IND 063384

CONTINUE 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 dated March 17, 2022, that provides a response to our February 28, 2022, letter which cited the reasons for placing Protocol MPG1, titled "An Open-Label Feasibility and Safety Study of MDMA-Assisted Group Therapy for the Treatment of Posttraumatic Stress Disorder in Veterans," on clinical hold 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:

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

Summarized below is the information needed to resolve these deficiencies.

We acknowledge that you provided the no overnight stay safety data from MP16 (N=4) and MAPP1 (N=15). We have further questions about the safety data from the adverse event (AE) table from the substudy in MAPP1 (table below):

1. Provide the cutoff values of systolic and diastolic blood pressure used to determine the threshold for AE reporting. Provide detailed information, including the amount of rise of mm Hg, for the cases in the table. Provide narratives, if available.

2. Provide additional details for the cases of "non-cardiac chest pain." Provide narratives, if available.

[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.

3. Provide the quantitative temperature information, both absolute value and change from baseline, for the cases of pyrexia. Provide narratives, if available.

4. Provide narrative for the cases of stress, intrusive thoughts, and nervousness and the definitions of these AE terms, if available.

5. We note that fewer AEs are reported in patients who did not stay overnight. Please describe how monitoring, vital signs, and AE reporting are conducted for the patients participating in the no overnight stay substudies.

Table 1: MAPS' TEAE Table from Response to Hold letter dated March 17, 2022.

Treatment-emergent AEs with Two-Fold Prevalence in MDMA Group over Placebo, by Overnight Stay

Preferred Term	MDMA-assisted therapy (N=46)		Placebo with therapy (N=44)	
	Overnight (N=37) n (%)	No Overnight (N=9) n (%)	Overnight (N=38) n (%)	No Overnight (N=6) n (%)
Muscle tightness	23 (62.2)	6 (66.7)	3 (7.9)	2 (33.3)
Decreased appetite	18 (48.6)	6 (66.7)	4 (10.5)	1 (16.7)
Nausea	9 (24.3)	5 (55.6)	5 (13.2)	0 (0.0)
Feeling cold	9 (24.3)	0 (0.0)	2 (5.3)	1 (16.7)
Bruxism	6 (16.2)	0 (0.0)	1 (2.6)	0 (0.0)
Dry mouth	5 (13.5)	0 (0.0)	2 (5.3)	0 (0.0)
Mydriasis	7 (18.9)	0 (0.0)	0 (0.0)	0 (0.0)
Dizziness postural	4 (10.8)	2 (22.2)	2 (5.3)	0 (0.0)
Hyperhidrosis	6 (16.2)	3 (33.3)	0 (0.0)	1 (16.7)
Non-cardiac chest pain	5 (13.5)	0 (0.0)	1 (2.6)	0 (0.0)
Blood pressure increased	5 (13.5)	0 (0.0)	0 (0.0)	0 (0.0)
Feeling jittery	5 (13.5)	0 (0.0)	0 (0.0)	0 (0.0)
Nystagmus	5 (13.5)	1 (11.1)	0 (0.0)	0 (0.0)
Pollakiuria	4 (10.8)	0 (0.0)	1 (2.6)	0 (0.0)
Restlessness	5 (13.5)	2 (22.2)	0 (0.0)	0 (0.0)
Musculoskeletal pain	4 (10.8)	0 (0.0)	0 (0.0)	0 (0.0)
Pyrexia	3 (8.1)	0 (0.0)	1 (2.6)	0 (0.0)
Vision blurred	4 (10.8)	0 (0.0)	0 (0.0)	1 (16.7)
Chills	3 (8.1)	0 (0.0)	0 (0.0)	0 (0.0)
Intrusive thoughts	3 (8.1)	1 (11.1)	0 (0.0)	0 (0.0)
Micturition urgency	3 (8.1)	0 (0.0)	0 (0.0)	0 (0.0)
Muscle twitching	3 (8.1)	0 (0.0)	0 (0.0)	0 (0.0)
Nervousness	3 (8.1)	0 (0.0)	0 (0.0)	0 (0.0)
Somnolence	3 (8.1)	0 (0.0)	0 (0.0)	0 (0.0)
Stress	3 (8.1)	1 (11.1)	0 (0.0)	0 (0.0)
Substance use	3 (8.1)	0 (0.0)	0 (0.0)	0 (0.0)
Vomiting	3 (8.1)	1 (11.1)	0 (0.0)	0 (0.0)

The clinical hold on Protocol MPG1 remains in effect until you have submitted the required information. Until 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 you have any questions, contact CDR Sarah Seung, Regulatory Project Manager, at [redacted]

Sincerely,

{See appended electronic signature page}

Tiffany R. Farchione, MD
Director
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/

TIFFANY R FARCHIONE
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