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Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
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28 August 2019

CLINICAL HOLD COMPLETE RESPONSE

RE: IND #063384, Serial No. 0123, Clinical Hold Complete Response to Partial Clinical Hold Letter dated 5 August 2019

Dear Division of Psychiatry Products/CDER,

Below is a complete response to the Partial Clinical Hold Letter dated 5 August 2019 for the MT2 study under the Breakthrough-Designated IND #063384. The MT2 protocol has been revised to align with the Agency's comments. Please reference the Summary of Changes for Protocol Amendment 1 Version 1 provided with this submission.

Prior to addressing the Agency's individual clinical hold concerns, the Sponsor will address the purpose of the MT1 and MT2 clinical research studies. On June 22, 2009, the Sponsor provided the rationale for conducting the MT1 study to the FDA in the submission cover letter, informing the agency of the importance of the MT1 study to "assist the sponsor in improving therapeutic skills in the male/female co-therapy teams conducting MAPS Phase 2 MDMA/PTSD studies and possible future Phase 3 multi-site studies." In training therapists to conduct MDMA-assisted psychotherapy research for treatment of PTSD, personal experience with MDMA can only be obtained legally through participation in a clinical trial with appropriate regulatory clearance. The design of the MT1 study was subsequently developed with input from FDA reviewers at the time. The MT1 study was designed as a placebo-controlled crossover study in order to train researchers to conduct MDMA-assisted psychotherapy research with a placebo control group. The majority of MT1 participants have later worked on the MAPP1 Phase 3 placebo-controlled PTSD study.

Many therapists who have participated in the MAPS-sponsored MT1 study publicly speak or write about their experience and how it has aided them in delivering MDMA-assisted psychotherapy because they were able to better understand the psychoactive effects of MDMA within a controlled trial (Nielson and Guss 2018). One wrote "My complete immersion in the session allowed me to walk away with a clearer image of how to be present with and for a client during their experience, and I felt more prepared to respond to what I would encounter as a therapist in an MDMA study" (Halberstadt 2014). Another wrote, "I underestimated how valuable the MDMA experience would be for me. It became instrumental to the way I'm now approaching the sessions and working with participants in the trial" (Love 2019). An important opportunity for facilitators learning to conduct MDMA-assisted psychotherapy is to experience MDMA themselves so they may better understand the techniques taught in the MDMA Therapy Training Program.

The proposed MT2 study is for trainees who wish to further expand their knowledge with their own MDMA experience, but do not need to prepare for research with a placebo-control group, such as Expanded Access facilitators enrolled in the MDMA Therapy Training Program. The MT1 and MT2 research studies also provide the opportunity to continue gathering safety and psychological effect data in healthy volunteers receiving MDMA-assisted psychotherapy. The MT2 protocol excludes participants with a current psychiatric disorder or a history of bipolar affective disorder type 1, or a history of a primary psychotic disorder, although they may have a

history of a mood disorder, anxiety disorder, insomnia, or ADHD. If participants have a history of an allowed disorder, it must be in remission without requiring ongoing medication during the Experimental Session.

Practitioners of psychotherapeutic methods such as trauma-focused cognitive behavioral therapy, prolonged exposure therapy, and psychoanalysis consider their personal experience with those modalities to be a beneficial part of their training. In the psychotherapy literature, clinician-specific non-pharmacological factors, such as personal experience in relationships with individuals of other racial or ethnic backgrounds, and personal resilience and competence have been empirically tested and were found to influence the psychotherapy treatment outcomes (Larrison, Schoppelrey et al. 2011, Green, Barkham et al. 2014).

The training value placed on the personal experience of MDMA by MAPS-trained researchers, almost all of whom have volunteered for the experience as a part of the MT1 clinical trial, is consistent with the views expressed by many of the early psychedelic therapists and researchers from the 1940s to the early 1980s who used psychedelic sessions to train therapists. Those who underwent personal therapy reported a better understanding of their patients' experience, including both the negative and positive effects of therapy. People who are unfamiliar with the effects of a given compound in a specific setting may hold inappropriate expectations or be unaware of aspects of the setting that may enhance or hinder therapeutic effects leading to over or under reporting of adverse events.

Investigators who researched d-lysergic acid diethylamide (LSD) in the course of psychotherapy reported that therapists who experienced LSD gained better insight into their patients' experiences during LSD-assisted psychotherapy and were thus better able to aid them. In the 1960s and early 1970s, over 100 people with pastoral and counseling jobs received LSD up to three times in a therapeutic context as part of the "Training Project for Mental Health Professionals" conducted at the Maryland Psychiatric Research Center, under Dr. Albert Kurland's IND for LSD. This was initiated in order to enhance the ability of mental health professionals to work with people who discussed LSD experiences with them. Daniel Helminiak STL, Ph.D., LPC, a Professor of Psychology at the University of West Georgia, one of the original participants in the "Training Project for Mental Health Professionals," reported long-term benefits to his ability as a therapist from undergoing a supervised experience with LSD.

In many psychotherapy training programs, trainees complete a full course of the type of psychotherapy they are learning to deliver. In addition, they participate as an observer under the supervision of an experienced psychotherapist working with a patient, as long as the patient agrees to this observation. This method of training emphasizes "learning by doing." Participants taught with experiential methods gain first-hand experience that is critical for learning to treat patients with PTSD. Experiential teaching is a gold standard in psychotherapy training.

The sponsor has surveyed Phase 3 researchers working on MAPS-sponsored studies, who were asked to consider the personal and professional impact of this experiential psychotherapy training on their lives. Similar to other studies conducted on students of experiential psychotherapy training courses reported in the scientific literature, Phase 3 researchers perceived multiple changes on both a professional level (i.e., skill acquisition and learning related to the therapeutic process) and a personal level (i.e., self-growth in a more private sphere) (Pascual-Leone, Wolfe et al. 2012). Training in MDMA-assisted psychotherapy presents a unique situation for a psychopharmacology program. As psychopharmacology is combined with psychotherapy in this treatment method, it is very helpful for facilitators to actually have experience with MDMA, since their primary role will be to help future patients process their experience with MDMA. This is not

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a typical requirement for a psychiatric drug trial, but it is appropriate for psychedelic-assisted psychotherapies. In psychedelic-assisted psychotherapy, the therapeutic setting and the mindset of the facilitators make critical contributions to the administration of the treatment, which is an inherently variable process. This differentiates the training needs for psychedelic-assisted therapies from other medications that are not prone to operator effects.

As MDMA-assisted psychotherapy continues to show a justifiable benefit:risk profile, with early phase clinical trials supporting Breakthrough Therapy Designation by the Agency, it is crucial to continue the MDMA Therapy Training Program with appropriate techniques that will prepare therapists interested in this modality.

We thank the agency for their review of this response letter. The clinical hold concerns are addressed below:

***Deficiency**: 1. 21 CFR 312.42(b)(1)(i): Unreasonable and significant risk of illness or injury to human subjects. Based on the study design of MT2 Amendment 2 and safety information submitted in your cover letter, the benefit:risk profile for MDMA in healthy subjects is unacceptable.*

Lack of scientific benefit:
a. You describe Protocol MT2 as an open-label safety study of up to 400 healthy volunteers. However, you state that a study of MDMA in 1286 healthy volunteers has already been conducted. You further state that this study will provide phase 1 healthy volunteer data to support new indications for MDMA-assisted psychotherapy.

***Information Needed to Resolve Deficiency:** You must justify the large number of healthy subject exposures in MT2 for an unapproved therapy when data already exists.*

SPONSOR RESPONSE:

The sponsor would like to clarify that 1286 healthy volunteers have not been exposed to MDMA under a MAPS-sponsored IND. As described in Section 2.2.2 of the protocol (Previous MDMA Research) and the 11th Edition of the MDMA Investigator's Brochure, MDMA has been administered to 248 people in studies under a MAPS-sponsored IND, and to 1286 individuals in clinical or research studies conducted without Sponsor support, giving a total of 1534 research participants in both Phase 1 and Phase 2 studies as of October 2018. There has been one healthy volunteer study to date conducted under a MAPS-sponsored IND (MT1) with systematic data collection. The number of healthy participants enrolled in the MT1 study as of the date of this response is 79. Systematically collected and monitored raw data are not available to the sponsor from the 1286 participants to the sponsor, rather this is a compilation of summary information from different studies in the published scientific literature. While this published data is supportive of the safety profile of exposure to MDMA in a controlled setting, it does not substitute for systematically assessed data from subjects receiving MDMA in a MAPS-sponsored IND study.

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The MT2 protocol was originally written for 400 participants in order to provide enough capacity for those therapists in training for MDMA pilot programs, the anticipated MAPS Expanded Access protocol (EAMP1) and potential post-approval prescription use. However, the sample size of the Expanded Access program has since been reduced per FDA request to 50 (with anticipated growth to follow pending review of safety data), therefore the MT2 protocol has now been revised to 150 participants (with anticipated growth to follow pending review of safety data) to be closer in alignment with anticipated growth in the MDMA Therapy Training Program to follow. The MT2 study will also provide additional exploratory healthy volunteer data on psychological effects and is part of MAPS' efforts to systematically collect more safety data on MDMA exposures. This was discussed with the Agency in the End of Phase 2 meeting per the minutes dated December 29, 2016, which stated the sponsor's intention to collect additional safety data in open-label studies. As the sponsor anticipates a gradual increase in the number of qualified facilitators who can treat patients with PTSD post-approval, continuing to collect additional safety data would be helpful as the sponsor prepares to introduce MDMA more broadly into the market.

The risk and duration of potential psychological distress in the MT1 study population was already described in the approved MT1 Protocol in Section 7.2.4 Psychological Risks and the Informed Consent Form. Based on the AE Clarification Letter provided under submission Serial No. 0121 under IND#63384, the sponsor feels strongly that these clarifications should be considered as the Agency reviews the benefit:risk profile of the MT1 and MT2 studies.

> "Psychological distress from MDMA could arise from the first indications of drug effects until the last effects have dissipated (approximately 3 to 5 hours after drug administration). Anxiety or distress during the session may last for as little as 15 minutes or for as long as 5 hours. … participants may confront emotionally intense or upsetting memories, thoughts, and feelings. Signs of psychological distress, panic, or other unpleasant psychological reactions may not be as strong as expected in people with psychiatric disorders, but may still be present..."

The sample size is justified on the basis of the training need and in order to gather more safety data. Further sample size justification relates to the goal of generating effect size estimates for improvement in self compassion and professional quality of life, effects on mood, and burnout, which is yet to be tested in a population of facilitators learning to deliver MDMA-assisted psychotherapy.

***Deficiency**:*
Lack of scientific benefit:
b. The overall objective of this study is to explore the safety and psychological effects of open-label, manualized, MDMA-assisted psychotherapy in healthy volunteers and to expand the knowledge of treatment providers who are learning to conduct MDMA-assisted psychotherapy or MDMA research. Your submission admits that the purpose of the study is to allow therapists to experience MDMA to aid in their training.

***Information Needed to Resolve Deficiency:** You must justify why MT2 is necessary when you already are currently conducting a similar study (MT1).*

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SPONSOR RESPONSE:

The MT1 study is a double-blind placebo-controlled crossover study that has currently enrolled 79 participants. The sponsor has requested to amend the MT1 Protocol from 100 to 120 participants to train additional researchers who are learning to conduct MDMA-assisted psychotherapy research with a placebo control group.

The MT2 study design is open-label for participants and is supplemental to the data generated from the placebo-controlled MT1 study. The proposed MT2 study is to provide valuable training experience for trainees who do not need to prepare for research with a placebo-control group. MT2 will allow for the collection of additional safety and other outcome data that will further help in determining both the safety profile of this therapy as well as suggesting other potential benefits.

The primary and exploratory outcome measures from the MT2 healthy volunteer study will provide important and relevant data which are not being captured in the MT1 study. Changes to professional quality of life and burnout can impact the quality of care patients receive. Recently, the World Health Organization classified burn-out as an occupational phenomenon deriving from workplace stress left unsuccessfully managed, which is classified in the International Statistical Classification of Diseases and Related Health Problems (ICD-11) under the diagnosis code of Z73.0. Burn-out is a syndrome conceptualized as resulting from chronic workplace stress that has not been successfully managed. It is characterized by three dimensions: 1) feelings of energy depletion or exhaustion; 2) increased mental distance from one's job, or feelings of negativism or cynicism related to one's job; and 3) reduced professional efficacy. The data gathered with the MT2 study is designed to measure possible changes in the study participants that would be likely to correlate with professional effectiveness and satisfaction.

***Deficiency**:*
Lack of scientific benefit:
c. The primary endpoint is the Self-compassion Scale. Lack of self-compassion is not a recognized psychiatric illness.

***Information Needed to Resolve Deficiency:** You must justify how the data obtained from this study will contribute to your development program for MDMA in psychiatric illness.*

SPONSOR RESPONSE:

MT2 is not a registration study and the information obtained is for research purposes only. MT2 is for training therapists, to gather additional safety data, and in addition is a feasibility study intended to study the development of self-compassion associated with the administration of MDMA to qualified trainees enrolled in the MDMA Therapy Training Program. This research study will collect data from participants to measure changes in self-compassion with a validated measure as the primary endpoint. Data from a healthy population of treatment providers may contribute to the sponsor's understanding of psychological mechanisms of action of MDMA-assisted psychotherapy and allow comparison of differences in self-compassion between treatment providers and PTSD patients. MT2 is hypothesized to demonstrate the benefit of exposure to MDMA in a treatment provider population, and potential correlations with professional quality of life and burnout.

Self-compassion is being measured in the Phase 3 PTSD trials of MDMA-assisted psychotherapy to continue to explore the relationship between PTSD symptom severity and self-compassion. Research supports the role of several components of self-compassion in recovery from PTSD, and recommends facilitating decrease in self-judgment, isolation, and over-identification and increase in self-kindness in PTSD patients as important contributors to the treatment of PTSD (Hoffart, Oktedalen et al. 2015). In a study examining the relationship between PTSD symptoms and components of self-compassion, PTSD symptoms ranked higher when initial self-judgement existed. Other studies have found that patients with PTSD may improve by combining elements of self-compassion into their treatment plans (Thompson and Waltz 2008). In an open trial, the addition of imagery re-scripting to prolonged exposure psychotherapy, with the goal of fostering self-compassion, was found to be helpful for PTSD patients who had previously not responded to standard prolonged exposure psychotherapy (Grunert, Weis et al. 2007). In pilot studies, both loving-kindness meditation and mindfulness-based stress reduction have shown promising results in the treatment of veterans with PTSD (Kearney, Malte et al. 2013, Kearney, McManus et al. 2014). Since neurobiological effects of MDMA increase compassion (see Section 5.2.3.2 Behavioral and Neuropsychological Effects of the MDMA Investigator's Brochure), the Sponsor hypothesizes that self-compassion will also increase in trainees as well as in PTSD patients.

***Deficiency**:*
Safety risk:
d. The safety data submitted from MT1 appears to reveal the potential for serious risk. You state that the benefit:risk ratio of MDMA-assisted psychotherapy in healthy volunteers remains favorable as the risks are lower than the PTSD population. However, there was a case of blindness, severe suicidality, and intentional self-harm in a population of 76 healthy subjects.

***Information Needed to Resolve Deficiency**: Given that the safety and efficacy of your proposed product has yet to be adequately characterized, you must justify why additional subjects (with, as you propose, a history of a mood or anxiety disorder) should be exposed to MDMA in an open-label design where all subjects would receive drug.*

SPONSOR RESPONSE:

The sponsor has submitted a formal clarification to the IND under Serial No. 0121 providing a clinical narrative that the AE for MT1 Subject [redacted] was determined at the time of evaluation by the site and sponsor to not be serious per protocol-defined criteria. Since the participant's life was never in danger and no medical intervention was required to ensure her safety, the Clinical Investigators deemed this AE to be non-serious. Rather, this experience represented an example of uncovering of deeper repressed feelings from the past that is a central goal of the MDMA experience and is beneficial to a facilitator learning to conduct MDMA-assisted psychotherapy. The Columbia Suicide Severity Rating Scale (C-SSRS) indicated a Suicidal Ideation category score of 4 during the experimental session, which does not necessarily indicate an immediate risk if the thoughts are fleeting, fairly easily controlled, and deterrents are strong. The C-SSRS scores demonstrate that the suicidal ideation had already diminished to passive ideation (category 1) by the end of the experimental session. The Safety Plan described in MT1 Protocol Amendment 3 Version 1 in Section 7.2.1 for participants who screen positive for suicidal ideation or intent was followed appropriately by the clinical site.

In addition, the verbatim term of the AE experienced by MT1 Subject [redacted] has been clarified with the participant by the site physician of the clinical site and should have been reported as Vision Blurred. The case of blurred peripheral vision was incorrectly coded as blindness. Upon the sponsor requesting clarification, the site physician re-contacted the participant. The

participant clarified that her peripheral vision was blurred for 3-4 hours. This resolved by the end of the experimental session with no treatment. There was no loss of vision. The verbatim term of the AE was revised to Blurred Peripheral Vision, which was coded using MedDRA Version 17.1 to the preferred term of Vision Blurred. This data clarification request and update in the database was completed after the database freeze for the MT2 protocol submission on May 21, 2019 under IND#63384, Serial No. 0117. With this clarification, there are now two participants who experienced an AE of Vision Blurred, for a study-wide prevalence of 2.6% (2 of 76 as of the data cut-off of the MT2 protocol submission). The sponsor believes that the benefit:risk ratio of MDMA in healthy volunteers remains acceptable with risks lower than in the PTSD population.

To ensure the exclusion of participants with psychiatric disorders, and those with history of a mood or anxiety disorder that is not in remission, the MT2 protocol has been amended to now include Independent Raters to assess each participant by screening with the validated diagnostic clinical interview, the Mini-International Neuropsychiatric Interview (MINI), instead of relying on investigator judgement. In addition, an enrollment confirmation step has been implemented which will require both site physician and sponsor Medical Monitor review of medical history, MINI results, concomitant medications, physical exam, and laboratory testing results. Participants will not be enrolled until the Medical Monitor approves of the enrollment packet.

***Deficiency**: 2. 21 CFR 312.42(b)(1)(ii): Unqualified clinical investigators*
Protocol MT2 states that all psychotherapy sessions will be conducted by at least one trained, qualified, and licensed therapist, who will be accompanied by an observer. The observer may be a second licensed therapist or a trainee who is enrolled in or has completed a therapy training program under the auspices of the sponsor (if both the therapist and participant agree). Each licensed therapist will hold a certificate from the MAPS Therapy Training Program specifying their approved status.

***Information Needed to Resolve Deficiency:** You must explain why the therapists' requirements will be safe for healthy volunteers when the proposed therapists are less qualified than in your phase 3 trials. (We remind you that subjects taking MDMA are in a vulnerable state and that you already have reported safety compliance issues.)*

SPONSOR RESPONSE:

In the MT2 protocol, participants do not suffer from PTSD. In addition, participants with current psychiatric disorders, and those with history of a mood or anxiety disorder that are not in remission, are excluded from the MT2 study based on the MINI diagnostic clinical interview. A single MT2 facilitator with appropriate qualifications and a second person assisting, with a site physician on call, should be sufficient to ensure the safety of a healthy volunteer participant who may temporarily be in a vulnerable state due to receiving MDMA. This is a research study and the intervention does not provide a patient/client psychotherapeutic relationship. The licensed MT2 facilitator would be responsible for identification of safety concerns, in addition to the site physician who is responsible for overall safety.

Each clinical site will include an appropriately qualified site Clinical Investigator (CI) who is personally responsible for the conduct of the MT2 study per the commitments they agree to in the FDA Form 1572. All CIs named in the IND are qualified by reason of their scientific training and experience to conduct the investigation described in the IND. The MT2 facilitators described below will work under the supervision of the site CI.

There will be a minimum of two licensed MT2 facilitators at each clinical site, with most study sites having more than two MT2 facilitators. All MT2 facilitators will be selected by the MDMA Therapy Training Team and will have completed the sponsor's supervision process while working on a previous PTSD study, or will have had extensive experience conducting MDMA-assisted psychotherapy and will have subsequently completed the MDMA Therapy Training Program up to the point of supervision. If a licensed MT2 facilitator does not have extensive experience delivering MDMA-assisted psychotherapy they will work with a more experienced MT2 facilitator as a team under supervision. The supervisors of the MDMA Therapy Training Program are only recommending the most skilled facilitators to be MT2 facilitators. This is being carefully tracked, and each site CI will receive a listing of approved recommended MT2 facilitators at the time of site selection. Once a licensed MT2 facilitator begins working on MT2 they will receive additional supervision which is described in the paragraphs below.

Clinical Investigator Qualifications

A Doctor of Medicine (MD) or a Doctor of Osteopathic Medicine (DO) will be designated as the CI or medical Co-lead CI (site physician) at each study site as previously requested by the FDA. The site physician will fulfill DEA Schedule I license and FDA medical oversight requirements. Each site will have appropriately qualified personnel who will be licensed to manage and administer Schedule I controlled substances and may authorize a delegate (per DEA requirements) to administer drug under their license. The site physician conducting the screening may delegate screening to qualified site personnel such as a second site physician, nurse practitioner, or physician's assistant. Potential participants in MT2 are required to complete an on-site physical exam, in addition to off-site clinical laboratory assessments, an electrocardiogram (ECG), and 1-minute rhythm strip during screening. Once all results are obtained, the CI and/or site physician will review all screening assessments against eligibility criteria. If, upon examination, there are questions raised about possible medical problems, the site physician will request additional tests, assessments, or measures as indicated. The site physician may also contact outside care providers with participant permission as needed. In addition, the sponsor Medical Monitor will review screening assessments in order to confirm participants for enrollment. The site physician and/or CI will review safety data during the conduct of the MT2 study and be responsible for reporting AEs to the sponsor. The site physician and/or CI will be on call and able to respond in case of a medical emergency during MT2 experimental sessions.

Facilitator Qualifications

The sponsor has further clarified the MT2 facilitator requirements in the MT2 Protocol Amendment 1 Version 1 to be comparable to lead facilitators working on Phase 3 trials and Expanded Access. Selected MT2 facilitators will have completed the MDMA Therapy Training Program and they must also be recommended by the program supervisors on the basis of demonstrated acceptable experience delivering MDMA-assisted psychotherapy or they will work with a more experienced MT2 facilitator under supervision. Each MT2 facilitator will hold an MDMA Therapy Training Program certificate specifying their approved status.

The licensed MT2 facilitator is required to be a physician or a mental health professional licensed to practice psychotherapy according to state and local requirements. For example, this could include a registered nurse if their licensing board allows psychotherapy, and documentation is provided to support this. Two people will be present with the MT2 participant for each study visit after enrollment in one of the two configurations as described in the table below.

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Table 1: MT2 Configurations

	Qualifications	
Level 1	Licensed MT2 facilitator	Licensed MT2 facilitator
Level 2	Licensed MT2 facilitator	Co-facilitator-trainee

Level 1 Configuration

Two licensed MT2 facilitators will be required to work in the Level 1 configuration during MT2 sessions until they have passed MT2-specific supervision requirements. MT2-specific supervision will be provided during meetings between the supervisor and the MT2 facilitators, which is also used in other psychotherapy training programs. Completion of MT2 supervision is determined by the MDMA Therapy Training Program Supervisors. To document completion of supervision, the licensed MT2 facilitators will be given a certificate specifying their approval to facilitate sessions in the Level 2 configuration.

Level 2 Configuration

The MT2 protocol allows for assistance from a Co-facilitator trainee if the MT2 study participant agrees to this observation. The MT2 participant may decline having the Co-facilitator-trainee present, however if this occurs the study visits will be conducted in the Level 1 configuration.

A licensed MT2 facilitator holding a Level 2 certificate will be allowed to work with a Co-facilitator-trainee as a second person in the room. The Co-facilitator-trainees will act under the direct supervision of an MT2 facilitator. The role of the Co-facilitator-trainee is primarily to assist the facilitator in modeling the process of MDMA-assisted psychotherapy in a live clinical setting, including the Preparatory, Experimental, and Integrative psychotherapy sessions. The MT2 facilitator will supervise the administration of MDMA, modeling the core principles of MDMA-assisted psychotherapy. The MT2 facilitator and site physician are responsible for participant safety. Co-facilitator-trainees agree to abide by the guidelines of the MDMA-Assisted Psychotherapy Code of Ethics in their interactions with MT2 participants, including maintaining confidentiality and professional boundaries.

Co-facilitator-trainees are required, at a minimum, to have a bachelor's degree and training in mental health, which includes students in a postgraduate internship-type program providing detailed knowledge of mental health interventions and treatments, or 1000 hours of behavioral health experience in addition to the MDMA Therapy Training Program. Trainees must be enrolled in or have completed the MDMA Therapy Training Program under the auspices of the sponsor and will have documentation of this training, i.e. registration in the sponsor's online learning portal for Therapy Training. The trainees will meet all co-facilitator qualifications as specified by FDA as required to work on approved MAPS-sponsored studies, such as the Expanded Access study EAMP1.

Safety from Two-Person Teams

The sponsor has previously used the approach of having two people in the room during MDMA-assisted psychotherapy with the intention to optimize efficacy regardless of cost, to provide a sense of safety for participants who suffer from PTSD due to sexual assault and abuse, and to provide a male/female team for participants with emotional issues related to problematic parenting and attachment, as well as other issues. Both configurations, Level 1 and 2, provide the required safety of two people in the room with each participant who is in a vulnerable state.

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In conclusion, the sponsor greatly appreciates the Agency's review of this response and the revised MT2 protocol. The MT2 protocol was submitted on May 21, 2019, and the protocol was placed on partial clinical hold 76 days later. To better address any future concerns, the sponsor requests that the agency provide a telephone call prior to placing a clinical hold on a research protocol in accordance with the U.S. FDA's internal SOP MAPP 6030.1 and Title 21 CFR § 312.42(c), similar to other sponsors of commercial INDs.

If the Agency has any further questions regarding this complete response to the Partial Clinical Hold Letter, please do not hesitate to contact Sponsor Designee, Amy Emerson, by telephone at [redacted] or by email at [redacted]

Sincerely,

Amy Emerson

Electronically signed by: Amy Emerson
Reason: I am the author of this document
Date: 2019-08-28 13:26:32-07:00

Amy Emerson
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