DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

IND 63384

SPECIAL PROTOCOL - AGREEMENT

Multidisciplinary Association for Psychedelic Studies
Attention: Amy Emerson
Executive Director and Director of Clinical Research
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 (FDCA or the Act) for +/-3,4-methylenedioxymethamphetamine (MDMA).

We acknowledge your request received on June 14, 2017 for a special protocol assessment (SPA) of a clinical protocol. The protocol is titled "A Randomized, Double-Blind, Placebo-Controlled, Multi-Site Phase 3 Study of the Efficacy and Safety of Manualized MDMA-Assisted Psychotherapy for the Treatment of Severe Posttraumatic Stress Disorder." We also refer to phone conversation between yourself and Keith Kiedrow, Project Manager, on July 21, 2017, in which you agreed to limit the scope of the SPA to the questions pertaining to the primary endpoint of the protocol, Questions 1 through 3.

We note that this protocol includes revisions discussed in our March 9, 2017, letter and in the May 11, 2017, meeting between you and the Division.

We have completed our review and, based on the information submitted, agree that the design and planned analysis of your study adequately address the objectives necessary to support a regulatory submission. We advise you that, if you make any changes to this protocol, this agreement may be invalidated. If you choose to revise this protocol, submit your modifications as "**Special Protocol Assessment – Amendment**." This agreement is subject to modification only as outlined in section 505(b)(4)(C) of the Act.

As stated in the "Guidance for Industry: Special Protocol Assessment," a special protocol assessment documents our agreement that the design and planned analysis of a study can adequately address objectives in support of a regulatory submission. However, final determinations for marketing application approval are made after a complete review of a marketing application and are based on the entire data in the application.

We also have the following responses to your questions.

1. Has agreement been reached through the SPA process on the Phase 3 protocol design as described in Section 8.0 and based on the MAPP1 Version 2 protocol submitted?

   FDA Response: The protocol design in Section 8 of MAPP1 Version 2 is acceptable. Clinical request not precluding agreement: Please describe the safety assessments during the open-label extension studies.

2. Has agreement been reached through the SPA process on the MAPP1 planned primary analysis as described in Section 8.0 to adequately address objectives in support of an NDA submission?

   FDA Response: Your primary endpoint of the CAPS-5 is acceptable. The MMRM analysis of CAPS-5 scores, as presented in your July 26, 2017, statistical analysis plan, is acceptable..

3. Has agreement been reached in the SPA process related to execution of the MAPP1 study as described in Section 8.0, if replicated in a confirmatory study MAPP2, to form the primary basis of an efficacy claim?

   FDA Response: Yes. Please note that your specific efficacy claim will depend on the studies' results.

If you have any questions please email Ann Sohn, Regulatory Project Manager, at [redacted].

Sincerely,

{See appended electronic signature page}

Mitchell V. Mathis, MD
Director
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 and this page is the manifestation of the electronic signature.

/s/

MITCHELL V Mathis
07/28/2017