IND 063384

CONTINUE 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 December 30, 2019 that provides a response to our September 27, 2019, letter which cited the reasons for continuing the partial clinical hold for IND 063384, specifically for Protocol MT2 entitled, "A Phase 1, Open-Label, Multi-Site Study to Assess Psychological Effects of MDMA-Assisted Psychotherapy when Administered to Healthy Volunteers," and the information needed to resolve the clinical hold issues.

We have completed the review of your submission and have concluded that removal of the clinical hold from the following proposed study is not warranted. Specifically, the following issues have not been resolved:

1. **21 CFR 312.42(b)(1)(i): Unreasonable and significant risk of illness or injury to human subjects**

   Information Needed to Resolve Deficiency: We disagree with your justification of scientific benefit for MT2, Amendment 2. You still have not provided sufficient justification for exposing healthy individuals to the risks of the study drug in your open-label protocol for MT2. It is not clear what, if any, potential benefit healthy volunteers may expect to experience. You must provide an adequate justification for your assertion that the benefits outweigh the risks for healthy individuals in Study MT2. You may need to consider an alternate study design for therapist training that does not involve drug exposure for healthy volunteers.

2. **21 CFR 312.42(b)(1)(ii): Unqualified clinical investigators**

   Information Needed to Resolve Deficiency: Your current description of the Clinical Investigator (CI) Qualifications in your Protocol MT2 remains unacceptable: The CI

and the medical physician are allowed to be off-site and delegate duties to less qualified staff (under 21 CFR 312.42(b)(1)(ii)) to prescribe and monitor the use of an unapproved, Schedule I substance. We do not agree with your justification. Given the known medical risks of the study drug, including previously reported adverse events from your own program, we continue to require the following CI requirements to ensure patient safety, as we discussed in our previous letter from September 27, 2019. You must revise your protocol accordingly:

- On-site physician (i.e., not on-call)

- Lead Facilitator should be a doctoral level PhD/MD-level psychotherapist (or equivalent).

- Co-Facilitator should have a bachelor's degree *and* be trained in mental health. An example of mental health training is a postgraduate internship-type program at an institute to gain more detailed knowledge of mental health interventions and treatments (e.g., mental health counselor, mental health certification for nursing, etc.).

Therefore, the clinical hold on Protocol MT2 remains in effect until you have submitted the required information, and we notify you that you may initiate this clinical study; you may not legally conduct this study under this IND.

Please identify your response to the clinical hold issues as a "**CLINICAL HOLD COMPLETE RESPONSE**."

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.

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
Office of Neuroscience
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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