to see if you have the human immunodeficiency virus (HIV) which is the virus that causes AIDS. If you choose not to have this test, you will not be able to take part in this study. If the tests find out that you have HIV, then we will have to submit a confidential report to the California Department of Public Health within seven days telling them of your positive test result. This is required by State law. We will also refer you for counseling and treatment.
- You will provide a sample of your urine to test for the presence of drugs of abuse. If this urine test is positive you will not be able to take part in the study, unless there is a medical reason for the positive test.

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- If you are a woman who can become or may be pregnant, we will use your urine sample for a pregnancy test as well. If the pregnant test is positive you will not be able to take part in the study.
- You will complete a questionnaire and we will interview about what you think about the study so far.

If necessary, we may ask you to allow us to get copies and review your medical record from your treating doctors. We will require a signed release form from you in order to do this.

If, based on the results of the screening tests and procedures, you qualify to take part in the study, we will schedule you for the next part of the study called "Preparatory Sessions and Baseline Measures".

Preparatory Sessions and Baseline Measures:

We will meet with you on three separate occasions for preparatory sessions before we schedule your first experimental session. Each of these visits will last about two hours and will be about 1 week apart. At each of these visits we will ask you about how you are doing and if there have been any changes in your health or the medications you are taking. We will ask you questions to check your symptoms. During each preparatory session, you will learn more about what to expect during the experimental sessions and we will video record these sessions as well. During these sessions, you will complete a number of different questionnaires about your mental health, emotions and quality of life. You will also complete a computer-based laboratory assessment (like a questionnaire) during one of the sessions.

It is during these sessions that we will have you stop taking any medication that you are not allowed to take while you are taking part in this study. We will have you stop taking the medication based on your therapist/doctor and the study doctor decide how to best have you stop it. This means that it may be done by lowering the dose over time until you are no longer taking the medication.

During the first session you will go on a tour of the study site to help prepare for the experimental sessions.

We will give you a card that says you are taking part in a research study involving the use of MDMA. This card will also include the telephone numbers to reach us (the researchers) and the Institutional Review Board. You can keep this card in your wallet to make it easier for you or anyone treating you in an emergency to contact us if you or they need to do so.

Stage 1 Experimental Sessions:

You will take part in two experimental sessions, when you will receive MDMA or placebo together with psychotherapy, each happening about one month apart. The placebo looks like MDMA but contains no active medicine. The first experimental session will occur after you have finished the third preparatory session.

We will "randomize" you into one of the study groups described below. Randomization means that you are put into a group by chance (like tossing a coin). A computer program will place you in one of the study groups. Neither you nor the study doctor can choose the group you will be in. You will have 2 out of 3 chances of receiving MDMA, and 1 chance out of 3 of receiving placebo. Neither your study doctor or his staff nor you will know which study group or drug (MDMA or placebo) you will be receiving. However should a medical emergency occur, this information will be made immediately available to your study doctor.

If, at the end of this study, we find that you were in the group that did not receive MDMA, there will be a second part of the study ('Stage 2') where you will be offered two additional experimental sessions with MDMA (no placebo is given). (Stage 2 is described below.)

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Each Experimental Session will last about 8 hours. We will schedule them so that they start at 9:00 am and end by 5:00 pm. Unless there are unusual circumstances, the Experimental Sessions will take place on Saturdays. The day after each session you will need to return to the study site for an "Integrative Session" at which we will check to see how you are doing. The details of these sessions are described below.

Before each Experimental Session you must:

- Not eat anything after midnight the evening before each session;
- Drink only beverages not containing alcohol after midnight the evening before each session;
- Not take any psychoactive drugs, with the exception of caffeine or nicotine, within the 24 hours before each session; and
- Not consume caffeine or use nicotine for 2 hours before and 6 hours after receiving the study drug (MDMA or placebo) or until therapists tells you it is safe to do so.

Before (about 9:00 am) you are to receive with the MDMA or placebo during each experimental session:

- We will collect a sample of your urine to test for drugs of abuse. You cannot take part in this study if your urine drug screen is positive for drugs of abuse.
- If you are a woman who can have children, we will use your urine sample for a pregnancy test. You cannot take part in this study if you are pregnant.

After you receive either MDMA or placebo (at 10:00 am) during each experimental session:

- We will measure and record your blood pressure, temperature, and pulse every hour until 5:00 pm (7 times total).
- We will ask you to rate the amount of distress you feel on a scale of 1 to 7 every hour until 5:00 pm (7 times total).
- Just before you are to receive the study drug (MDMA or placebo) and about 6 hours after you receive it, as a standard safety precaution, we will ask you about thoughts you might have about hurting or killing yourself.
- We will remain with you for seven hours after you take the study drug (MDMA or placebo).
- During each 8 hour session, you may sit or lie down in a comfortable position. You can ask for an eyeshade or headphones.
- We will ask to talk to you at least every hour, but you can talk to us or remain silent whenever you wish.
- Two hours after you take the study drug (MDMA or placebo) during the Experimental Session 2, we will take a sample of your blood (about 2 tablespoons) from a vein in your arm to measure the amount of hormones in your body.
- Two hours after you take the study drug (MDMA or placebo), you will complete the same computer-based laboratory assessment you completed during the Preparatory Sessions.
- We will give you food and drinks during each session at your request.
- If you request it and we agree to it, your support partner may stay with you during some of the experimental session, starting at an agreed-upon time. When your support partner arrives, they will stay in the waiting room until there is a good time for them to come into the experimental session.

You can go home after each experimental session is over (5:00 pm or so). However, you will have to make arrangements so that you do not drive yourself home. We ask that this arrangement be made 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 after having taken MDMA.

If you live more than 30 miles away from the study site (LA BioMed), we will offer you and your support partner a hotel room at a location close to the study site. If you live less than 30 miles away from the study site, someone or your support partner will drive you home or to the hotel and back to the study site the next day for another study visit to see how you are doing.

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If you find you need to talk with the study doctor or a member of his study team or you are having other problems and need to contact them, your support partner may contact us for help.

You will complete some questionnaires about feelings you might have experienced during or after the experimental session. You can complete these questionnaires at any time between the end of the experimental session and the start of the integrative session on the next day. During the time between the end of the experimental session and the start of the integrative session the next day, we ask that you use the time as a period of rest and reflection in a quiet setting.

Integrative Session - Therapy After Experimental Sessions

On the next day, you will have a non-drug (integrative) therapy session 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 experimental sessions. Each Integrative Session will last about 60 to 90 minutes. Your support partner will need to wait outside the therapy room during this visit.

Before starting integrative therapy on the day after each experimental session, we will ask you to guess whether you got MDMA or placebo. However, we will **not** tell you if your guess is correct. As an extra safety measure, we will ask you if you have had any thoughts of harming yourself.

After the integrative therapy session, we will interview you about your social anxiety symptoms and you will complete questionnaires about your mental health.

Time Between Each Experimental Session (about 1 month)

After the integrative sessions, we will telephone you every day for a week to see how you are feeling and whether you should return to see the study doctor or a member of his study team before your next scheduled psychotherapy session. We will also ask you about any thoughts of harming yourself on Day 2 and Day 7 of these telephone check-ins. These telephone calls will take about 5 to 15 minutes, though they can be as long as you need them to be.

You may schedule additional meetings with the study doctor or a member of his study team besides those that are scheduled as part of the study. You can contact them at any time. You can reach one of them by telephone 24 hours a day throughout this entire research study.

You will have integrative therapy with the researchers on two more visits every two weeks during the month after the experimental session. These integrative sessions will last 60 to 90 minutes. You and the researchers will also talk about ways to use what you learned to help work on treating your social anxiety, face and solve difficulties you may have faced during the experimental sessions and gain the most benefit and understanding from the experimental sessions. We will ask you about any thoughts of harming yourself. At each integrative session, we will interview you about your social anxiety symptoms and you will complete questionnaires about your mental health.

At the very last integrative session (about 1 month after Experimental Session 2), we will take a sample of your blood (about 2 tablespoons) from a vein in your arm to measure the amount of hormones in your body. You will also complete additional questionnaires about your feelings and the computer-based laboratory assessment.

Follow-up Period

During the next five months, you won't have any office visits scheduled for the study. You may go back to taking any medications if you need them for psychological problems and you can change your outside therapist or any therapy you receive outside of the study.

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To keep track of any medications, therapies or if you have to go the doctor, we 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 your last integrative therapy visit and the 6-month follow-up visit.

Just as you agreed to do during the rest of the study, you will need to avoid taking any MDMA or Ecstasy outside of the research study.

Every month during the follow-up period, you will need to complete questionnaires about your mental health. We may mail these questionnaires to you for you to fill out. If so, they will come with an envelope that is already stamped and have only the researcher's address on it. Do not put your name on the questionnaire as it will have your study identification (ID) number. This will help us to maintain your confidentiality should these questionnaires get lost. Alternatively, you may complete the questionnaires online using a secure internet connection, to keep everything confidential. We will explain how to do this and will be available to answer your questions.

6-Month Follow-Up Visit

About 6 months after your last experimental session, you will return to the study site for a study visit. During this visit, we will ask you questions about any thoughts of harming yourself, any changes in medications or your psychiatric health, including any benefits or harms, since your last visit. We will interview you and ask you about your thoughts on being in this research study. You will complete a questionnaire on the effects of being in this research study, any thoughts you have about the good and bad points of MDMA-assisted therapy, and your thoughts about taking MDMA. You will also complete questionnaires about your mental health. We will take a final sample of your blood (about 2 tablespoons) from a vein in your arm to measure the amount of hormones in your body.

After you complete these tests, you will find out if you received MDMA or placebo. If you learn that you had the placebo, you may choose to receive two additional experimental sessions of therapy with two different doses of MDMA, followed by three integrative therapy sessions after each one**.** If you received MDMA during Stage 1 you cannot take part in Stage 2.

Stage 2 Experimental Sessions - Open-Label MDMA

If you received placebo in Stage 1, you can take part in Stage 2. If you take part in Stage 2, you will have eight more visits. During the first experimental session in Stage 2, you will receive 75mg of MDMA. During the second experimental session (about 1 month after the first session), you will receive 125mg of MDMA. All the procedures during Stage 2 will be the same as those done in Stage 1, except you will know that you will receive MDMA during the experimental sessions. We will take samples of your blood (about 2 tablespoons each time) from a vein in your arm during both the experimental sessions and the third integrative session after each experimental session in Stage 2. There is no 6 month follow-up period after your last integrative session.

Signing this consent form means you agree to take part in Stage 2 should you qualify; however, you can change your mind at any time and stop without taking part in Stage 2. There won't be another follow-up period after Stage 2**.**

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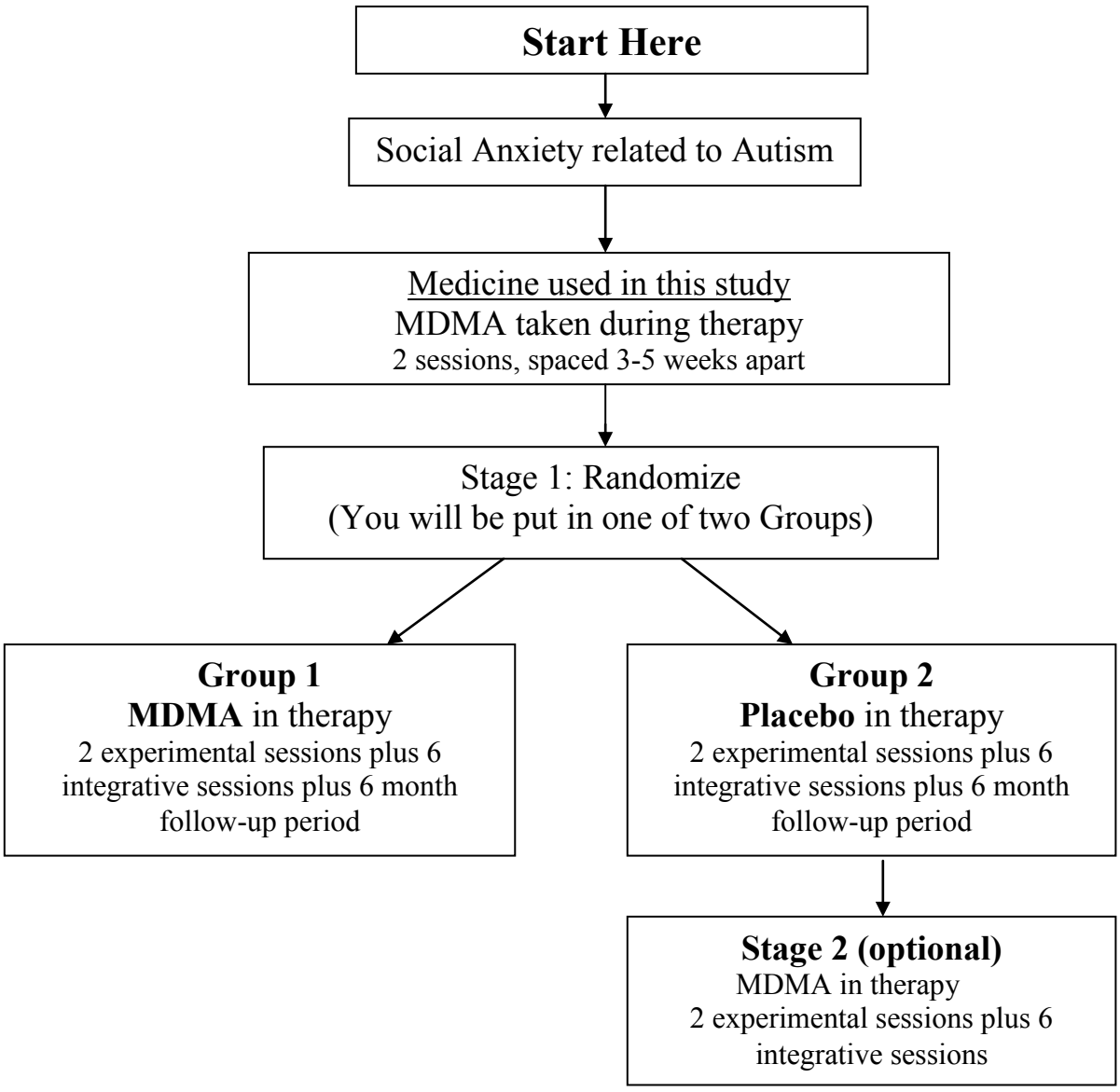
Study Plan

Another way to find out what will happen to you during the study is to read the chart below. Start reading at the top and read down the list, following the lines and arrows.



What are my responsibilities if I take part in this research?

If you take part in this research study, you are responsible for coming to all study visits, following the study doctor's and his study team's instructions, taking the study drug (MDMA or placebo) as told and completing all therapy sessions, questionnaires, and interviews.

How long will I be in the study?

This study can take up to eight months or 14 visits if you receive MDMA in Stage 1 of this study. It can last for an additional two months or 8 more visits if you receive the placebo in Stage 1 and agree to take part in Stage 2.

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Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from the MDMA can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

Your doctor, the sponsor of the study (MAPS), 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 psychological problems,
- 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.

If you have very high blood pressure, get sick, or have an important and strong lasting reaction (unwanted effect or health problem) during or after an experimental session, you or the study doctor may decide that you should not take part in the next experimental session. You may make this decision to stop taking part in the study for any reason. If the study doctor decides to take you out of the study, he will let you know that he is doing this and tell you his reason for doing this. If you are taken out of the study or decide you do not want to receive treatment in the study, the study doctor will ask you to complete some final questionnaires about your mental health. If you decide you do not want to continue in the study during an experimental session, we will ask you to stay in the office until the study doctor thinks that you are well enough to leave and that all the effects of the drug have worn off. If this happens, we will also ask you to allow us to interview you about your thoughts on being in the study and for you to complete the same questionnaires you completed at the beginning of the study during the follow-up visit in 6 months.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

If you stop being in the study, already collected data (information collected from and about you while you are in the study) may not be removed from the study database. We will ask whether we can collect data from your routine medical care. If you agree, we will handle this data the same as research data.

What treatments and/or procedures are experimental?

We are carrying out all of the procedures and/or treatments described above for research or experimental purposes. MDMA is an experimental drug, and has not been approved for use by the U.S. Food and Drug Administration (FDA) for medical use except in research studies.

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What side effects or risks can I expect from being in the study?

You may have side effects while on the study. We will watch everyone taking part in the study carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be anything from mild to very serious. Your study doctor or his/her staff may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the MDMA. In some cases, side effects can be serious, long lasting, or may never go away.

You should talk to your study doctor about any side effects that you have while taking part in the study even if you think they may not be caused by the medicines.

Risks and side effects related to **MDMA** include those which are:

Likely

- Fatigue
- Anxiety
- Lack of appetite
- Increased blood pressure
- Increased heart rate
- Dry mouth
- Tight jaw/teeth grinding
- Decreased ability to concentrate
- Slight changes in vision, hearing or other senses
- Headache
- Insomnia (trouble sleeping)
- Thirst
- Restlessness

Less Likely

- Nausea
- Feeling down
- Feeling cold
- Dizziness
- Impaired balance/gait
- Reduced immune system function (making you more susceptible to infections)
- Perspiration (sweating)
- Feeling weak
- Need for more sleep (feeling sleepy)

Rare but serious

- Potential for addiction (becoming dependent on the drug)
- Very high blood pressure
- Fast heartbeat (tachycardia)
- Irregular heartbeat
- Overheating (feeling hot)
- Liver disease
- Water intoxication (drinking too much water)

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

There may be unknown side effects or risks from the use of MDMA. Other possible risks of MDMA may include the following:

Physical Risks:

Serious problems: There have been some serious problems, and even deaths, associated with the use of Ecstasy outside of controlled settings (outside of research studies). In research studies (clinical trials), none of these serious problems have happened. Outside of medical settings, these problems have included high fever, brain swelling associated with drinking too much liquid, convulsions (seizures), and liver damage. Since you will be receiving moderate amounts of uncontaminated MDMA in a controlled setting with trained and experienced researchers who will be closely monitoring your physical and psychological reactions, these problems are not expected to occur either during or after the experimental sessions. While this does not guarantee that they will not occur, it does mean that if they do occur, the researchers are prepared to respond in a safe and professional manner.

Changes in vision, hearing or other senses: Most people that took part 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 12-33 out of every 100 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 doses used in this study, the increases in blood pressure and heart rate are likely to be moderate. Average increase in systolic blood pressure is 35 mmHg (measurement unit for blood pressure) and average diastolic blood pressure increase is 20 mmHg. Heart rate may increase by about 30 beats per minute (BPM).

In previous studies, blood pressure rose well above normal levels in a few people (a little less than 1 out of every 20, and usually in subjects receiving higher doses of MDMA than will be administered in this study) after receiving MDMA, but they 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 ask you about and check you for heart problems during the screening for this study. While this doesn't guarantee that no heart problems will occur, it does reduce the risk of this happening.

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 may become dependent on (addicted to) MDMA. One study found that up to 6% (a little more than 1 out of every 20) of people using Ecstasy for recreational purposes were dependent on it. However, three studies of people who had received MDMA in a research study found that they did not want to try MDMA again outside of the study. People who have recently (in the last 2 months) had problems with drug abuse should not take part in this study.

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Mental Risks:

Anxious or jittery feeling: Some people in previous studies (about 4 out of every 25) 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 therapy. If you are not able to deal with these experiences in a way that helps you, the researchers 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. We will encourage you to ask your support partner to call us immediately if you have any thoughts about hurting or killing yourself so we can help you resolve them safely. If necessary, we may prescribe anti-anxiety medication or medication for sleep. Some recreational users of Ecstasy have become severely anxious, depressed or paranoid (thinking that other people are out to get them).

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.

Mood: Some after-effects of MDMA may be noticeable up to 2 or 3 days later. While some people felt that their mood is better, about 3 out of every 20 felt that it was worse after receiving MDMA in other research studies.

Possible Risks to Brain Function: One study conducted by the sponsor in 20 people with PTSD found that two doses of 125mg MDMA spaced a month apart did not lead to differences in how well their brain functioned from a placebo control. The dose you will receive in this study will be similar to or less than this amount, and you will only receive it twice, just like in the previous study. 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, which may or may not contain MDMA, 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.

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.

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. They also 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.

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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 those studies were far higher than those typically taken by humans in either recreational or laboratory settings.

Worsening of Symptoms: You may experience a worsening of your social anxiety symptoms while taking part in this study. This may occur when you are stopping your current medications and if you receive placebo (no active medicine). This may also occur if you receive MDMA during this study.

Other Risks:

You should not drive or use machinery immediately after each experimental session (up to 24 hours afterwards). This is because the study drug (MDMA) may cause drowsiness, lack of co-ordination or slower reaction time.

If you are tested for drugs of abuse within three days of each experimental session, you may test positive. The researchers will provide you with an information card in case you are tested for drugs of abuse. If you are tested for drugs of abuse while you are taking part in this study, you can have the person(s) testing you call us to verify that you are taking part 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.

This study involves 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. If you are not comfortable with giving blood for tests, please let us know because it is an important part of taking part in this study.

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. If this happens, you should talk with your outside therapist and the study doctor. If you have to start taking medicine again, then the study doctor will have to take you out of the study.

Reproductive Risks - Females: Effects of MDMA on the growth and development of an unborn baby are not known; 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 doctor and the sponsor (MAPS) will ask you about and keep track of the pregnancy. If this happens, you will need to stop being in the study and they 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 (intrauterine devices), and barrier method used along with spermicide for at least one month afterward your final study visit/session. We 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.

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If you are a woman that can become pregnant, we will give you a pregnancy test at the start of the study and again before each experimental session to see if you are pregnant. If, at any time during the study, you think that you may be pregnant or are worried that you may become pregnant, you must notify us immediately. If you should become pregnant during the study, we will help you get proper advice and help you and your unborn baby get proper care while you are pregnant. However, you are responsible for the costs of the care for your pregnancy.

For more information about risks and side effects, ask your study doctor.

Are there benefits to taking part in the study?

Your mental health symptoms may improve while taking part 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 of autistic adults with social anxiety in the future.

What other choices do I have if I do not take part in this study?

One alternative to being in this study is to decide not to take part in it. This study does not offer you a treatment for your social anxiety but is rather looking to see if MDMA can be studied further as a possible treatment. This study is looking to find the appropriate dose for a possible future study.

You may decide to try other treatments for social anxiety. There are other medicines, Valium (diazepam), Xanax (alprazolam), or Prozac (fluoxetine) 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 researchers can discuss the alternatives and their potential risks and benefits with you. Talk to your doctor about your choices before you decide if you will take part in this study.

Will my personal and medical information be kept private?

We will do our best to make sure that the personal information in your medical record is kept private. However, we cannot guarantee total privacy. We may have to give out your personal information if required by law. If information from this study is published or presented at scientific meetings, we will not use your name and other personal information. **To ensure confidentiality, we will only provide the sponsor with your data (study information) containing your study ID (not your name).**

When not in use, we will keep your medical record (containing all information collected from you during and for the study) in a locked office. **Absolute confidentiality cannot be guaranteed, but every effort will be made to maintain your confidentiality**.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The sponsor, Multidisciplinary Association of Psychedelic Studies (MAPS);
- The U.S. Food and Drug Administration and similar regulatory agencies in other countries;
- The Department of Health and Human Services (DHHS) agencies;
- The Research Advisory Panel of California or State regulatory agencies; and
- The Institutional Review Board (IRB).

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Video recordings: The researchers (study doctor and study team), the sponsor (MAPS) staff and other researchers that the study doctor has given permission to who are seeking to better understand the principles of MDMA-assisted therapy will listen to or watch these recordings. No identifying information (such as your name) will be written on or attached to the recordings. You may listen to or watch the recordings 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 ask to view the recording. You have the right to view your study records and ask for changes if the information is not correct.

What are the costs of taking part in this study?

The sponsor of this study, MAPS, will cover the costs that are directly related to this study. This includes the costs for all therapy sessions that are a part of this study (includes all experimental and integrative sessions), 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.

If you live more than 30 miles from the study site, you will be reimbursed for one night (the night after each experimental session) in a hotel room at a hotel close to the study site that will be comfortable for you and your support partner.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor, [redacted] if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at [redacted]. If you cannot reach your study doctor, you may call the hospital emergency department (adult, [redacted]) or the hospital Psychiatric Emergency Department at [redacted].

You will get medical treatment if you are injured as a result of taking part in this study. If you are injured as a direct result of the study medicines or procedures required by this study, we will provide you with appropriate medical care including treatment and hospitalization if necessary. The sponsor of this study agrees to pay for such medical care including treatments and hospitalizations that are not covered by your health insurance or other third party provider.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time (unless if it's during an experimental session, in which case you are agreeing to remain in the treatment room until the doctor agrees that it is safe for you to leave). No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from [redacted].

By signing below, you will be agreeing to allow the researchers to decide what to do with any surplus tissue (blood) removed from your body during the research described above.

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We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

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Who can answer my questions about the study?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at [redacted]

This research has been reviewed and approved by a John F. Wolf, M.D. Human Subjects Committee, which is located at 1124 W. Carson St., Building N-14 in Torrance, CA. You may talk to them at (310) 222-3624 or email them at compliancehs@labiomed.org for any of the following:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

Have you taken part in any research studies within the past three months? *Circle "Yes" or "No"*

Yes **No**

If "YES", please describe: _____

If you want more information about this study, ask your study doctor.

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SUBJECT'S STATEMENT OF CONSENT

I have been given a copy of this consent form in its entirety (all pages). I have read it or it has been read to me. I understand the information and have had my questions answered. You will receive a copy of this signed informed consent form as well as a copy of the Human Subject's Bill of Rights. I agree to voluntarily take part in this study.

By signing this consent form, I have not waived any of the legal rights which I otherwise would have as a participant in a research study.

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.

Your signature documents your permission to take part in this research.

Signature of subject	Date
Printed name of subject	
Support partner's signature	Date
Printed name of support partner	
Witness to Subject Signature	Date
Signature of person obtaining consent	Date
Printed name of person obtaining consent	

Video and Audio Recording of Sessions:
I agree to have my sessions video and/or audio (voice only) recorded for the purposes described in this consent form.
Circle your choice (Yes or No) and sign below.

Yes No

Signature of subject	Date

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SUPPORT PARTNER'S STATEMENT OF CONSENT

"A Placebo-controlled, Randomized, Blinded, Dose Finding Phase 2 Pilot Safety Study of MDMA-assisted Therapy for Social Anxiety in Autistic Adults"

My participation in this study as a Support Partner is voluntary. I may refuse to take part in or I may stop taking part in this study as a Support Partner 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 medical center. The researchers and/or the sponsor may stop my participation in this study at any time without my consent if they decide it is in my best interest or if I do not follow the researchers' instructions.

I have been told that my role as a Support Partner includes:

- Providing reliable transportation, as required, to and from office visits and taking part in study visits, as appropriate.
- Driving the participant home or to another secure location following sessions. No participant will be allowed to drive themselves home after experimental sessions.
- Remaining available to attend to basic comfort needs and to talk with the participant in person for 24 hours after experimental sessions.

I have been given a copy of this consent form in its entirety (all pages). I have read it or it has been read to me. I have been given sufficient opportunity to consider participating in this study as a Support Partner. All of my questions so far about the study and my participation in it have been answered. You will receive a copy of this signed informed consent form as well as a copy of the Human Subject's Bill of Rights. I agree to voluntarily take part in this study.

By signing this consent form, I have not waived any of the legal rights which I otherwise would have as a participant in a research study.

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.

Your signature documents your permission to take part in this research.

Signature of support partner	Date
Printed name of support partner	
Witness to support partner's signature	Date
Signature of person obtaining consent	Date
Printed name of person obtaining consent	

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For the Investigator:

I certify that I am the principal investigator and am responsible for this study, for ensuring that the subject is fully informed in accordance with applicable regulations, and for advising the Human Subjects Committee of any adverse reactions that develop from the study.

Principal Investigator:_____

Date _____

Principal Investigator: [redacted]
Telephone Number: [redacted]

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HUMAN SUBJECT'S BILL OF RIGHTS

Anyone asked to take part as a subject in a medical research study or asked to agree on behalf of someone else, has the right to understand the following:

1. What the study is about and why it is being done.

2. What you will have to do if you take part in the research study and what treatments, drugs or medical devices, if any, will be used.

3. Any pain or discomfort you may expect to feel and what risks you might run, if any, from taking part in the research study.

4. What benefit to your health, if any, you might get from taking part in the research study.

5. Other non-research treatments, drugs or medical devices that may be available to treat your illness and a comparison of the risks and benefits of these other treatments with the one you are being asked to agree to receive.

6. What medical treatment, if any, will be available to you after the research study, if medical complications arise as a result of the study.

7. You will be given a chance to ask questions about the research study, until you are satisfied that you understand what is involved. You should expect your questions to be answered clearly, fully and honestly.

8. If you agree to take part in the research study, you can later change your mind at any time without being penalized. Leaving the study will not affect your usual medical care.

9. You will not be pressured, forced, misled, given wrong facts, bribed or unfairly influenced to get you to agree to take part in the experiment.

10. You will be given a copy of any consent form you sign for the research study.

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