PARTICIPANT INFORMATION AND CONSENT FORM AND HIPAA AUTHORIZATION

TITLE: A Multi-Site Open-Label Safety Extension Study of Manualized MDMA-Assisted Therapy for the Treatment of Participants with Posttraumatic Stress Disorder

PROTOCOL NO.: MAPPUSX
WCG IRB Protocol # 20210317

SPONSOR: Multidisciplinary Association for Psychedelic Studies (MAPS)
3141 Stevens Creek Blvd #40547
San Jose, CA 95117

<<CF-Main Header Block - Investigator>>

STUDY RELATED PHONE NUMBER(S): <<CF-Main User Defined #1>>

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

Experimental Subject's Bill of Rights

Any person who is requested to consent to participate as a subject in a research study involving a medical experiment, or who is requested to consent on behalf of another has the right to:

(a) Be informed of the nature and purpose of the experiment.
(b) Be given an explanation of the procedures to be followed in the medical experiment and any drug or device to be used.
(c) Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment, if applicable.
(d) Be given an explanation of any benefits to the subject reasonably to be expected from the experiment if applicable.
(e) Be given a disclosure of any appropriate alternative procedures, drugs, or devices that might be advantageous to the subject, and their relative risks and benefits.
(f) Be informed of the avenues of medical treatment, if any, available to the subject after the experiment or if complications should arise.
(g) Be given an opportunity to ask any questions concerning the experiment or other procedures involved.
(h) Be instructed that consent to participate in the medical experiment may be withdrawn at any time, and the subject may discontinue in the medical experiment without prejudice.
(i) Be given a copy of a signed and dated written informed consent form when one is required.

Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

Purpose of the Participant Information and Consent Form
This consent form describes the research study and your role as a participant. This consent form may have words in it you do not clearly understand. Please read this form carefully before you decide to be in this study. You may ask the study staff any questions about the information provided.

The purpose of this form is to give you information about the study. The form describes the purpose, procedures, benefits, risks, discomforts and your rights as a part of the study.

If you sign the form, you are giving your permission to participate. Signing this form does not guarantee that you will be enrolled in the study or that you are obligated to participate or unable to withdraw from the study. You should participate only if you want to. Before you decide whether to participate, you should think about how the tests and study visits will affect your schedule, family, and work.

You can review this consent form to think about or discuss with family or friends before deciding whether or not to participate.

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

The sponsor is paying for this research study. Your study doctor, research team and therapy pair will be paid for their time to conduct this research study. <<CF-Main Financial Disclosure>>

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

Signing this form will not result in you losing any of your rights. You may refuse to take part in this study or withdraw from this study at any time without penalty or loss of benefits to which you are otherwise entitled.

Background
You are being asked to participate because you were previously involved in a Phase 3 clinical trial sponsored by the Multidisciplinary Association for Psychedelic Studies (MAPS, www.maps.org) and you were either randomized to placebo or you were unable to complete the study due to the Coronavirus Disease 2019 (COVID-19) global pandemic or other external circumstances.

The purpose of this multi-center study is to provide information on whether the drug 3,4-methylenedioxymethamphetamine (MDMA) combined with therapy is safe and helpful for people who have post-traumatic stress disorder (PTSD). MDMA is an experimental drug, which means that it has not been approved by the Food and Drug Administration (FDA) for sale for medical use in the United States (U.S.). MDMA is also a controlled drug (illegal to use outside of research) and is sometimes known as “Ecstasy” or “Molly” (which is supposed to contain MDMA, but often contains other drugs instead of or in addition to MDMA). MDMA is a chemical that is structurally similar to some stimulant chemicals, like methamphetamine, which is both a major drug of abuse and an FDA-approved treatment for Attention Deficit/Hyperactivity Disorder. MDMA is also similar to some psychedelic (hallucinogenic) chemicals, like mescaline, which is found in peyote cactus. MDMA has already been used legally in research and illegally in uncontrolled environments, such as nightclubs. While much is known about MDMA and its risks, much remains unknown about this drug.

The study is sponsored by a U.S. based non-profit organization, MAPS. MAPS has completed twelve studies of MDMA-assisted psychotherapy in the U.S., Canada, and Israel for PTSD and other diagnoses.

Before MDMA became illegal in 1985, some psychologists and psychiatrists combined it with therapy to help people with psychological problems or challenges, including PTSD and couples therapy. Though we do not know exactly why it may help people with PTSD, we know that MDMA may increase positive mood and change 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 distressing. 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, help people work through thoughts, memories and emotions related to PTSD and other past experiences.

Study Information

Type of Study
This study is open-label, meaning you will receive MDMA. There will be approximately 100 participants enrolled in this study.

Length of Study
The length of active participation in the study will be about 22 weeks but may be more or less, depending on the length of screening, how long you need to safely stop your medications (as needed), and scheduling. Participation in the study requires a large time commitment from you over the active study period.

Due to the COVID-19 pandemic or other unforeseen circumstances, there may be delays in your study schedule including visits and Study Drug Sessions. The

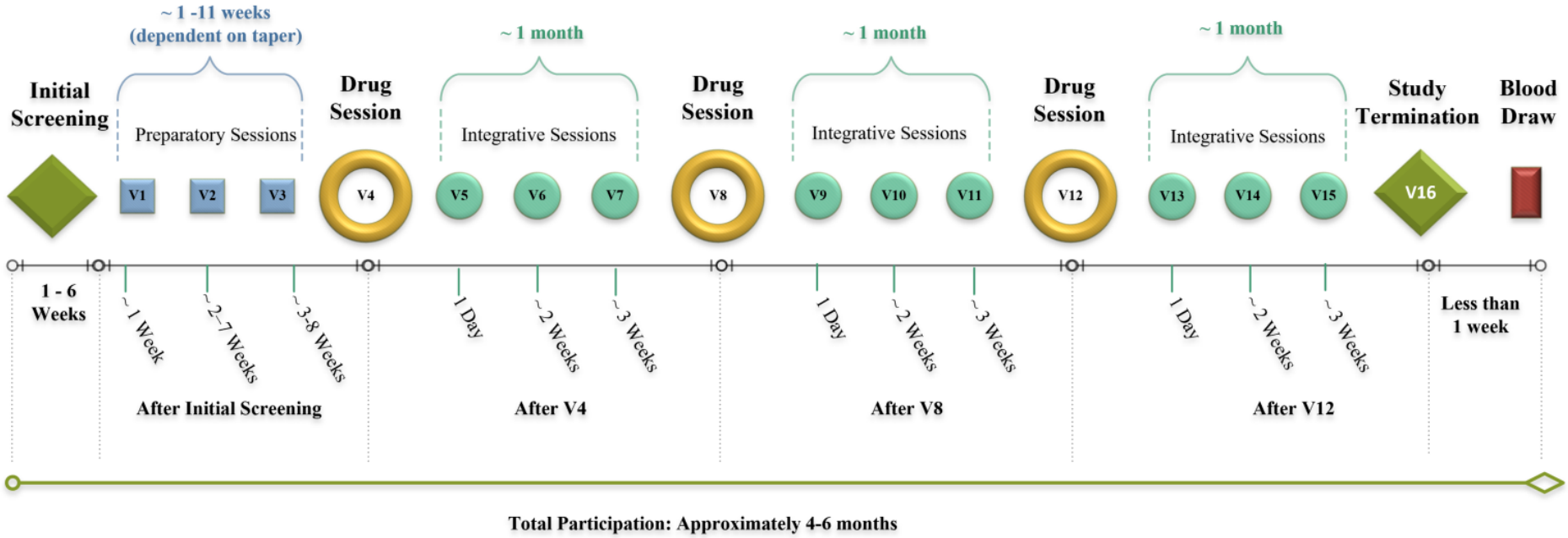
Study team will be closely following federal and local safety guidelines regarding COVID-19 and will keep you as informed as possible about any potential changes to the study schedule.

Types of Visits and Duration
Below are the planned visits for this study:

- **Screening Visits**: Multiple visits at the study location, lab, and/or doctor's office, an online meeting with an evaluator, and phone/video calls from the study team.
- **3 Preparatory Visits (approximately 90 minutes each)**: Three introductory therapy sessions at the start of participation in the study, spaced about one week apart.
- **3 Study Drug Sessions (approximately 8 hours long plus an overnight stay)**: Three visits about 1 month apart. You will be given MDMA during these visits along with therapy.
- **9 Integrative Sessions (approximately 90 minutes each)**: Three sessions after each Study Drug Session. These are about 1 week apart and will involve you talking to your therapists about your thoughts and feelings.
- **Questionnaires (60 minutes)**: Completion of questionnaires at Visit 3 (the third Preparatory Visit) and Visit 16 (Study Termination).

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

Study Structure Overview



Total Participation: Approximately 4-6 months

Procedures/What Will Take Place in the Study

Screening/Evaluation and Beginning of Study
If you agree to be in this study, you will first sign this Informed Consent Form and HIPAA Authorization before any study-related procedures are done.

Before you can be enrolled in the study, the study team must first make sure that you qualify for the study and that you are generally physically healthy. This screening process can take up to 10 weeks. The order of assessments in screening may vary, but this form lists all the activities in the screening period. Some of these meetings may take place online or in-person.

At the initial meeting, you will be asked to:

- Provide information about yourself, including answering questions about difficult experiences you may have had during your childhood and other times in your life
- Complete questionnaires about your past trauma(s), PTSD symptoms, substance use, and thought patterns
- Answer questions about thoughts you might have had in your life about harming yourself or ending your life

If you are initially eligible, screening will continue with the following medical assessments with a study doctor. There may be multiple visits or online meetings, where you will be asked to do the following:

- Provide your medical and psychiatric history, including past medical records since your participation in the previous study
- Provide information about past and current medications
- A brief physical exam, including taking vital signs (blood pressure, heart rate, and body temperature) and measuring your height and weight
- An electrocardiogram (ECG) and rhythm strip, which are recordings of the electrical activity of your heart
- Provide a small sample of your blood (about 2 teaspoons) for the sole purpose of ensuring your safety and compatibility with the study, including tests of metabolism, liver function, and alcohol use. We also may test for the Hepatitis C virus (HCV).
    - If you have positive test results for HCV, we will notify you. If the state we are practicing in requires that we notify state health authorities of positive results, we will do so. You may still be able to participate in the study after you have been evaluated (and potentially treated) by a doctor. If you do not want to be tested, you should not take part in this research study.
- A urine test for drugs that may be addictive. Urine drug screen will be reviewed in order for you to take part in the study. We will not report findings of drugs to any authorities.
- A urine pregnancy test if you are able to get pregnant. Your urine pregnancy test must be negative for you to take part in the study.

You will also have an online meeting with an evaluator who will ask you questions about:

- Your emotional and psychiatric history
- Drug use
- Thoughts you may have about harming yourself or ending your life
- Other thought patterns you may have

If there are other medical concerns during screening, you may be asked to do additional testing with your primary care physician or another doctor. The study doctors will explain any tests they are asking you to do.

Due to COVID-19, your therapy pair and study doctor may ask you additional questions about your health in advance of any on-site visit. They may ask you to wear a mask or other protective equipment. They may take your temperature or ask for other precautions, such as COVID-19 testing. If there are any costs associated with COVID-19 screening or protective equipment required by your therapy pair or study doctor, the sponsor will pay for those costs.

Additional Cardiac Testing
You may need additional testing by a cardiologist if you have hypertension, diabetes, or another medical condition. The cardiologist will explain these tests in detail. They may include a nuclear exercise stress test, echocardiogram, and/or carotid ultrasound. These extra tests may occur over one or two visits to a cardiologist's office. The visits will take between 1 and 3 hours each.

The cardiologist may generate medical records with your name on them.

The study doctors will use the results of these tests to assess whether your heart is healthy enough to take MDMA in the study.

In addition to the risks or discomforts listed in the following sections, there may be other risks that are currently not known. Also, the risks or discomforts described may occur more often or be more severe than has been seen before.

Nuclear Exercise Stress Test
Exercise testing is a way of learning how your heart responds to strenuous exercise. For this test, you will go to a doctor's office that is specifically prepared for this kind of procedure. There are two parts to this test. First, you will receive a radiotracer (radioactive dye) in your blood followed by imaging (pictures) of your heart. You will then exercise on a treadmill or stationary bicycle. About 2 minutes before stopping (or until signs of difficulty appear, such as shortness of breath or tension in your chest), you will receive a second radiotracer. Another set of imaging will be done about 60 minutes later. The whole procedure will therefore take about 3 hours to complete. The exposure to radiation is very low. There are no known side effects to receiving the radiotracers.

The radiotracer is injected using a needle placed in a vein in the arm (similar to a blood draw). This is a fine, small gauge needle; it could cause brief minor pain where it is inserted, possible bruising, and rarely, infection or fainting.

The nuclear exercise testing may cause discomfort, fatigue, and shortness of breath. Rarely, more serious problems such as fainting, falling, or irregular heartbeat have been reported. In less than one in 10,000 cases, heart attacks have occurred. The doctor performing these testing procedures will monitor you continuously during the test and will stop the test if it appears that you are having problems or if you ask to stop the test.

The radiotracer contains a small amount of radiation. This is not necessary for your medical care, is for research purposes only, and is necessary to obtain the desired information. The total “effective” radiation dose you will receive is comparable to 3.3 times the yearly dose from environmental radiation in the US, which is allowed by the FDA for individuals participating in basic research studies, and has not been shown to involve a risk of cancer.

Stress Echocardiogram
Your study doctor may order this type of exercise testing, instead of the one mentioned above. This will depend on availability of the testing and your study doctor’s clinical opinion. For this test, you will also go to a doctor’s office that is specifically prepared for this kind of procedure. There are two parts to this test. In the first part of the test, a cardiac scientist performs an echocardiogram, using an ultrasound machine. An echocardiogram checks how your heart functions when resting. In order to obtain the image, you will be asked to lie on your left side. To ensure good contact between your skin and the probe, surgical jelly is placed at several different sites on your chest. In the second part of the test, your heart is exercised or ‘stressed’. If you can walk easily, you can walk on the treadmill. The speed and slope of the treadmill will increase gradually. This makes your heart do more work. When your heart is working as hard as possible, you stop exercising and quickly lie down on the bed. More echocardiogram pictures are taken. The test will be stopped if you have chest pain, become very tired or very short of breath, or if you ask to stop.

Echocardiogram
An echocardiogram (echo) is a graphic outline of the heart's movement. During an echo test, ultrasound (high-frequency sound waves) from a hand-held wand placed on your chest provides pictures of the heart's valves and chambers and helps the sonographer evaluate the pumping action of the heart. Echo is often combined with Doppler ultrasound and color Doppler to evaluate blood flow across the heart's valves.

There are no known risks associated with the echo procedure, because it uses harmless sound waves, similar to how doctors record pictures of fetuses in pregnant people. The gel may feel cold when it is first placed. Some people with sensitive skin can develop a rash from the gel.

Carotid Ultrasound

A carotid ultrasound is a painless test that uses high-frequency sound waves to create pictures of the insides of your carotid arteries, which are inside your neck. The ultrasound will show the doctor if there is any buildup of plaque inside your carotid arteries. If there is too much plaque, it can cause blood clots, which can cause a stroke.

There are no known risks associated with the carotid ultrasound procedure, because it uses harmless sound waves, similar to how doctors record pictures of fetuses in pregnant people.

Beginning of Study
If you pass the initial screening and choose to participate, you will be enrolled in the study and we will schedule your first preparatory session with your therapy pair.

If you are taking certain medications, you may need to stop taking them before your first Study Drug Session. The study doctor will discuss the medication plan with your prescribing doctor. Only stop medications if the study doctor gives you specific instructions for how to stop. Your symptoms of PTSD may worsen with discontinuation of your current medications. Some PTSD medications can cause thoughts of harming yourself or ending your life if you stop taking them too quickly and without the care of a doctor. **This is very important. Do not stop taking the medications before you are supposed to.**

You must let your therapy pair know about any change in medicines or medical conditions or procedures, such as surgery, within 48 hours of it happening.

You will need to give your therapy pair the name and contact information (phone number or email) of a relative, spouse, or close friend. Your therapy pair will contact this person only if you have a medical emergency, if you are at risk of hurting yourself or someone else, or if the study team cannot get in touch with you and need to know you are okay.

Preparatory Sessions
During the Preparatory Period, you will have the following sessions:

- Visit 1: Preparatory Session 1 (90 minutes)
- Visit 2: Preparatory Session 2 (90 minutes)
- Visit 3: Preparatory Session 3 (90 minutes therapy + 55 minutes questionnaires)

Most of these visits will take place in person at the study site; your therapy pair will let you know if any of the preparatory sessions can or will take place remotely on a computer.

Preparatory Sessions are 90-minute therapy sessions. The third Preparatory Session has an additional 55 minutes of questionnaires. During each Preparatory Session, the therapists will get to know you and discuss with you the traumatic incidents that led to your PTSD, the ways PTSD symptoms are affecting your life, and what you would like to achieve during the study.

If the study staff have medical concerns about your health, they will provide you with that information so you can get follow-up care.

If you are eligible to continue in the study at the third Preparatory Session, you will complete about 55 minutes of psychological questionnaires. These questionnaires are an essential part of the research and will help establish the baseline data for your participation in the study. During the third Preparatory Session and several times throughout the study, you will be asked questions about thoughts or feelings you might have about harming yourself or ending your life. Your study therapists will ask these questions so that they can assess your safety and track any changes in suicidal thoughts or feelings throughout the study. While these questions may be difficult to respond to, it is important for you to answer them honestly. The study therapists will support you in processing any difficult emotions or reactions to these questions.

The therapy pair will give you a card with contact information for the therapists, a study 24-hour emergency phone number, and the Institutional Review Board (IRB), which is a group of scientists and non-scientists that protects the rights and welfare of study participants. You can keep this card in your wallet to contact the therapy pair if you need to.

Study Drug Sessions
After you have met all of the inclusion criteria and none of the exclusion criteria of the study and if you qualify for the study after the Preparatory Sessions, you may be eligible to be enrolled in the study to receive study drug sessions.

There will be a total of 3 full day Study Drug Sessions during the study which will occur about 4 weeks apart. The first Study Drug Session will occur after you have had three Preparatory Sessions. During the first Study Drug Session, you will receive an 80 mg dose of MDMA. MDMA capsules also contain mannitol (a sweetener) and magnesium stearate (a lubricant). You will receive another dose (40 mg) of MDMA 1.5 to 2 hours later, unless you or the therapy pair decide that it is not in your best interest to receive the second dose. During the second and third Study Drug Sessions, you and your therapy pair can decide if you would like to take the same dose you took in your first Study Drug Session, or if you would like to try a higher dose (120 mg). You will receive a supplemental dose of either 40 mg or 60 mg of MDMA 1.5 to 2 hours later, unless you or the therapy pair decide that it is not in your best interest to receive the second dose. The goal will be to decide on the optimal dose for you.

We will ask you to make some lifestyle changes prior to the Study Drug Sessions.

For 1 week before each Study Drug Session:

- You cannot take any herbal supplements that have not been discussed and approved with the therapy pair and study doctor. Examples of herbal supplements include milk thistle, gingko, ginseng, etc. Please talk to your study doctor about all herbal supplements and vitamins (such as multivitamins, Vitamin D, etc.) that you take.
- You may need to stop taking prescription and non-prescription medications before each Study Drug Session, which may require more or less time than one week. Your

medications will be reviewed by the study doctor in advance and the requirements will be shared with you. **Do not stop taking any medications without the study doctor instructing you when and how to do so.**

- Some prescription medications, such as birth control or blood pressure medication should be continued as normal. Talk to your study doctor to ensure you understand the requirements.
- Non-prescription medications may include over-the-counter medicines like pain relievers, antacids, allergy medications, nasal sprays, etc. Talk to your study doctor about all over-the-counter medications you take to ensure you understand the requirements.

After midnight before each Study Drug Session:

- You must not eat any food, drink any alcohol, or use cannabis.
- You can drink non-alcoholic liquids during this time, such as water or juice.

For 2 hours before each Study Drug Session:

- You cannot use nicotine or caffeine.

For 6 hours after the first dose of MDMA at each Study Drug Session:

- You cannot use nicotine or caffeine.

If you are taking certain opioid medications for pain management, you can stay on these medications during treatment, although the study team may ask you to reduce the dose before each Study Drug Session and stop taking them for 12 hours before and at least 24 hours after the first dose in each Study Drug Session. If your pain becomes too severe to handle during this period, or you have side effects from not taking your medication. Please inform the study team of any symptoms you may have or any changes in the medications you are taking during your study participation so they can guide you as to which medications are safe to use during the study.

On the morning of the Study Drug Session, before the first dose of MDMA:

- You will be asked to provide a urine sample to test for drugs of abuse and for pregnancy
- You will be asked to answer questions about thoughts you might have about harming yourself or ending your life
- You will be asked to discuss your goals with the therapy pair and get answers to any questions you may have.

After urine testing, you will receive capsules containing a dose of MDMA. After taking the dose, you will then sit or lie down in a comfortable position. You can ask for eyeshades if you wish. You will listen to music during much of each Study Drug Session, either through headphones or room speakers. Lying or sitting in a comfortable position and listening to music are meant to bring out thoughts and feelings, including those about past traumatic experiences. The therapy pair will remain with you, and they will help you if you need them

to. They will speak with you and ask you to talk to them at least once an hour, but you can talk to them whenever you wish. There may be times when the therapy pair will suggest that you stop talking for a while in order to pay attention to your thoughts and feelings. There will be beverages available, including juices or sports drinks, and you will be encouraged to drink an adequate amount of fluid. You can drink whenever you wish to do so, within the limits of the amount that is safe for your body. In the afternoon, food will be provided.

Approximately 2 hours after you take the first dose, you may take a second dose containing about half the amount of the first dose if the study doctor thinks it is appropriate for you. The second dose may make the effects last longer. If you choose not to, or if you or the therapy pair decide that it is not in your best interest to receive the second dose, then you will not receive the second dose.

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

If you are confused or upset 8 or more hours after the start of a Study Drug Session, the therapy pair will stay with you until you have fully recovered. If the therapy pair thinks you are at risk of hurting yourself or others, they will either remain with you all night or admit you to a hospital until you are no longer at risk. The therapy pair will ask you how you feel at the beginning and end of the Study Drug Session and on several occasions during the phone follow-up period.

You need to agree to call the study doctors if any of the following things happen while you are on study:

- You have an increase in symptoms that you have taken medication for in the past
- You have a new symptom or medical issue
- You need to contact your outside therapist other than for the usual appointments
- You start or stop taking a prescription medicine or an over-the-counter medicine that you have not previously cleared with the therapy pair
- You go to the hospital for any reason.

If you have very high blood pressure, get sick, or have an uncomfortable and strong lasting negative reaction (unwanted effect or health problem) during or after a Study Drug Session, you or the therapy pair may decide that you should not have the next Study Drug Session. You may also make the decision to stop treatment in the study for any reason.

If the therapy pair decides you can no longer participate in the study for medical reasons after you have taken the dose of MDMA, they will let you know that they are doing this and

their reason. They will help you find a therapist who can continue to help you with your PTSD, if needed. If you can no longer participate in the study or decide you do not want to receive study drug in the study, the study researchers may ask you to complete some final questionnaires about your PTSD symptoms. If you decide you do not want to continue in the study during a Study Drug Session, you will still have to stay in the office until the therapy pair thinks that you are stable enough to leave and all the side effects of the drug have worn off. If this happens, you will also be asked to take part in some of the same interviews and questionnaires you completed at the beginning of the study. This is optional.

Overnight Stay
You will spend the night after each Study Drug Session in a room at the study site with an attendant who will be staying in a room nearby. If you find you need to talk with the therapy pair or are having other problems and need to contact the therapy pair, you or the attendant can contact them immediately.

Integrative Sessions
There will be three Integrative Sessions after each Study Drug session. Some or all of these visits may be conducted remotely. The morning after each Study Drug Session, you will have a 90-minute non-drug therapy visit to help you express, understand, and connect any thoughts or feelings you may be having about your symptoms and their causes. The therapy pair will encourage you to think and talk about your experience during the Study Drug Session. You may not drive until after the Integrative Session. **Do not drive if you are feeling tired, less alert, or having difficulty concentrating.**

After you return home from the therapy session, the therapy pair will talk to you by phone every other day for 14 days to ask how you are feeling. They will ask if you have had any thoughts of harming yourself or ending your life. They will also ask about medications you are taking. These calls will take about 5 to 15 minutes, though can be as long as you need them to be. You can call the therapy pair at any time. If they are unavailable, a study team member will be available at the 24-hour number provided on the contact card.

After each Study Drug Session, you will have two more Integrative Sessions, about 1 and 3 weeks after. Your therapy pair will let you know if any can be conducted remotely. At each, the therapy pair will ask you if you are having thoughts of harming yourself or ending your life. At each third Integrative Session, you will be asked to complete a questionnaire about stressful events in your life.

If there are delays in following the usual study schedule, the therapy pair will call you at least once a week to talk about how you are doing. These calls will take about 15 minutes.

Study Termination
About 1 month after the last Study Drug Session and 2 months after the last Study Drug Session, you will meet with your therapy pair to end your study participation. Your therapy pair will let you know if this meeting can happen remotely or if you need to come to the study

site. You will fill out the same questionnaires from the start of the study (about 1 hour). You will be asked if you have had any thoughts of harming yourself or ending your life.

The researchers will measure your blood pressure and weight. These tests will help the therapy pair tell if your symptoms have changed or stayed the same over time.

Possible Risks, Benefits or Alternatives
You may have changes in health while on the study, which could be due to MDMA or therapy, or events in your own life not related to the study. However, doctors do not know all the possible side effects. Side effects may be mild or very serious. You should talk to your study doctor about all changes in health you experience while taking part in the study, whether you think they are related to the study or not.

Risks of MDMA
MDMA has not been widely tested in humans, but as of October 01, 2022, 1,974 people have been given MDMA in clinical research settings. Some of the effects that have been observed are listed below.

Side effects that are typically not severe but are more frequently reported at active doses of MDMA and at least twice as often as placebo include:

Most Common (≥20% of patients):

- Muscle Tightness (about 65%)
- Lack of appetite (about 52%)
- Nausea (about 30%)
- Sweating (about 20%)

Common (≥10% to 19% of patients):

Feeling cold, restlessness, big pupils, dizziness, jaw clenching, eye wiggling, increased blood pressure, feeling jittery, chest pain not related to heart issues, dry mouth.

Less Common (<5% to 9% of patients):

Blurry vision, frequent urination, recurrent thoughts, vomiting, stress, muscle pain, increased body temperature, chills, substance use (cannabis use), urgent urination, muscle twitching, feeling sleepy, nervousness.

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

Serious problems
Within all MAPS-sponsored studies to date, only one serious reaction related to MDMA occurred in a participant who had a medical history of pre-existing heart issues (irregular

heart rhythm) and who experienced an episode of changes in heart rhythm after receiving MDMA. This participant recovered without any complications.

Blood pressure and heart rate
MDMA typically causes a transient increase in blood pressure and heart rate, similar to what happens with moderate exercise. These transient increases in blood pressure and heart rate usually have returned to normal by the end of the visit, approximately 6-8 hours after the first dose.

In the Study Sponsor's past studies, participants did not report any discomfort, nor did they require any treatment, due to increased blood pressure and heart rate after taking MDMA. Although these increases in blood pressure are similar to what happens after moderate exercise, they could cause serious problems in individuals with pre-existing heart or blood vessel conditions. These serious problems could include an irregular heartbeat, heart attack, or stroke. We will test you for pre-existing heart problems before you 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.

Driving Limitation
Due to known potential risks described above, you should not drive of use machinery immediately after Study Drug Visits (up to 24 hours afterwards).

Possible Negative Effects on the Brain
Previous studies (conducted by the Study Sponsor) of brain scans of people before and after they got between one and three doses of MDMA did not show any changes or injury to the structure of the brain following MDMA. MDMA did decrease the reaction of the brain to challenging content in PTSD patients, which was an improvement. Findings from this study suggest that the amount of MDMA you will receive in this study will not produce any lasting negative changes in your brain.

Emotional Openness
MDMA is considered an "empathogenic" drug. This means people who use it may experience increased empathy and sociability. After taking the study drug, you may feel more emotionally open, friendly, extroverted, or talkative. You may also feel closer to the Study Team or more trusting of them, or you may even feel loving or sexual feelings toward them. The Study Team is aware of the effects of the drug. They have been trained on how to appropriately care for someone who has taken MDMA and have signed a code of ethics that prohibits any sexual or romantic relations between researchers and participants in the study, including after participation in the study has ended. If you have any concerns that you are uncomfortable addressing with the Study Team, please contact the IRB via the phone number provided on this consent form.

Risks of Being in the Study
It is possible that you may experience some risks associated with being in the research study outside of the scope of MDMA. These potential risks are described in the following sections.

Positive Drug Test
If you are given a drug test within three days of each Study Drug Visit, you may test positive for MDMA. The Study Team will provide you with an information card in case you are given a drug test. This card may not protect you from discipline at work or loss of employment. The Study Team will discuss when and how to present the information card. The card will not prevent you from being stopped or cited if you are driving erratically or poorly, so you should not operate machinery or drive a car for 24 hours or more and until you feel back to your normal self.

Emotional Discomfort
The interviews you have and questionnaires you complete during the study may make you feel upset at the review of your emotional experiences, or you may feel boredom or fatigue. Answering questions about thoughts you might have of harming yourself or ending your life may be upsetting.

The medical tests done during health screening for the study may show something abnormal that needs further evaluation by the Study Doctor or your personal doctor, which may cause emotional discomfort. You can decline any testing you do not want to complete, but we may not be able to enroll you in the study without medical confirmation for your safety. The Study Doctors will explain all test results to you and refer you to the appropriate medical providers, as needed.

Trauma Therapy
The treatment being tested in this study is a combination of a drug (MDMA) combined with therapy. Any therapy, including MDMA-assisted therapy, can be a challenging process when it addresses emotionally painful experiences, and symptoms may become more pronounced at times. During the study (and/or after) you could experience increased anxiety, sadness, or other difficult feelings and thoughts, including the possibility of suicidal thoughts. Tell your study therapists if you are having any new or worsening symptoms. If your experience does worsen, it does not necessarily mean that the study will not help you. You should only continue in the study if you and the Study Therapists agree it is in your best interest. The Study Therapists and doctor will provide you therapeutic support or alternative medications if needed. It is important that you understand this possibility before deciding whether or not to participate.

Psychological Distress
Both the therapeutic process and MDMA may expose underlying psychological distress. Psychological distress could arise following a Study Drug Visit or non-drug therapy visits or at the end of the study as a result of the process of integrating feelings, perspectives, insights, or may arise more generally around ending the study.

The Study Therapists can discuss with you if you have any need for additional integration support during the study and can provide referrals at the end of the study for continuing integration support as needed.

Your pre-existing symptoms and diagnosis related to your PTSD may not improve and may become worse during the study or after.

You may start Preparatory Visits but are not eligible to continue onto the Study Drug Visits due to the results of your screening evaluations. This may lead to disappointment and distress at not being able to participate in the research study.

Temporarily Discontinuing your Regular Medications

As you will be required to discontinue the use of psychiatric medicines (as for depression or anxiety, for example) as part of the study, you may start to have new or recurring symptoms. There is also a risk that you may have thoughts of harming yourself or ending your life when you stop taking medicine, especially if you have had these thoughts before. If this happens, talk with your prescribing doctor, your Study Therapists, and your Study Doctor. If you need to start taking medicine again, the Study Doctors will need to re-evaluate your eligibility and there is a chance that you will not be able to continue in the study. Your health and safety takes priority over your continued participation in the study. There are some allowable medicines on study; your doctors will discuss these with you if needed.

COVID-19 Transmission
Study participation will involve several consecutive overnight visits at the study site, including three 6-8 hour Study Drug Visits. This personal interaction may increase your risk of becoming infected with SARS-CoV-2 (coronavirus that causes COVID-19 disease). The Study Team will follow local and national COVID-19 prevention guidelines for healthcare workers and all precautions will be taken to reduce this risk, such as screening for symptoms before in-person visits, using face masks, cleaning surfaces, and washing hands. For your safety and the safety of Study Team, we recommend that you also follow the local and national safety guidelines for prevention of COVID-19, which may include wearing a face mask while in public, maintaining 6-feet distance between yourself and others outside of your household, and other physical distancing guidelines in order to reduce the potential for COVID-19 infection. The Study Team will ask you about your habits prior to in person visits, and together you will figure out a safe plan for reducing risk while attending in-person visits. This plan may include testing for the virus, isolating at home if exposed, or other changes to your habits. These recommendations may change as the impact of the COVID-19 pandemic changes over time and your Study Team will update you as needed.

Remote Visits
Some of the non-Study Drug Visits, including Screening, Preparatory, and Integration visits, may be scheduled via telemedicine. The Study Team will discuss your options for telemedicine visits with you. There may be benefits to remote visits, such as convenience and reduced risk of COVID-19 transmission. There may be risks, including potential breach of security and technological difficulties or interruptions. It is critical that you do not share the links to online meetings with anyone unauthorized to attend.

Loss of Privacy
Absolute confidentiality and security cannot be guaranteed; however, every effort will be made to maintain your confidentiality. This is described more in the section titled “Your Rights as a Study Participant.”

Discomfort During Blood Tests
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.

Risks of ECG
You may have skin irritation from the contacts used.

Reproductive Risks
Effects of MDMA on the growth and development of an unborn baby or nursing children are not known. Therefore, you will not be allowed to be in the study if you are pregnant, planning to get pregnant, or are nursing.

- If you are able to become pregnant, you will be tested at the start of the study, before each Study Drug Visit, and once after the final Study Drug Visit to see if you are pregnant.
- If you are male assigned at birth and your female partner becomes pregnant during the study, we will request to follow-up with your partner’s pregnancy. If this is the case, we will provide a separate consent form for your partner. Taking part in the partner pregnancy follow-up is voluntary and will not affect your participation in the study.
- If, at any time during the study, you think that you may be pregnant or may become pregnant, you must tell the Study Team immediately.
- If you become pregnant after you have had at least one Study Drug Visit, the Study Doctors and the Study Sponsor will ask you about and keep track of your pregnancy and will ask about the outcome of your pregnancy.
- If you become pregnant, you will no longer receive study drug but may remain in the study for follow-up purposes.
  If you should become pregnant during the study, the Study Doctors will refer you to the appropriate medical providers, as needed.

Not being able to become pregnant is defined as permanent sterilization, postmenopausal, or assigned male at birth. Those who are able to become pregnant must use one of the allowed contraception methods during the study and for 10 days after the last Study Drug Visit:

- Intrauterine device (IUD)
- Intrauterine hormone-releasing system (IUS)
- Non-oral hormonal methods (including injected, intravaginal, implanted, or transdermal)

- Does not engage in sexual activities that could result in pregnancy
- Oral hormones plus a barrier contraception or double barrier contraception
- Vasectomized sole partner

Two forms of contraception are required with any barrier method or oral hormones (i.e., condom plus diaphragm, condom or diaphragm plus spermicide, oral hormonal contraceptives plus spermicide or condom). If you do not engage in sexual activities that could result in pregnancy, you will still need to select a back-up method, in the case that you choose to while participating in this study. The Study Team will explain these methods to you and will help you decide which might be best for you, and they can suggest to you where you can get more information and advice.

Study Termination
This is a time-limited study. You may require further treatment after you complete the study. This may be because the study treatment did not help you, or it was helpful but did not fully resolve your symptoms, or because the process of trauma therapy itself can worsen symptoms in the course of addressing trauma. This may mean more time and treatment are needed for resolution.

You may feel increased feelings of distress at the termination of the study. Your therapists will support you by helping you find another therapist or by providing appropriate resources for further follow-up.

New Findings
If any new information becomes available about MDMA while you are in this study, the Study Team will tell you about it as soon as possible.

Possible Benefits
Your symptoms of PTSD may improve, stay the same, or get worse during or after taking part in this study. There is no guarantee that you will benefit from taking part in this research study. Information obtained from this study may help doctors and researchers to improve treatment for PTSD and other mental health conditions in the future.

Alternatives
One alternative to being in this study is to decide not to take part. You may decide to try other treatments for PTSD. In the U.S., the FDA approved paroxetine (Paxil) and sertraline (Zoloft) for PTSD Evidence-based psychotherapies for PTSD include Cognitive Processing Therapy (CPT), Cognitive Behavioral Therapy (CBT), Prolonged Exposure (PE), and Eye Movement Desensitization and Reprocessing (EMDR). If you are currently taking medication or doing therapy, you could continue those. There may also be other investigational therapies available. The Study Team can discuss alternatives with you. If you decide not to participate in this research, the Study Team will offer you referrals for other care which may be available to you.

Your Rights as a Study Participant

Confidentiality
All information collected will be treated and handled as confidentially as possible. To ensure confidentiality, your information will be stored in secure electronic systems at the participating sites until securely transferred to a remote storage facility. These records will be stored after the end of the study in keeping with the regulatory and ethics board regulations governing your study site. Absolute confidentiality and security cannot be guaranteed, but every effort will be made to maintain your confidentiality. The information collected about you usually will not directly identify you (for example, by name, address, or social security number). Instead, your initials and a code number will be used for your information.

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

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

- The sponsor, MAPS, and the people they hire.
- The FDA, Health Canada, the Israeli Ministry of Health, and similar agencies in other countries.
- The Institutional Review Board (IRB) that reviewed this research. The IRB is a group of scientists and non-scientists who review the ethics of research. The goal of the IRB is to protect the rights and welfare of study participants.<<CF-Main SMO Company 1>><<CF-Main Affiliated IN Language 1>>
- Members of the study team.

These people may look at your records to make sure the study has been done the right way. They also want to make sure that your health information has been collected the right way, or for other reasons that are allowed under the law.

You have the right to review any medical records related to this study, including lab results and cardiac testing. At the end of the study, your therapist team or study doctor will provide a summary of study procedures, side effects or other health issues on study, and medications taken. After the study is complete, you may request a summary of your data.

The results of this research study may be presented in meetings, presentations, or in publications, where your identity will not be disclosed. To help make scientific knowledge accessible, the data collected in this study will be shared with other researchers.

Audiovisual recordings
By signing this document, you are agreeing to audio and video recording of your study visits and online evaluations. The purpose for recording study visits and online evaluations is:

- To maintain accurate records of the study visits and online evaluations
- To verify that the therapy, assessments, and evaluations are carried out properly, according to the protocol
- To conduct further research on MDMA and MDMA-assisted therapy

For the above purposes, authorized researchers and therapists may view these recordings. Researchers and therapists are selected by the sponsor and agree to protect the confidentiality of the recordings and all identifying information.

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

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

These recordings will be stored in remote data storage centers. No personally identifying information will be used to label the audiovisual recordings. A copy will be transferred to the sponsor for secure electronic storage on the web to allow for viewing purposes described above. Electronic systems used will include measures to protect confidentiality of your identity and protection of this audiovisual data. The sponsor takes data security seriously and works to consistently maintain and improve the security of its systems. Total security cannot be guaranteed.

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

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

After the study is complete at all locations, you may request access to view the video recordings from your study visits. You may contact the study site with any questions about video recording, or to request access to your records.

Payment for Study Participation
In order to remove some financial barriers to participation, you may be reimbursed for direct costs of participation (travel or dependent care costs, for example) at certain study visits as they are completed. If you do not complete a visit, you may not be reimbursed for costs

associated with it. As a nonprofit organization, MAPS has limited funds to reimburse participants for financial assistance, and you have the option to decline funds if they are not needed. Options for reimbursement will be offered as outlined below:

- Visits 1-4 (Preparatory Sessions through Study Drug Session 1): $375
- Visits 5-8 (Integrative 1.1 through Study Drug Session 2): $375
- Visits 9-12 (Integrative 2.1 through Study Drug Session 3): $375
- Visits 13-16 (Integrative Session 3.1 through Study Termination): $375

OR You will not receive any payment for participating in this research study.

<<CF-Main Payment for Part. Paragraph>>

Cost
The sponsor of this study, MAPS, will cover the costs that are directly related to the research and have been outlined in this document. This includes the costs for screening to see if you are eligible for the study, including medical and psychological testing. This also includes the Study Drug Sessions, including study drug, therapy, and psychological testing. You, your private medical insurance (if any), or public health insurance plan will not be charged for any procedures done solely for the purpose of the study. You or your insurance company will remain responsible for ongoing treatment not included in the study. You may talk to the study staff and your insurance company about what is covered.

If there are any costs associated with COVID-19 screening or protective equipment required by your therapy pair or study doctor, the sponsor will pay for these costs.

Treatment and Compensation for Study-Related Injury
If you get sick or injured during this study, call the study doctor immediately. Some study-related injuries or sickness can be treated by the study doctor. If the study doctor cannot treat a study-related emergency, they will arrange to transport you to the nearest hospital.

Treatment of a study-related injuries, sickness, or emergency would first be billed to your health insurance provider, if you have health insurance. If your health insurance plan does not cover clinical trial-related claims that occurred during the course of the study, or you do not have health insurance, then the sponsor will cover any treatment costs directly related to the study. To cover those costs, the sponsor carries third-party insurance

The sponsor has no plans to cover the costs of ongoing treatment unrelated to the study due to pre-existing conditions, or the cost of your time spent getting treatment for pre-existing conditions before receiving treatment in the study.

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

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 which you are otherwise entitled if you decide not to take part.

In addition, you may withdraw from (leave, stop being in) the study at any time. There will be no penalty or loss of benefits to which you are otherwise entitled 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 if you would be willing to complete final assessments.

If you decide to stop being in the study or are removed from the study, the data collected about you up to that point will remain part of the study and will not be removed from the study database. Your video recordings will be retained.

Withdrawal
Your study team, the Sponsor, or the government authority in your country (the FDA) have 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 serious reaction from the study drugs
- If you need a treatment not allowed in this study, such as restarting a psychiatric medication
- If you do not keep appointments or follow study procedures
- If you do not take the study drug as instructed
- If you become pregnant
- If the study is canceled by the FDA, Health Canada, Israeli Ministry of Health, IRB, or the Sponsor.

The Sponsor, the FDA, Health Canada, Israeli Ministry of Health, or the IRB may decide to stop the study at any time. If the study is stopped, the data collected about you up to that point will remain part of the study and will not be removed from the study database.

Contact for Questions
If you have questions, concerns, or complaints, or think this research has hurt you or made you sick, talk to the research team at the phone number(s) listed above on the first page, or contact the sponsor's compliance hotline at 833-254-1732.

This research is being overseen by an Institutional Review Board ("IRB"). An IRB is a group of people who perform independent review of research studies. You may talk to them at 1-855-818-2289 or Researchquestions@wcgirb.com if:

- You have questions, concerns, or complaints that are not being answered by the research team.

- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

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

PARTICIPANT'S STATEMENT OF CONSENT

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 otherwise entitled at this site. The staff and/or the Sponsor may stop my participation in this study at any time without my consent if they decide it is in my best interest or if I do not follow their instructions.

I agree to have my screening assessment audio and video-recorded during this study.

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

By signing this consent form, I have not waived any of the legal rights which I otherwise would have as a participant in a research study. I have been told that I will be given a signed and dated copy of this consent form<<CF-Main California Bill of Rights>>.

Signature of Participant	Date
Printed Name of Participant	

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

Signature of Person Obtaining Consent	Date

Printed Name of Person Obtaining Consent

HIPAA Authorization

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

In working with the sponsor, the study doctor 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, and audiovisual recordings. 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 such as the U.S. FDA and the Institutional Review Board (IRB) 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 Institutional Review Board (IRB) <<CF-Main SMO Company 2>><<CF-Main Affiliated IN Language 2>>
- The U.S. Food and Drug Administration (FDA).
- Other regulatory agencies.

FOR CA SITES ONLY: [Your records may also be inspected by the Research Advisory Panel of California (RAPC) or by State and Federal regulatory agencies.] <<CF-Main User Defined #3>>

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. We may also share the data collected in this study with other researchers. Any data or recordings shared that could contain identifiable information will require the researchers to maintain a data use agreement with confidentiality parameters for your data.

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.

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.

If you do not withdraw this authorization, it will remain in effect.

If the research site is located in California, Delaware, Illinois, Indiana, Washington, or Wisconsin this authorization will expire on December 31, 2070.

There is no expiration of this authorization except for research conducted in the states listed above.

You have the right to review and copy your health information. However, your access to this information may be delayed until the study is complete.

You do not have to sign this form. If you do not sign this authorization, you cannot participate in this research study. If you withdraw this authorization in the future, you will no longer be able to participate in this study. Your decision to withdraw your authorization or not to participate will not involve any penalty or loss of access to treatment or other benefits to which you are otherwise entitled.

For IL Sites Only:[You have the right to review any mental health information collected about you and shared with others.] <<CF-Main User Defined #4>>

Authorization
HIPAA Authorization: I authorize the release of my medical records and personal health information related to this study to the IRB, the FDA, other regulatory agencies as described above, and ([for CA sites only] The Research Advisory Panel of California (RAPC). However, as the sponsor (and its representatives) is not considered a covered entity, I waive my right to the HIPAA privacy rule and my health information may be shared between their representatives. The study site where you will complete study visits is/is not a covered entity. I have been told that I will receive a signed and dated copy of this authorization for my records.

_____ _____
Signature of Participant Date

_____
Printed Name of Participant

_____ _____
Signature of Person Obtaining Authorization Date

Printed Name of Person Obtaining Authorization