IND 063384

PARTIAL CLINICAL HOLD

Multidisciplinary Association for Psychedelic Studies
Attention: Amy Emerson
Executive Director &
Head of Clinical Development and Regulatory Affairs
1115 Mission Street
Santa Cruz, CA 95060

Dear Ms. Emerson:

Please refer to your investigational new drug application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for 3,4-methyelenedioxy-methamphetamine (MDMA).

We also refer to your amendment dated May 21, 2019.

The study you proposed, protocol MT2, titled “A Phase 1, Open-Label, Multi-Site Study to Assess Psychological Effects of MDMA-Assisted Psychotherapy when Administered to Healthy Volunteers," is on clinical hold and may not be initiated.

The following are the specific deficiencies and the information needed to resolve the deficiencies.

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.

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).

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.

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.

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.)

Until you have submitted the required information, and we notify you that you may initiate the clinical study, you may not legally conduct the identified clinical study under this IND.

Please identify your response to the clinical hold issues as a "**CLINICAL HOLD COMPLETE RESPONSE**." To facilitate a response to your submission, submit this information in triplicate to the IND. In addition, send a copy of the cover letter to CDR Sarah Seung.

Following receipt of your complete response to these issues, we will notify you of our decision within 30 days.

If we have additional comments or information requests not related to this clinical hold, we will notify you. Your responses to any non-hold issues should be addressed in a separate amendment to the IND.

Please cite the IND number listed above at the top of the first page of any communications concerning this application

SUBMISSION REQUIREMENTS

The Electronic Common Technical Document (eCTD) is CDER and CBER's standard format for electronic regulatory submissions. The following submission types: **NDA, ANDA, BLA, Master File** and **Commercial INDs** must be submitted in eCTD format. Submissions that do not adhere to the requirements stated in the eCTD Guidance will be subject to rejection. For more information please visit FDA.gov.[1]

The FDA Electronic Submissions Gateway (ESG) is the central transmission point for sending information electronically to the FDA and enables the secure submission of regulatory information for review. Submissions less than 10 GB must be submitted via the ESG. For submissions that are greater than 10 GB, refer to the FDA technical specification *Specification for Transmitting Electronic Submissions using eCTD Specifications*. For additional information, see FDA.gov.[2]

SECURE EMAIL

Secure email is required for all email communications from FDA when confidential information (e.g., trade secrets, manufacturing, or patient information) is included in the

[1] http://www.fda.gov/ectd

[2] http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway

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If you have any questions, contact CDR Sarah Seung, Regulatory Project Manager, at [redacted] or [redacted].

Sincerely,

{See appended electronic signature page}

Tiffany R. Farchione, MD
Director (Acting)
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

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