IND 063384

PARTIAL CLINICAL HOLD

Multidisciplinary Association for Psychedelic Studies (MAPS)
Attention: Amy Emerson
Chief Executive Officer
3141 Stevens Creek Blvd #40563
San Jose, CA 95117

Dear Ms. Emerson:[1]

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-methylenedioxy-methamphetamine (MDMA).

We also refer to your amendment(s) dated November 8, 2021.

The study you proposed, protocol MPG1, titled "An Open-Label Feasibility and Safety Study of MDMA-Assisted Group Therapy for the Treatment of Posttraumatic Stress Disorder in Veterans," is on partial clinical hold and may not be initiated, except as specified.

21 CFR 312.42(b)(2)(i): Unreasonable and significant risk of illness or injury to human subjects

An overnight stay must be required for Protocol MPG1. You have not yet provided sufficient safety data from your no-overnight stay substudies to allow this study to proceed without an overnight stay.

You may not legally initiate or resume Protocol MPG1 until you have submitted the required information and we notify you that you may initiate or resume clinical studies.

Please identify your response to the clinical hold issues as a "**CLINICAL HOLD COMPLETE RESPONSE**." An incomplete response will not start the review clock. Your complete response submission should reference, by date, any information previously submitted necessary to fully respond to these clinical hold issues.

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

[1] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

In addition, we have the following recommendations and/or requests that are not clinical hold issues. Your responses to any non-hold issues should be addressed in a separate amendment to the IND.

1. Please provide an explanation for changing the description of MDMA doses from the MDMA HCl equivalents (e.g., 120 mg initial dose, 40 or 60 mg supplemental dose) as in your other many protocols dating back almost two decades to MDMA (101 mg, 34 mg, or 50 mg). This change creates the appearance of new and different dosing in MPG1, especially in Table 6, and can be confusing.

2. Please explain why the MDMA dosing is 120 mg followed by a supplemental dose of 40 or 60 mg in the MPG1 protocol submitted November 11, 2021. In your protocol (MPVA6 Amendment 5) submitted September 17, 2021, we note that you changed the MDMA dose to 120 mg followed by 40 mg based on new CMC information.

3. Further, please explain the dosing discrepancies in the initial dose of MDMA in your current protocol. If all supplemental doses will be the same for participants based on what is available, does the supplemental dose change between cohorts? If there is no efficacy difference in the 40 or 60 mg supplemental dose (assuming the second dose is tolerated) why is the manufacturing not consistent with the lower dose?

    a. In one place in the protocol it says, “Initial doses per Experimental Session include *101* mg MDMA, followed 1.5 to 2 hours later by a supplemental dose of 34 or 50 mg MDMA (equivalent to 120 mg followed by 40 or 60 mg MDMA HCl).”

    b. In another place it says, “This open-label study will examine the effects of a divided-dose of 134 mg to 150 mg of MDMA (equivalent to 160 mg to 180 mg MDMA HCl) administered in two Experimental Sessions. Participants will receive an initial dose of *100* mg and a supplemental dose of 34 mg or 50 mg MDMA (equivalent to 120 mg and a supplemental dose of 40 mg or 60 mg MDMA HCl) at 1.5-2 hours after initial ingestion, unless tolerability issues emerge with the initial dose or the participant declines. Strength of supplemental dose will be the same for all participants and will be determined by drug supply availability at the start of the trial.”

4. We acknowledge that MPG1 is a feasibility study. Please clarify if you intend on further evaluation of the group MDMA-assisted therapy model. As MPG1 is currently designed, we consider this study to be strictly exploratory. Your current design will not provide an adequate comparison of efficacy between individual and group Experimental and Integrative sessions.

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.[2]

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.[3]

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

Sincerely,

{See appended electronic signature page}

Tiffany R. Farchione, MD
Director
Division of Psychiatry
Office of Neuroscience
Center for Drug Evaluation and Research

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

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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.

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