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Additional Information

Facilities

Introductory, MDMA-assisted and integrative psychotherapy [redacted] rooms, including a private bathroom and kitchen and include a refrigerator and microwave. The main room is comfortably furnished and private. There is artwork on the walls, and stained glass in some windows. Subjects may sit or lie on a couch. The offices are furnished with beds that allow for two people to remain overnight. The offices are lower than ground level. They can be heated, and fans are used for cooling. The offices have an enclosed courtyard. The office will contain equipment for assessing blood pressure, pulse, and body temperature and an automatic external defibrillator. [redacted] One therapist can reach the offices within five to ten minutes of contact if necessary.

Abuse Liability

The Drug Enforcement Administration placed MDMA in Schedule 1, a category reserved for drugs with high abuse potential and no known medical use. MDMA was scheduled shortly after people started using it in non-medical settings, as nightclubs or at parties (Beck and Rosenbaum 1994). Despite its classification as a Schedule 1 drug, self-administration studies in nonhuman animals and findings concerning prevalence of ecstasy abuse and dependence do not suggest that its abuse liability is high. Rats, mice and monkeys will self-administer MDMA (Fantegrossi et al. 2004; Schenk et al. 2003; Trigo et al. 2006). However, monkeys will "pay" higher prices in lever presses for psychostimulants than they will for MDMA (Lile et al. 2005; Wee and Woolverton 2006). Studies assessing prevalence of problematic ecstasy use or dependence suggest that a small percentage of individuals, especially those with prior psychological difficulties, may develop ecstasy use or dependence (Huizink et al. 2006; Lieb et al. 2002), though studies of non-representative samples have reported higher rates of dependence (Cottler et al. 2001). Most regular ecstasy users report taking ecstasy no more often than once a week (von Sydow et al. 2002). Taken together, an examination of findings in humans and nonhuman animals suggests that MDMA possesses moderate abuse potential that is higher than that reported for "classic hallucinogens" like psilocybin, but lower than that reported for psychostimulants such as cocaine or methamphetamine.

Appendix A: Visit by Visit Description

Participants who consent to take part in the study will undergo the following sequence of events:

- *Randomized sessions*
- **Screening/Evaluation (Visit 3)**; A two to three hour long medical and psychiatric evaluation. A physician working with the investigators will perform medical history and physical examination and ECG. The independent assessor will diagnose psychiatric disorders with the SCID, and will perform a face to face interview and administer the ASIQ to assess suicide risk. The physician or principal investigator will draw blood for laboratory tests. The independent rater will administer the CAPS and the participant will complete the BDI. The independent rater will administer the RBANS and PASAT. If a participant meets study eligibility criteria after evaluation, he or she will be scheduled for an introductory psychotherapy session. The independent assessor will re-evaluate any participant who undergoes the screening and baseline evaluation prior to discontinuing psychiatric medication. During re-evaluation, the independent assessor will administer the CAPS and the participant will complete the PDS and BDI during a visit occurring after an interval of at least five times drug half-life.
- **Introductory Psychotherapy visits (Visits 4-6)**: Three 60 to 90 minute introductory psychotherapy sessions with both psychotherapist investigators. These sessions will help the therapists and participant to learn about each other and discuss the participant's goals, hopes and fears in relation to upcoming MDMA-assisted psychotherapy, and the events and procedures that will occur during MDMA-assisted psychotherapy. Introductory sessions will be recorded to audio and video, and participants will have an opportunity to review the recordings. On the third introductory session, participants will receive instructions and restrictions relating to food and drug consumption for the night before and morning of the MDMA-assisted session. Participants must be randomized to one of the two conditions (active placebo or experimental dose) prior to the first MDMA-assisted psychotherapy session.
- **MDMA-assisted Psychotherapy Session 1 (Visit 7):** First eight-hour long randomized (active placebo versus experimental dose) MDMA-assisted psychotherapy session. Participants arrive at approximately 9:00 AM to undergo urinary drug and pregnancy tests, with positive test results either delaying or rescheduling the session to withdrawal from the study. The investigators will administer a capsule containing either 25 or 125 mg MDMA at 10:00 AM, and participants will be encouraged to sit or lie down comfortably for the duration of the session. The investigators will measure blood pressure and pulse once prior to drug administration and every thirty minutes for the duration of the session, with more frequent measures taken if blood pressure or pulse exceed established cut-offs. The investigators will measure body temperature every 60 to 90 minutes with tympanic thermometer. The participant will complete the SUD every sixty to ninety minutes. One and a half to 2.5 hours later, if the therapists deem it appropriate and the participant agrees to it, a supplemental dose of 12.5 or 62.5 mg MDMA will be administered. The entire session will be recorded to audio and video and participants may receive a copy of the session recording upon request. The male and female therapist will remain with the participant for the duration of the session up until eight hours later (approximately 6:00 PM). A significant other may remain with the participant during the experimental session or at some time after it has ended. The significant other can remain overnight with the participant but does not have to do so. All participants will remain at the offices of Dr. Pacey overnight. A same-sex attendant versed in caring for people

undergoing difficult psychological experiences will remain with the participant during the overnight stay.

- **Integrative Psychotherapy On the Day After Experimental Session (Visit 8):** A ninety-minute long psychotherapy session with both psychotherapist-investigators always occurring on the morning of the day after MDMA-assisted psychotherapy. The participant will discuss his or her thoughts, feelings, memories or experiences that occurred during the experimental session and the participant and investigators will seek to integrate this material into everyday life. The session will be recorded to audio and video and participants may listen to or view recordings upon request. The participant and both therapist-investigators will complete a measure of beliefs concerning participant condition assignment prior to starting psychotherapy, and the participant will complete the ASIQ after completing psychotherapy.
- **Integrative Psychotherapy Sessions Between Experimental MDMA-assisted Session 1 and 2 (Visit 9-10, 10.x):** Two or more sixty to ninety minute psychotherapy sessions with both psychotherapist-investigators during which they and the participant continue to integrate material from MDMA-assisted psychotherapy sessions. The investigators and participant may schedule additional integrative sessions upon participant request and therapist-investigator mutual agreement. These sessions will be recorded to audio and video and participants may view session recordings upon request.
- **MDMA-Assisted Psychotherapy Session 2 (Visit 11):** The second eight-hour long session of MDMA-assisted psychotherapy with either active placebo or experimental dose MDMA with both therapist-investigators. Participants arrive at approximately 9:00 AM to undergo urinary drug and pregnancy tests, with positive test results either delaying or rescheduling the session to withdrawal from the study. The investigators will administer a capsule containing either 25 or 125 mg MDMA at 10:00 AM, and participants will be encouraged to sit or lie down comfortably for the duration of the session. The investigators will measure blood pressure and pulse once prior to drug administration and every thirty minutes for the duration of the session, with more frequent measures taken if blood pressure or pulse exceed established cut-offs. The investigators will measure body temperature every 60 to 90 minutes with a tympanic thermometer. The participant will complete the SUD every sixty to ninety minutes. One and a half to 2.5 hours later, if the therapist-investigators deem it appropriate and the participant agrees to it, a supplemental dose of 12.5 or 62.5 mg MDMA will be administered. The entire session will be recorded to audio and video and participants may receive a copy of their session recordings upon request. The male and female therapist will remain with the participant for the duration of the session up until eight hours later (approximately 6:00 PM). A significant other may remain with the participant, arriving sometime during the experimental session or after the experimental session is over. All participants will remain [redacted] Significant others may remain overnight with participants but do not have to do so.
- **Integrative Psychotherapy One Day after MDMA-assisted Psychotherapy 2 (Visit 12)**: A ninety-minute long psychotherapy session with both psychotherapist-investigators that will take place on the day after the second experimental session. The participant and investigators will discuss participant thoughts, feelings, memories or experiences from one or both experimental sessions, working to integrate this material into everyday life. The session will be recorded to audio and video. Participants may listen to or view recordings upon request. The participant and both therapist-investigators will complete a measure of beliefs concerning participant condition assignment prior to starting psychotherapy, and the participant will complete the ASIQ after completing psychotherapy.

- **Integrative Psychotherapy After MDMA-Assisted Session 2 (Visits 13-14, 14.x)**: At least two sixty to ninety minute psychotherapy sessions with both therapist-investigators occurring after the second MDMA-assisted psychotherapy session. The participant and both therapist-investigators will continue to work toward integrating experimental session material. Additional psychotherapy sessions may be scheduled at the request of the participant. These sessions will be recorded to audio and video, and participants can listen to or view recordings upon request.
- **MDMA-Assisted Psychotherapy Session 3 (Visit 15):** The third eight-hour long session of MDMA-assisted psychotherapy with either active placebo or experimental dose MDMA with both therapist-investigators. Participants arrive at approximately 9:00 AM to undergo urinary drug and pregnancy tests, with positive test results either delaying or rescheduling the session to withdrawal from the study. The investigators will administer a capsule containing either 25 or 125 mg MDMA at 10:00 AM, and participants will be encouraged to sit or lie down comfortably for the duration of the session. The investigators will measure blood pressure and pulse once prior to drug administration and every thirty minutes for the duration of the session, with more frequent measures taken if blood pressure or pulse exceed established cut-offs. The investigators will measure body temperature every 60 to 90 minutes with a tympanic thermometer. The participant will complete the SUD every sixty to ninety minutes. One and a half to 2.5 hours later, if the therapist-investigators deem it appropriate and the participant agrees to it, a supplemental dose of 12.5 or 62.5 mg MDMA will be administered. The entire session will be recorded to audio and video and participants may receive a copy of their session recordings upon request. The male and female therapist will remain with the participant for the duration of the session up until eight hours later (approximately 6:00 PM). A significant other may remain with the participant, arriving sometime during or after the experimental session. All participants will remain [redacted]. Significant others may remain overnight with participants but do not have to do so.
- **Integrative Psychotherapy One Day after MDMA-assisted Psychotherapy 3 (Visit 16)**: A ninety-minute long psychotherapy session with both psychotherapist-investigators that will take place on the day after the third experimental session. The participant and investigators will discuss participant thoughts, feelings, memories or experiences from one or both experimental sessions, working to integrate this material into everyday life. The session will be recorded to audio and video. Participants may listen to or view recordings upon request. The participant and both therapist-investigators will complete a measure of beliefs concerning participant condition assignment prior to starting psychotherapy, and the participant will complete the ASIQ after completing psychotherapy.
- **Integrative Psychotherapy After MDMA-Assisted Session 3 (Visits 17-18, 18.x)**: At least two sixty to ninety minute psychotherapy sessions with both therapist-investigators occurring after the third MDMA-assisted psychotherapy session. The participant and both therapist-investigators will continue to work toward integrating experimental session material. Additional psychotherapy sessions may be scheduled at the request of the participant. These sessions will be recorded to audio and video, and participants can listen to or view recordings upon request.
- **Evaluation Six weeks After Third MDMA-assisted Session (Visit 19)**: A ninety to 120 minute long (1.5-2 hour long) evaluation. The independent assessor will administer the CAPS, RBANS and PASAT, and the participant will complete the BDI and PDS.
- **Study Blind Broken for Individual Subject (Visit 19)**: A 30 to 60 minute long meeting with the therapist-investigators. The participant and both therapists will learn participant condition assignment. The independent rater will remain blind to participant condition

assignment. If the individual received active placebo MDMA, then he or she will receive consent materials for the open-label study segment, Stage 2. Any participant who received active placebo and does not consent to take part in Stage 2 will complete the RRPQ.

- *Open-label Sessions for Active Placebo Participants (Stage 2)*
- **Consent for stage 2 (Visit 20):** A 30 to 60 minute meeting with the investigator therapists for participants who learn they received active placebo. They will receive consent materials concerning the open-label study segment. They must give written informed consent to take part in this study segment. Visit 20 may occur on the same day as Visit 19.
- **Stage 2 Baseline Evaluation (Visit 21**): Baseline evaluation for stage 2 (active placebo participants only). CAPS, PDS and BDI scores from the evaluation six weeks after the third experimental session (Visit 19) will serve as baseline scores except in the case where thirty days have passed between those evaluations and the time when the participant entered Stage 2, in which case the independent assessor will perform and additional evaluation, administering the CAPS and BDI prior to entry into Stage 2.
- **Review and Introductory Psychotherapy (Visit 22)**: A sixty to ninety minute psychotherapy session with both therapist-investigators and the participant enrolled in Stage 2. The participant and therapist-investigators will re-acquaint themselves with each other, and the participant will review information about MDMA-assisted therapy and all three will discuss, review and possibly revise goals for MDMA-assisted psychotherapy. The session will be recorded to audio and video. Participants may listen to or view recordings upon request.
- **Open-label MDMA session 1 (Visit 23):** The first eight-hour long open-label session with a full dose of MDMA (125 mg), **applicable for participants in Stage 2 only.** This option is not applicable to participants enrolled in Stage 2. Participants will undergo urinary drug and pregnancy testing, and 125 mg MDMA will be administered at approximately 10:00 AM. Participants will be encouraged to sit or lie down comfortably for the duration of the session and the male and female therapist-investigators will remain with the participant throughout the session. The entire session will be recorded to audio and video, and participants will receive copies of their open-label session recordings. One and a half to 2.5 hours later, if the investigators believe it appropriate and the participant agrees to it, a second dose of 62.5 mg MDMA will be administered. Blood pressure and pulse will be assessed prior to drug administration and at 30-minute intervals for the duration of the session, with more frequent measures taken only if the established thresholds for normal blood pressure and pulse have not been exceeded. The investigators will measure body temperature every 60 to 90 minutes with a tympanic thermometer. The SUD will be administered every sixty to ninety minutes. A significant other may arrive during the experimental session or after the session is over. All participants will remain [redacted] Significant others may remain overnight with participants but do not have to do so.
- **Integrative Psychotherapy One Day after Open-Label MDMA Session 1** (Visit 24): A 90-minute psychotherapy session with both therapist-investigators on the morning of the day after the first open-label MDMA-assisted psychotherapy session. This session will employ similar procedures and serve a similar goal to integrative psychotherapy sessions after experimental MDMA-assisted therapy sessions. This session will be recorded to audio and video. Participants can listen to or view recordings upon request.
- **Integrative Psychotherapy Between Open-Label Session 1 and 2 (Visits 25-26, 26.x)**. At least two 60 to 90-minute psychotherapy sessions with the two therapist-investigators scheduled to occur in the time interval between the first and second Stage 2 open-label

MDMA-assisted session. The therapists and investigator will continue working on integrating MDMA session material into everyday life. These sessions will be recorded to audio and video, and participants can review session recordings upon request. Participants will complete the ASIQ after completing psychotherapy.

- **Open-label MDMA session 2 (Visit 28):** The second eight-hour long open-label session with a full dose of MDMA (125 mg), **applicable for participants in stage 2 only.** Participants not enrolled in Stage 2 may decline to take part in this session. Participants will undergo urinary drug and pregnancy testing, and MDMA will be administered at approximately 10:00 AM. Participants will be encouraged to sit or lie down comfortably for the duration of the session and the male and female therapist-investigators will remain with the participant throughout the session. The entire session will be recorded to audio and video, and participants may receive copies of their open-label sessions upon request. One and a half to 2.5 hours later, if the investigators believe it appropriate and the participant agrees to it, a second dose of MDMA will be administered. Blood pressure and pulse will be assessed prior to drug administration and at 30-minute intervals for the duration of the session, with more frequent measures taken only if the established thresholds for normal blood pressure and pulse have not been exceeded. The investigators will measure body temperature every 60 to 90 minutes with a tympanic thermometer. The SUD will be administered every sixty to ninety minutes. A significant other may arrive during or after the experimental session to remain with the participant. All participants will remain [redacted] Significant others may remain overnight with participants but do not have to do so.
- **Integrative Psychotherapy One Day after Open-Label MDMA Session 2** (Visit 29): A 90-minute psychotherapy session with both therapist-investigators on the morning of the day after the second open-label MDMA-assisted psychotherapy session. This session will employ similar procedures and serve a similar goal to that of integrative psychotherapy sessions after experimental MDMA-assisted psychotherapy. The session will be recorded to audio and video, and participants can listen to or view session recordings upon request. Participants will complete the ASIQ after completing psychotherapy.
- **Integrative Psychotherapy Between Open-Label MDMA 2 and 3 (Visits 30-31, 31.x).** At least two 60 to 90-minute psychotherapy sessions with the two therapist-investigators scheduled to occur in the time interval between the second and third Stage 2 open-label MDMA-assisted session. These sessions will be recorded to audio and video, and participants can listen to or view session recordings upon request. These will be the final integrative sessions for participants not enrolled in stage 2. The therapists and investigator will continue working on integrating MDMA session material into everyday life.
- **Open-label MDMA session 3 (Visit 32):** The third eight-hour long open-label session with a full dose of MDMA (125 mg) for participants enrolled in Stag 2. Participants will undergo urinary drug and pregnancy testing, and MDMA will be administered at approximately 10:00 AM. Participants will be encouraged to sit or lie down comfortably for the duration of the session and the male and female therapist-investigators will remain with the participant throughout the session. The entire session will be recorded to audio and video, and participants will receive copies of open-label session recordings. One and a half to 2.5 hours later, if the investigators believe it appropriate and the participant agrees to it, a second dose of MDMA will be administered. Blood pressure and pulse will be assessed prior to drug administration and at 30-minute intervals for the duration of the session, with more frequent measures taken only if the established thresholds for normal blood pressure and pulse have not been exceeded. The investigators will measure body

temperature every 60 to 90 minutes with a tympanic thermometer. The SUD will be administered every sixty to ninety minutes. A significant other may arrive sometime during the experimental session or after it has ended or near the end of the session to remain with the participant. All participants will [redacted]. Significant others may remain overnight with participants but do not have to do so.

- **Integrative Psychotherapy One Day after Open-Label MDMA Session 3** (Visit 33): A 90-minute psychotherapy session with both therapist-investigators on the morning of the day after the third open-label MDMA-assisted psychotherapy session. This session will employ similar procedures and serve a similar goal to that of integrative psychotherapy sessions after experimental MDMA-assisted psychotherapy. This session will be recorded to audio and video. Participants can listen to or view their recordings upon request. Participants will complete the ASIQ after completing psychotherapy.
- **Integrative Psychotherapy After Open-Label Session 3 (Visits 34-35, 35.x)**. At least two 60 to 90-minute psychotherapy sessions with the two therapist-investigators scheduled to occur in the time interval after the third open-label session. The therapists and investigator will continue working on integrating MDMA session material into everyday life. These sessions will be recorded to audio and video, and participants can listen to or view session recordings upon request.
- **Evaluation Six weeks after Third Open-Label Session for Participants Enrolled in Stage 2 (Visit 36):** A ninety to 120-minute visit with the independent assessor and the therapist-investigators for participants enrolled in Stage 2 occurring six weeks after the third open-label session. The independent assessor will administer the CAPS and the participant will complete the BDI and PDS.
- **Study Termination for Stage 2 Participants (Visit 37):** After completing CAPS, PDS and BDI, the participant will meet for approximately a half hour (0.5 hours) with the therapist-investigators. The participant will complete the RRPQ.

Appendix B: Case Report Forms

These are sample case report form drafts for the study "A Randomized, Active Placebo-controlled Pilot Study of 3,4- methylenedioxymethamphetamine (MDMA)-assisted Psychotherapy in 12 Subjects with Posttraumatic Stress Disorder (PTSD)-Canada."

The series of case report forms represents the series of events from screening up through the first experimental session of MDMA-assisted psychotherapy. The series does not include CRFs for subsequent experimental sessions or open-label sessions as the information contained is identical or nearly identical in content and format.

CONTAINS

SCREENING AND BASELINE EVALUATION
INTRODUCTORY PSYCHOTHERAPY
FIRST EXPERIMENTAL SESSION
INTEGRATIVE PSYCHOTHERAPY
FINAL EVALUATION
MEDICATION AND ADVERSE EVENTS

Participant Demographics

Date signed consent _____-_____-_____ Date of Enrollment _____ - _____ - _____
dd mmm yy dd mmm yy

Date of Birth: _____-_____-_____
dd mmm yy

Sex: ☐ Male ☐ Female

Ethnic Origin: ☐ Asian
☐ African American
☐ Caucasian
☐ Latino/a / Hispanic
☐ Middle Eastern
☐ First Nation
☐ Native Hawaiian/Other Pacific Islander
☐ Biracial, Specify _____
☐ Other, Specify _____

Physical Examination

Height	Height	Body Temperature
_____ ☐ In ☐ cm	_____ ☐ lb ☐ kg	_____ ☐ F ☐ C

Blood Pressure (mm Hg) _____/____ Heart Rate (BPM) _____

Urine Pregnancy Test
☐ Positive
☐ Negative
☐ Not Applicable (Subject is Male, Non-child bearing potential)

Urine Drug Screen
☐ Positive
☐ Negative

ECG

☐ Normal
☐ Abnormal*, NOT clinically significant
☐ Abnormal*, clinically significant

If "Abnormal," please describe in the space provided below

_____

_____

Study Entry Criteria

Subject screened under protocol version: ☐ Original ☐ Amendment # _____

Did subject meet all study entry criteria specified in the protocol ☐ Yes ☐No

If No, please mark nature of deviation in the chart below and on the following pages

Inclusion not Met / Exclusions Met	**Criterion number** (as listed in protocol)	**Protocol deviation entry granted?**	**If yes, date granted (dd-mmm-yy**
☐ Inclusion not met ☐ Exclusion met	__________	☐ Yes ☐ No	__ __ - __ __ __ - __ __
☐ Inclusion not met ☐ Exclusion met	__________	☐ Yes ☐ No	__ __ - __ __ __ - __ __
☐ Inclusion not met ☐ Exclusion met	__________	☐ Yes ☐ No	__ __ - __ __ __ - __ __
☐ Inclusion not met ☐ Exclusion met	__________	☐ Yes ☐ No	__ __ - __ __ __ - __ __
☐ Inclusion not met ☐ Exclusion met	__________	☐ Yes ☐ No	__ __ - __ __ __ - __ __
☐ Inclusion not met ☐ Exclusion met	__________	☐ Yes ☐ No	__ __ - __ __ __ - __ __

Non Psychiatric Medical History

Does the subject have any significant Non Psychiatric past diagnosis (including allergies, abnormalities, injuries, sexually transmitted diseases, major surgeries requiring in-patient hospitalization) or current diagnosis/condition?

☐ YES ☐NO

If Yes, specify below.

NOTE: If the Diagnosis date is not known write UNK, try to provide at least a year.
Newly diagnosed or worsening conditions or diseases after this visit are considered adverse events.

Diag #	Diagnosis	Start date mm-dd-yyyy	Ongoing?	Stop Date mm-dd-yyyy
			☐Yes ☐No	
			☐Yes ☐No	
			☐Yes ☐No	
			☐Yes ☐No	
			☐Yes ☐No	
			☐Yes ☐No	
			☐Yes ☐No	
			☐Yes ☐No	
			☐Yes ☐No	
			☐Yes ☐No	
			☐Yes ☐No	
			☐Yes ☐No	
			☐Yes ☐No	
			☐Yes ☐No	
			☐Yes ☐No	
			☐Yes ☐No	

Baseline Clinical Labs Visit #1 **Date of Result** _____-_____-_____

If any clinically significant lab results, please record in Adverse Event CRF *dd mmm yy*

Comprehensive Metabolic Profile	Result	Unit	Clinically Significant?
AG ratio			☐ Yes ☐ No
Albumin			☐ Yes ☐ No
Alkaline Phosphatase			☐ Yes ☐ No
AST (SGOT)			☐ Yes ☐ No
ALT (SGPT)			☐ Yes ☐ No
Bilirubin Total			☐ Yes ☐ No
BUN			☐ Yes ☐ No
Bun/Creatinine			☐ Yes ☐ No
Calcium			☐ Yes ☐ No
Chloride			☐ Yes ☐ No
Creatinine			☐ Yes ☐ No
Globulin			☐ Yes ☐ No
Glucose			☐ Yes ☐ No
Potassium			☐ Yes ☐ No
Protein Total			☐ Yes ☐ No
Sodium			☐ Yes ☐ No

Urinalysis	Result		Clinically significant?
Specific gravity			☐ Yes ☐ No
PH			☐ Yes ☐ No
Protein			☐ Yes ☐ No
Glucose			☐ Yes ☐ No
Ketones			☐ Yes ☐ No
Occult blood			☐ Yes ☐ No
Leukocyte Esterase			☐ Yes ☐ No
Nitrite			☐ Yes ☐ No
Bilirubin			☐ Yes ☐ No
Urobilinogen			☐ Yes ☐ No

Thyroid Panel with TSH	Result		CS= Clinically significant
Thyroxine			☐ Yes ☐ No
Thyroid hormone binding ratio			☐ Yes ☐ No
Thyroid Stimulating Hormone			☐ Yes ☐ No
Free Thyroxine Index			☐ Yes ☐ No

Past Psychiatric Medical History

Record any Psychiatric Diagnosis made prior to visit 1. If Diagnosis date is not known write UNK, try to provide at least a year.

Diagnosis	**Diagnosis Start date** mm-dd-yyyy	**Ongoing?**	**Stop Date** mm-dd-yyyy
		☐Yes ☐ No	
		☐Yes ☐ No	
		☐Yes ☐ No	
		☐Yes ☐ No	
		☐Yes ☐ No	

Type and Duration of Previous Therapy

Record any non drug therapy prior to visit 1 using the codes provided to the side of this chart. If date is not known write UNK, try to provide at least a year. Record any drug therapy on the Psychotropic Medication page.

Type	Other Therapy Type	# Sessions	Per	Start Date mm-dd-yyyy	Ongoing ?	Stop Date mm-dd-yyyy
		_____	☐ Week ☐ Month ☐ Total		☐ Yes ☐ No	
		_____	☐ Week ☐ Month ☐ Total		☐ Yes ☐ No	
		_____	☐ Week ☐ Month ☐ Total		☐ Yes ☐ No	
		_____	☐ Week ☐ Month ☐ Total		☐ Yes ☐ No	
		_____	☐ Week ☐ Month ☐ Total		☐ Yes ☐ No	
		_____	☐ Week ☐ Month ☐ Total		☐ Yes ☐ No	

Type of Psychotherapy Code
1 = CBT (Cognitive Behavioral Therapy) **2** = Behavioral **3** = Prolonged Exposure
4 = EMDR **5** = IPT (Interpersonal Therapy) **6** = Psychodynamic
7 = Holotropic Breathwork **8** = Group Psychotherapy **9** = Other

History of Suicide Attempts or Thoughts

Suicidal Tendencies: Check the box that in your opinion most represents the frequency which the subject has thoughts of death or suicide, as determined via psychiatric interview.

☐ None at all
☐ Slight: occasional thoughts of death without suicidal thoughts
☐ Mild: frequent thoughts of being better off dead/occasional thoughts of suicide (without a plan)
☐ Moderate: often thinks of suicide or has thought of specific method
☐ Severe: frequent suicidal thoughts, mentally rehearsed plan, has made a suicide gesture
☐ Extreme: made recent preparations for serious suicide attempt
☐ **Very**

Adult Suicidal Ideation Scale at Screening

Score at Screening: _____

Past Use of Ecstasy

Has the subject ever used "Ecstasy"? ☐ YES ☐NO

If Yes, # of Occasions _____

If **Yes**, when

☐Within the last six months
☐Seven to 11 months ago
☐12 to 24 months ago
☐25 to 36 months ago
☐37 to 48 months ago
☐49 to 60 months ago
☐61 months to 120 months
☐Over 120 months ago.

Past Substance Use

Previous Alcohol Abuse/dependence ☐ yes ☐ no # of prior treatments_____

In the last six months ☐ yes ☐ no

Previous Drug Abuse/dependence ☐ ***yes*** ☐ ***no # of prior treatments_____***

In the last six months ☐ ***yes*** ☐ ***no***

CAPS Scoring – Baseline PTSD Diagnosis Visit #3 **Date of Evaluation** _____-_____-____
mmm dd yy

Criterion A met (traumatic event)	Specify	Criterion met? ☐ YES ☐ NO	**Frequency**	**Intensity**
B (re-experiencing) sx (≥ 1)?	Score	Criterion met? ☐ YES ☐ NO		
C (Avoidance) (≥ 3)?	Score	Criterion met? ☐ YES ☐ NO		
D (Hyperarousal) (≥ 2)?	Score	Criterion met? ☐ YES ☐ NO		
E (duration ≥ 1 month)?	Duration in Months	Criterion met? ☐ YES ☐ NO		
F(Distress/impairment)		Criterion met? ☐ YES ☐ NO		
CURRENT PTSD (Criteria A-F)		Criterion met? ☐ YES ☐ NO		
PTSD Global	Score			

☐ **Check this box if assessment occurred after screening and appropriate drug washout**

Associated Features

#25	#26	#27	#28	#29	#30

PDS and BDI Scoring– Baseline Visit #3 **Date of Evaluation** _____-_____-____
mmm dd yy

Posttraumatic Stress Diagnostic Scale (PDS) Stage 3 Outcome #1

PTSD Diagnosis	
Symptom Severity Score	
Symptom Severity Rating	
Level of Impairment of Functioning	

Beck Depression Inventory (BDI)

_____ BDI score

☐ Check this box if assessment occurred after screening and appropriate drug washout

Psychiatric History: SCID-Baseline diagnoses Visit #1 **Date of Evaluation** _____-_____-____
dd mmm yy

DSM Diagnosis	Yes	No
PTSD		
Unipolar Depression		
Panic Disorder		
Generalized Anxiety Disorder		
Bipolar Affective Disorder-1		
Bipolar Affective Disorder-II		
Dissociative Identity Disorder		
Psychosis		
Eating Disorder		
if Yes Active Purging?		
Borderline Personality Disorder		
Substance Abuse or dependence (60 days)		
Other DSM IV diagnosis-1		
Other DSM IV diagnosis-2		

General Well Being -Non-Experimental Sessions- Baseline

	Visit Date	**Subject Demeanor and State of Mind** enter code	**Subject currently** enter code
Visit #4			
Visit #5			
Visit #6			

1= Very stable and calm
2= Stable and calm
3= Slightly stable and calm
4= Slightly distressed
5= Distressed
6= Very distressed

A= Does not face risk of significant deterioration.
B= Probably faces risk of significant deterioration.
C= Faces risk of significant deterioration.

Experimental Session # 1 Visit #7

Review of Inclusion and Exclusion Criteria

Has the subject refrained from consuming prohibited food or beverages? ☐**Yes** ☐**No**

Have all meds finished tapering? ☐**Yes** ☐**No** ☐**NA**

Urine Pregnancy Test
☐ Positive
☐ Negative
☐ Not Applicable (Subject is Male, Non-child bearing potential)

Urine Drug Screen
☐ Positive
☐ Negative

Does subject continue to meet **All Inclusion** and **No Exclusion Criteria**? ☐**Yes** ☐**No**

If No Specify_____

Dosing

Date _____-_____-_____
dd mmm yyyy

Record time initial dose MDMA administered _____

Record Bottle number of active placebo/ experimental MDMA _____

Second Dose of active placebo/experimental dose MDMA Administered?

☐**Yes** ☐**No**

If yes, Record time second dose was administered _____

Record Bottle number of MDMA _____

Vital Signs -Experimental Session #1 Visit #7

Mark point where supplemental dose given. Make no mark if supplemental dose not given.

Monitoring: Blood Pressure and Pulse

Postdrug (h.min)	Time	SBP	DBP	Pulse
15 min predrug				
5 min predrug				
30 min postdrug				
1 hour post-drug				
1 h 30 min postdrug				
2 h postdrug				
2 h 30 min postdrug				
3 h postdurg				
3 h 30 min postdrug				
4 h postdrug				
4 h 30 min postdrug				
5 h postdrug				
5 h 30 min postdrug				
6 h postdrug				
6 h 30 min postdrug				
7 h postdrug				
7 h 30 min postdrug				
8 h postdrug				

Temperature

Postdrug (h.min)	Time	BT ☐F ☐ C
15 min predrug		
1 hour post-drug		
2 hours post-drug		
3 hrs post-drug		
4 hrs post-drug		
5 hrs post-drug		
6 hrs post-drug		

Record any additional time points here:

SUDS -Experimental Session #1 Visit #7

Postdrug (h.min)	**Time**	**SUDS**						
15 min predrug		1	2	3	4	5	6	7
5 min predrug		1	2	3	4	5	6	7
1 h postdrug		1	2	3	4	5	6	7
2 h postdrug		1	2	3	4	5	6	7
3 h postdrug		1	2	3	4	5	6	7
4 h 30 min postdrug		1	2	3	4	5	6	7
6 h postdrug		1	2	3	4	5	6	7
7 h postdrug		1	2	3	4	5	6	7
8 h postdrug		1	2	3	4	5	6	7

Record any additional time points here:

		1	2	3	4	5	6	7
		1	2	3	4	5	6	7
		1	2	3	4	5	6	7
		1	2	3	4	5	6	7

Integrative Psychotherapy After Experimental Session #1 (Visit 8)

Subject Belief of Condition Assignment Visit #8

Indicate what condition the subject believes they were assigned

- ☐ Low dose MDMA
- ☐ Experimental Dose MDMA

Indicate the subject's certainty about this belief of condition assignment

- ☐ Not at all certain
- ☐ Somewhat certain
- ☐ Certain
- ☐ Very certain

Adult Suicidal Ideation Scale After Experimental Session 1

Please administer the ASIQ after completion of integrative psychotherapy during Visit 8. Record the total score below.

Score: _____

Spontaneously Reported Side Effects Post Experimental Session #1 Visit #7-9

Please record the maximum intensity of any spontaneously reported effects for 7 days after drug administration. Report Duration for the first 24 hours.

Visit/Day	Visit 7 Day 0	Visit 7 Day 0	Visit 8 Day 1	Phone Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
	Duration in hours	Intensity	Intensity	Intensity	Intensity	Intensity	Intensity	Intensity	Intensity	Intensity
Report Max Intensity for the 24 hour period 0= None Reported 1= Mild 2= Moderate 3= Severe	Report Duration to the nearest ½ hour for the first 24 hours only									
Check None if no symptoms are reported for the 24 hour period		☐ None	☐ None	☐ None	☐ None	☐ None	☐ None	☐ None	☐ None	☐ None
Anxiety										
Difficulty Concentrating										
Dizziness										
Drowsiness										
Dry mouth										
Fatigue										
Headache										
Heavy legs										
Impaired gait/balance										
Increased irritability										
Increased private worries										
Insomnia										
Jaw clenching, tight jaw										
Lack of appetite										
Low mood										
Nausea										
Need more sleep										
Nystagmus										
Parasthesias										
Perspiration										
Restlessness										
Sensitivity to cold										
Thirst										
Weakness										

General Well Being Visit #8-10

Complete at Visit 8; Since the Experimental Session at Visit 7 the subject has:

☐ worsened ☐ remained pretty much the same ☐ improved

	Date	**Subject Demeanor and State of Mind** enter code	**Subject currently** enter code
Visit # 8			
Phone Day 1			
Phone Day 2			
Phone Day 3			
Phone Day 4			
Phone Day 5			
Phone Day 6			
Phone Day 7			
Visit #9			
Visit #10			

1= Very stable and calm
2= Stable and calm
3= Slightly stable and calm
4= Slightly distressed
5= Distressed
6= Very distressed

A= Does not face risk of significant deterioration.
B= Probably faces risk of significant deterioration.
C= Faces risk of significant deterioration.

Additional Non-Drug Psychotherapy

☐ Check this box if the participant did not schedule any additional non-drug psychotherapy sessions in the period between Visit 8 and Visit 10. If this box is checked, then draw a diagonal line through the page. If any additional non-drug psychotherapy visits were scheduled, complete general well-being ratings for all additional visits and draw diagonal lines through any empty rows. Label each additional non-drug psychotherapy session with a fraction after 10, using consecutive numbers for each session (as 10.1, 10.2, etc).

Number of additional Visits = _____

General Well Being

	Date	**Subject Demeanor and State of Mind** enter code	**Subject currently** enter code
Visit 10.__			
Visit 10.__			
Visit 10.__			
Visit 10.__			
Visit 10.__			
Visit 10.__			
		1= Very stable and calm **2**= Stable and calm **3**= Slightly stable and calm **4**= Slightly distressed **5**= Distressed **6**= Very distressed	**A**= Does not face risk of significant deterioration. **B**= Probably faces risk of significant deterioration. **C**= Faces risk of significant deterioration.

Final Evaluation (Visit 19)

CAPS Scoring – PTSD Diagnosis Visit #19

Date of Evaluation _____-_____-_____
dd mmm yy

Criterion A met (traumatic event)	Specify	Criterion met? ☐ YES ☐ NO	**Frequency**	**Intensity**
B (re-experiencing) sx (≥ 1)?	Score	Criterion met? ☐ YES ☐ NO		
C (Avoidance) (≥ 3)?	Score	Criterion met? ☐ YES ☐ NO		
D (Hyperarousal) (≥ 2)?	Score	Criterion met? ☐ YES ☐ NO		
E (duration ≥ 1 month)?	Duration in Months	Criterion met? ☐ YES ☐ NO		
F(Distress/impairment)		Criterion met? ☐ YES ☐ NO		
CURRENT PTSD (Criteria A-F)		Criterion met? ☐ YES ☐ NO		
PTSD Global	Score			

Associated Features

#25	#26	#27	#28	#29	#30

Final Evaluation (Visit 19)

PDS and BDI **Date of Evaluation** _____-_____-____
dd mmm yy

Posttraumatic Stress Diagnostic Scale (PDS)

PTSD Diagnosis	
Symptom Severity Score	
Symptom Severity Rating	
Level of Impairment of Functioning	

Beck Depression Inventory (BDI) Visit #15

_____ BDI score

RBANS- Evaluation Visit #19 **Date of Evaluation** _____-_____-_____
dd mmm yy

Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)

RBANS	Index Score	%ile
Immediate Memory		
Visuospatial/Constructional		
Language		
Attention		
Delayed Memory		
Total Scale		

Paced Auditory Serial Addition Task (PASAT) – Baseline Visit #4

PASAT	Raw	%ile
1		
2		
3		
4		
Total		

General Well Being Visit # ____ (16, 26, 35)

	Visit Date	**Subject Demeanor and State of Mind** enter code	**Subject currently** enter code
Visit # 19			

1= Very stable and calm
2= Stable and calm
3= Slightly stable and calm
4= Slightly distressed
5= Distressed
6= Very distressed

A= Does not face risk of significant deterioration.
B= Probably faces risk of significant deterioration.
C= Faces risk of significant deterioration.

Please check only one ☐ Visit 20 (End Randomized) ☐ Visit 37 (End Stage 2))

Reactions to Research Participation Questionnaire (RRPQ)

Please write in the numbers corresponding to the three top-ranked reasons for participating (the numbers to the left of each reason on the form. Write the number "1", "2" or "3") for each reason.

_____ 1. I was curious	_____ 4. I don't know	_____ 7. For the money
_____ 2. To help others	_____ 5. Thought it might improve my access to health care	_____ 8. I didn't want to say no
_____ 3. To help myself	_____ 6. Felt I had to	_____ 9. Other: _____

Please write in the scale scores the RRPQ below.

1. Participation 1 _____
2. Personal Benefits 2 _____
3. Emotional Reaction 3 _____
4. Perceived Drawbacks 4 _____
5. Global Evaluation 5 _____

☐ Check here if participant did not continue on to Visit 19

Date of Termination _____-_____-_____
dd mmm yy

Last Visit # Completed _____

Did the subject complete the protocol ☐ Yes ☐ No

If the answer to the item above is **"No"** indicate the reason for early termination

- ☐ Protocol violation
- ☐ Adverse event
- ☐ Death (Please Fill out Death Report
- ☐ Investigator withdrew subject
- ☐ Subject wished to withdraw
- ☐ Lost to follow-up
- ☐ Other_____

Subject Number ___ ___ ___ ___	CRF DRAFT	Visits 3 through Termination
PI: Pacey, I.	Concomitant Medication CRF	Page X1 Series ____ √ if Last Page

Non Psychotropic Concomitant Medications

At Visit 3 record all non psychotropic medications currently being taken and check the prestudy box (include start date if known) Provide diag# (from Med Hx page). Record all new prescription and non-prescription non psychotropic medications taken after visit 3 through termination visit. Provide AE# (from AE page) or other Reason for Treatment. Check the continuing box if continuing at study termination. ☐ **CHECK IF NONE**

Medication	**Route**	**Dose**	**Start Date (dd/mmm/yy)**	**Stop Date (dd/mmm/yy)**	**Reason for Treatment Complete at least one column**		
					Med HX Diag #	AE#	Other
			☐Prestudy	☐continuing			
			☐Prestudy	☐continuing			
			☐Prestudy	☐continuing			
			☐Prestudy	☐continuing			
			☐Prestudy	☐continuing			
			☐Prestudy	☐continuing			
			☐Prestudy	☐continuing			
			☐Prestudy	☐continuing			
			☐Prestudy	☐continuing			
			☐Prestudy	☐continuing			
			☐Prestudy	☐continuing			

Subject Number ___ ___ ___ ___	CRF DRAFT	Visits 3 through Termination
PI: Pacey, I.	Psychotropic Medication CRF	Page X2 Series_____ √ if last page

Psychotropic Medication and Tapering

- Record psychotropic medications previously used **and** psychotropic medications subject is on at visit1. Check the Prestudy box (include start date if known) and provide Disorder Code. Check Tapered box for medications tapered from V2 or V3. Provide route, dose and stop date for all medications.
- Record **all new psychotropic medications** taken after visit 1 through termination visit. Provide route, dose and start date. Provide AE# (from AE page) and check Rescue box if used as a rescue medication or complete Other Reason for Treatment. Check the Continuing box if continuing at study termination. ☐ **CHECK IF NONE**

Medication	Route	Dose	Start Date (dd/mmm/yy)	Stop Date (dd/mmm/yy)	Reason for Treatment Complete at least one column		
					Prestudy Disorder Code#	AE#	Other
			☐Prestudy	☐Tapered ☐ Con't		☐Rescue	
			☐Prestudy	☐Tapered ☐ Con't		☐Rescue	
			☐Prestudy	☐Tapered ☐ Con't		☐Rescue	
			☐Prestudy	☐Tapered ☐ Con't		☐Rescue	
			☐Prestudy	☐ Tapered		☐Rescue	
			☐Prestudy	☐Tapered ☐ Con't		☐Rescue	
			☐Prestudy	☐Tapered ☐ Con't		☐Rescue	
			☐Prestudy	☐Tapered ☐ Con't		☐Rescue	
			☐Prestudy	☐Tapered ☐ Con't		☐Rescue	

***Code for prestudy disorders**

1= Depression
2 = Anxiety
3 = Panic Disorder
4 = Pain management (routine)
5 = Pain management (PRN)
6 = Illness-related anxiety
7 = Obsessive-Compulsive Disorder (OCD)
8 = PTSD

Adverse Events

☐ **CHECK IF NONE**

AE #	Adverse event Diagnosis	Serious? a	Onset date (dd/mmm/yy)	Resolution date (dd/mmm/yy)	Severity b	Frequency c	Action taken for Study d	Action taken-treatment e

a
Serious?
1 = Serious*
2 = Not serious

* Serious = Fatal, life-threatening, requires prolonged hospitalization, results in persistent or significant disability, or requires medical or surgical intervention to prevent one of the outcomes defined as "serious" listed above.

b
Severity
1= Mild
2 = Moderate
3 = Severe

c
Frequency
1 = Single/Intermittent
2 = Continuous

d
Action Taken: Study
1 = None
2 = Interrupted session
3 = Delayed experimental session
4 = Discontinued experimental session
5 = Removed from study

e
Action Taken: Treatment
1 = None
2 = Procedure or therapy
3 = Blood or Blood products
4 = Withdrawn from study due to AE
5 = Prescription Med
6 = Non Prescription Med
7 = Hospitalization
8 = IV Fluids
9 = Other specify

f
Outcome
1 = Full recovery/retu
2 = Persists, diminish
3 = Persists, worseni
4 = Persists, the sam
5 = Alive with sequela
6 = Death

VIDEOTAPING OF HUMAN SUBJECTS

SUBJECT INFORMATION AND CONSENT FORM (Stage 1) FOR VIDEOTAPING

Study Title: A Randomized, Active Placebo-controlled Pilot Study of 3,4-methylenedioxymethamphetamine (MDMA)-assisted Psychotherapy in 12 Subjects with Treatment-Resistant Posttraumatic Stress Disorder (PTSD)-Canada

PROTOCOL NO.: M-P4

Study Sponsor: Multidisciplinary Association for Psychedelic Studies (MAPS)
3 Francis St., Belmont, MA 02478
Phone: 617 484-8711 Fax: 617 484-8427

Investigator: **Dr. Ingrid Pacey M.B. B.S. FRCP**

Address (es):
3369 West 4th Ave.
Vancouver BC V6R 1N6

Daytime telephone number(s): **604-732-9309**

24-hour contact number(s):

Cellular number(s):

PURPOSE OF THE SUBJECT INFORMATION AND CONSENT FORM

This consent form applies to your decisions about what the study doctors should do with videotapes of sessions in the research study for which you already signed an informed consent form, the study, "A Randomized, Active Placebo-controlled Pilot Study of 3,4-methylenedioxymethamphetamine (MDMA)-assisted Psychotherapy in 12 Subjects with Treatment-Resistant Posttraumatic Stress Disorder (PTSD)-Canada."

If you have completed the study, you are now going to be asked what you would like the study doctors to do with the recordings of your study sessions.

PURPOSE AND BACKGROUND

The purpose of this study consent is to ask you about your decisions about the videotapes of non-drug and MDMA-assisted psychotherapy during this study. Sessions will be recorded to video so that the study doctors will have accurate records of the session and so that they can gather more information about drug-assisted psychotherapy sessions. They plan to write up a series of standard instructions and methods for doing the therapy

called a manual for this therapy. The manual will help other scientists and therapists perform MDMA-assisted psychotherapy. The study doctors may also use the video recordings to train therapists for future research studies. If they use video recordings as part of this training program, you can either give permission for these recordings to be shown to people in the program with or without any identifying information removed. The study doctors will record each introductory, MDMA-assisted and non-drug psychotherapy session to video. They will begin recording MDMA-assisted psychotherapy starting shortly before you take MDMA and continuing for the whole six to eight hours of the experimental session with the exception of some periods of silence. You can stop the recording at any point in time, and you may request that portions of the video recordings be erased after they are recorded. Neither your full name nor your address will be included on the tape. You can ask to have other identifying information, such as your face, be removed from any video recordings used in programs for training therapists to learn to do MDMA-assisted psychotherapy. The study doctors and other scientists involved in this study and the sponsor of this study may review these videotapes to refine and improve this experimental treatment. All participants will receive a recording of each experimental session. The study doctors will provide a copy or permit you to view recordings of non-drug assisted psychotherapy sessions if you want to view them.

At the end of the study, when you have completed all of the questionnaires and measures, you can now make one of three decisions about video recordings and a decision about audio recordings of your study sessions. These include erasing all or some of the recordings of your study sessions and not saving a copy, having all facial images removed from copies of recordings shown to therapists in a training program to learn to do MDMA-assisted therapy, or allowing the study doctors to show people learning how to do MDMA-assisted psychotherapy video recordings of your psychotherapy sessions that still have your face or facial images in the recordings.

ALTERNATIVES

If you consented to be in this study, you can either agree to have your therapy session videorecordings shown to therapists in a program for training in MDMA-assisted psychotherapy without removing any additional identifying information, you can have them shown to people learning to do MDMA-assisted psychotherapy only if identifying information, such as your face, are removed from the recordings, or you can have the recordings erased.

CONFIDENTIALITY

All information collected will be treated and handled as confidentially as possible.

The study doctors will listen to or watch the video and audio recordings and no identifying information will be written or otherwise attached to the recordings. If you allow it, other scientists or therapists could watch the recordings to learn how to do MDMA-assisted psychotherapy.

VIDEOTAPING OF HUMAN SUBJECTS

Absolute confidentiality cannot be guaranteed.

This does not limit the duty of the researchers, study doctors and others to protect your privacy.

When not in use, information will be stored in a locked office. Any copies of the video recordings used for training purposes will also be kept in a locked office.

LEGAL RIGHTS

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

VOLUNTARY PARTICIPATION

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

You can stop the recordings at any time during the session or request to have part or all of them erased afterwards.

In addition, you may withdraw your consent to use the audio or video tapes at any time. There will be no penalty if you decide to withdraw from the research study. You must notify your study doctor that you wish to withdraw your consent. This notice will let the study doctors know that you do not wish to have experimental sessions videotaped or audiotaped. If you decide to stop the audio and/or videotaping component, you may still participate in the research study testing MDMA-assisted psychotherapy for PTSD.

QUESTIONS

If you have any questions about this study, its procedures, risks, benefits or your alternatives or rights or if at any time you feel you have experienced a research-related injury, contact:

Dr. Ingrid Pacey MBBS
3369 West 4th Ave.
Vancouver BC V6R 1N6
Office: 604-732-9309
Cell:

If you have other questions about other effects of MDMA, you can contact Rick Doblin, Ph.D., President of MAPS, the organization sponsoring this study.

The address is:

Rick Doblin, Ph.D.
3 Francis St.
Belmont, MA 02478
USA
Tel: 617 484-8711

VIDEOTAPING OF HUMAN SUBJECTS

SUBJECT'S STATEMENT OF CONSENT

"A Randomized, Active Placebo-controlled Pilot Study of 3,4-methylenedioxymethamphetamine (MDMA)-assisted Psychotherapy in 12 Subjects with Treatment-Resistant Posttraumatic Stress Disorder (PTSD)-Canada –

Your participation in this study and decision about your video recordings is voluntary. Your decision will not affect your current or future regular medical care or any benefits to which you are entitled at this site, or your participation in "Randomized, Active Placebo-controlled Pilot Study of 3,4-methylenedioxymethamphetamine (MDMA)-assisted Psychotherapy in 12 Subjects with Treatment-Resistant Posttraumatic Stress Disorder (PTSD)-Canada."

You have read the information in this consent form and it has been discussed with you. All of your questions so far about the study and your participation in it have been answered. You freely decided what will be done with your video recordings.

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

Your signature below indicates your consent to have your experimental sessions videotaped.

☐ If you check the box to the left, you are indicating that you would like the study doctors to erase the video recordings of all or some of your sessions so that no copy will be saved.

☐ If you check the box to the left, you are indicating that you wish to have images of your face removed from any video recordings that may be shown to therapists as part of a program training therapists to do MDMA-assisted psychotherapy.

☐ If you check the box to the left, you are indicating that you do not wish to have images of your face removed from any video recordings that may be shown to therapists as part of a program training therapists to do MDMA-assisted psychotherapy.

	SUBJECT		
Printed name			
Signature			
Date			

VIDEOTAPING OF HUMAN SUBJECTS

	PERSON ADMINISTERING CONSENT
Printed name	
Signature	
Date	

	INVESTIGATOR
Printed name	
Signature	
Date	

SUBJECT INFORMATION AND CONSENT FORM (Stage 1)

Study Title: A Randomized, Active Placebo-controlled Pilot Study of 3,4-methylenedioxymethamphetamine (MDMA)-assisted Psychotherapy in 12 Subjects with Treatment-Resistant Posttraumatic Stress Disorder (PTSD)-Canada

PROTOCOL NO.: M-P4

Study Sponsor: Multidisciplinary Association for Psychedelic Studies (MAPS)
3 Francis St., Belmont, MA 02478
Phone: 617 484-8711 Fax: 617 484-8427

Investigator: **Dr. Ingrid Pacey M.B. B.S. FRCP**

Address (es):
3369 West 4th Ave.
Vancouver BC V6R 1N6

Daytime telephone number(s): 604-732-9309

24-hour contact number(s):

Cellular number(s):

PURPOSE OF THE SUBJECT INFORMATION AND CONSENT FORM

This consent form describes a research study and your role as a participant. Please read this form carefully. Do not hesitate to ask anything about the information provided; it is expected that you will have questions about it. After reading the consent form, the study doctors will give you a short quiz to spot any parts of the study that need to be explained even further or in a better way than in the consent form, but your being in the study will not be related to your answers on the quiz.

You are being asked to participate in this research study because you have been diagnosed with posttraumatic stress disorder (PTSD) and because your symptoms have failed to go away after psychotherapy or medications for PTSD.

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

PURPOSE AND BACKGROUND

This small, early study is designed to provide information on whether MDMA-assisted psychotherapy is safe and helpful for subjects with posttraumatic stress disorder (PTSD). The study doctors plan to use the results of this study to design further studies.

MDMA is experimental, which means it has not been approved by Health Canada for medical use, except within research studies like this one. MDMA is illegal to use outside of research and is sometimes known as "Ecstasy" (which is supposed to contain MDMA but can often contain other drugs instead of or in addition to MDMA).

Before it became illegal, some psychotherapists combined MDMA with psychotherapy ("talk therapy") to help people with psychological problems, sometimes including PTSD. Though we do not know why it helps people with PTSD, we know that MDMA increases positive mood and also changes the way we see and think about the world around us, making it easier to think about and recall upsetting experiences, and people say they feel caring and forgiving toward themselves and others after MDMA. Most types of therapy that treat PTSD involve facing the trauma and PTSD symptoms and going over trauma-related emotions. Doing this reduces fear, defensiveness, avoiding things, places or feelings that trigger unwanted feelings or thoughts, and feeling emotionally numb or distant from relationships. If MDMA can temporarily decrease fear and avoidance and increase trust and connection between the person with PTSD and their therapist, then MDMA will make the therapy stronger and more likely to work. It is possible that these effects, when combined with psychotherapy, help people confront and go through the thoughts, memories and emotions related to PTSD.

This study will compare 125 and 62.5 mg MDMA, the study high dose, with the study low dose of 25 and 12.5 mg MDMA. The study low dose is an "active placebo" meaning it will produce some but not most of the effects of the study high dose of MDMA.

Length

This study can take up to four months and 19 visits if you get the study high dose from the beginning. The study can last an additional two and a half months and twelve more visits if you get the study low dose and decide to go on to have MDMA-assisted therapy in a second part of the study, "Stage 2."

Subject Responsibilities

If you and Dr. Pacey agree that you can and want to be in the study, you will have to come to all study visits. You will have to avoid taking any psychiatric medications from the beginning of the study up until your last study visit unless the study doctors make a specific exception, such as giving you medication for sleep or anxiety if needed temporarily between experimental sessions. If you are taking psychiatric medication, you will need to give Dr. Pacey permission to talk with your doctor about how best to stop taking your medication.

If you are currently seeing a psychotherapist, you may not begin any new psychotherapy or change the frequency or length of visits with your psychotherapist until after the final evaluation session.

For your safety, it is very important to tell the study doctor about all medications you are taking, including herbal or "natural" remedies, and to check with the study doctor before you begin taking a new medication while in this study.

PROCEDURES/WHAT WILL HAPPEN TO YOU

SCREENING/EVALUATION AND BEGINNING OF STUDY

Before you can be in the research study, the study doctors must first make sure that you qualify for the study and that you are generally physically healthy. The screening process will take about 3 to 4 hours.

The tests will include the following:

- A questionnaire about your PTSD symptoms and how you deal with them in your everyday life. Your score on this questionnaire will be used to decide if you can be in the study. The study doctor asking you these questions will be a different person from the study doctors.
- A questionnaire that you complete yourself on your PTSD symptoms
- A questionnaire about feelings of depression or other symptoms or feelings you might experience.
- Questions about your medical history, including questions about your emotional and psychiatric history. This may include any previous medical or psychiatric problems or treatment and may include questions about difficult experiences you may have had during childhood or at other times of your life.
- A questionnaire about thoughts and feelings you might have about hurting or killing yourself.
- Two different tests of attention, memory and different types of problem solving. These are not tests of intelligence.
- A physical examination that will include measures of your blood pressure, pulse, temperature, and body weight.
- An ECG (electrocardiogram) will also be taken, which is a recording of the electrical activity of your heart.
- A sample of your blood (about 2 tablespoons) and a urine sample for routine laboratory testing, including tests of metabolism and liver function.
- A urine test for drugs of abuse. Your urine drug screen must be negative to take part in the study.
- A urine pregnancy test if you are a woman and are able to get pregnant. Your urine pregnancy test must be negative for you to take part in the study.

BEGINNING OF STUDY

If you have decided that you want to be in the study and if the study doctors find that you are eligible, you will schedule your first introductory psychotherapy session with the two therapist-investigators. If you were taking psychiatric medicines when the study doctors first checked to see if you could be in the study, you will have your PTSD and depression symptoms measured again after you have stopped taking your medication.

SCHEDULE OF EVENTS 1

Time is counted from the first study visit after you are selected to be in the study. These are the events up until you learn if you got study low dose or study high dose MDMA

	Screen /Start Study	Intro & Preparation			MDMA & non-Drug Therapy 1				MDMA & Non-drug Therapy 2				MDMA & Non-Drug Therapy 3				End Random
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Screening	x																
Measure symptoms	x																x
Psychotherapy		x	x	x		x	X	x		x	x	x		x	x	x	
Attention and Memory Tests	x																x
Psychotherapy With MDMA					X				X				X				
Medical Exam	x																
Learn dose you got																	x

INTRODUCTORY PSYCHOTHERAPY SESSIONS:

You will meet with the study doctors on three separate occasions before the first experimental session. These visits will last from 60 to 90 minutes. During each introductory session, you will discuss the traumatic incidents that led to your PTSD, the ways PTSD symptoms are affecting your life and what you would like to achieve during these sessions. You will also learn more about what to expect during experimental sessions. The introductory session will be recorded to audio and video, so that the study doctors will have accurate records of the session and so that they can gather more information about drug-assisted psychotherapy sessions. You can ask the study doctors to let you hear or see these recordings if you wish.

SELECTION OF DRUG – MDMA OR PLACEBO?

Each subject in this study will be randomly assigned (by chance, as if by flipping a coin) to get either 25 and 12.5 or 125 and 62.5 mg MDMA. This study will have 12 subjects. Eight (67%), will receive the study high dose of 125 and 62.5 mg and four (33%) will receive the study low dose of 25 and 12.5 mg MDMA. You will take the same dose on each of the three experimental sessions.

Neither you, the person measuring your PTSD symptoms, or the study doctors will know who is getting the study high dose of MDMA and who is getting the study low dose ("double-blinded") until after the study is completed. However, this information is available if needed in an emergency.

EXPERIMENTAL SESSIONS:

There will be three experimental sessions (with either the study low dose or high dose MDMA), each happening three to five weeks apart. The first experimental session (study low dose or high dose MDMA) will occur after you have had three introductory sessions.

Each experimental session will last approximately eight hours, though both study doctors will remain with you for a longer period of time if necessary.

You must not eat or drink any alcohol after midnight on the night before each session, though you can drink non-alcoholic liquids during this time, such as water or juice.

First, you and the study doctors will discuss your goals for the experimental session, and the study doctors will answer any questions you still have about this session.

Before an experimental session:
- Your urine will be tested for drugs of abuse.
- If you are a woman who can become pregnant, a urine pregnancy test

Throughout an experimental session
- Your blood pressure and pulse will be measured every 30 minutes.
- Your temperature will be measured every hour.
- You will also complete a very brief, simple test of how comfortable or distressed you feel by marking a number on a sheet of paper that coincides with the way you feel at that moment. You will complete it every 60 to 90 minutes throughout each experimental session.
- The study doctors will check in on you every hour or so to see how you are doing

The experimental session will be audiotaped and videotaped, so that the study doctors will have accurate records of the session and so that they can gather more information about drug-assisted psychotherapy sessions. The study doctors can give you copies of these recordings for you to keep and watch if you want them.

After urine test results come back, you will receive a capsule containing 25 or 125 mg MDMA. After taking the capsule, you will sit or lie down in a comfortable position. You can ask for an eye shade if you wish. You will listen to music through headphones during much of each experimental session. Periodically you will be asked to remove the headphones to talk to the study doctors, and you may also remove them yourself if you want to talk to the study doctors or for periods of silence. Lying or sitting in a comfortable position and listening to music are meant to bring out thoughts and feelings, including thoughts and feelings about the trauma. Both study doctors will remain with you, and they will help you if you need them to do so. They will speak with you and ask you to talk to them at least once an hour, but you can talk to them whenever you wish. There may be times when the study doctors will suggest that you stop talking for a while in order to pay attention to your thoughts and feelings. There will be water, juices or Gatorade available to drink whenever you wish within the limits of what is safe for your body,

and you will be encouraged to drink an adequate amount of fluid. Later on, food will also be provided.

Approximately one and a half to two and a half hours later, you and the study doctors will talk about taking a second dose of MDMA. The second dose will be half the amount of the first dose. If you and the study doctors agree, then you will take the second dose. If you or the study doctors notice problems after the first dose of MDMA, then you will not get the second dose of MDMA.

The study doctors will continue to measure blood pressure, pulse and temperature, and they will watch for any side effects (unwanted effects or health problems), which will be treated if they occur. If this happens, the study doctors will let you know what they are doing.

If you are still confused or very upset eight or more hours after the start of the experimental session, the study doctors will stay with you until you have recovered more fully. If the study doctors think you are at risk for hurting yourself or someone else, they will either remain with you all night or have you stay in a nearby hospital until they are certain you are not at risk. If the study doctors decide that the effects of the drug have worn off and you are in an appropriate frame of mind, they will leave the office with the attendant in charge.

You will be spending the night in a comfortably furnished room [redacted] If you request and Dr. Pacey agrees, you may also have someone of your choosing stay with you at the office during or after an experimental session. An attendant who will be the same sex as you will stay in another room at the same location from the time after you are done with the experimental sessions until the non-drug session on the next day. The attendant will offer dinner and breakfast, assist you with any physical needs if requested, and contact Dr. Pacey to speak with her or to have her return to the office at your request or if the attendant considers it necessary.

On the next day, you will have a non-drug therapy session with the study doctors. You will need to arrange ahead of time to have someone take you home from this non-drug session, because we don't know how MDMA will affect you and some people report feeling tired or less alert. If you cannot find anyone to take you home, the study doctors will either call a taxi or make arrangements with a volunteer they know who is familiar with the study.

After you return home, the study doctors will telephone you every day for a week to inquire about how you are feeling and determine whether you should see Dr. Pacey before your next scheduled non-drug psychotherapy session. These telephone calls will take approximately 5 to 15 minutes, though they can last as long you need them to be. You may schedule additional meetings with the study doctors besides those that are scheduled as part of the study.

You can contact the study doctors at any time. The study doctors will give you a card with telephone numbers for reaching Dr. Pacey, the organization sponsoring the study, or the Institutional Review Board – IRB Services (an independent committee that reviewed the ethical aspects of this study to help protect the rights and welfare of study participants). Dr. Pacey will be on call (reachable by telephone or pager) 24 hours a day throughout the research study, except