DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

IND 63384

ADVICE/INFORMATION REQUEST

Multidisciplinary Association for Psychedelic Studies (MAPS)
Attention: Amy Emerson
Director of Clinical Research
1215 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 N-methyl-3,4-methylenedioxyamphetamine (MDMA).

Please also refer to your submission dated March 1, 2013 containing protocol MAA-1, "A Placebo-controlled, Randomized, Blinded, Phase 2 Pilot Study of MDMA-assisted Therapy for Social Anxiety in Autistic Adults."

We have the following comments and recommendations:

1. The study is reasonably safe to proceed as currently written.

2. Risk of Serotonin Syndrome: Because of the risk of serotonin syndrome, we recommend that patients treated with serotonergic drugs undergo a washout period of longer than 5 half-lives of the drug; the pharmacodynamic effects of such drugs are longer-lasting than the pharmacokinetic effects. Patients treated with fluoxetine should have a washout period of at least one month, because the active metabolite norfluoxetine has a longer half-life than fluoxetine.

3. CYP2D6 Inhibition by MDMA: MDMA is a potent inhibitor of CYP2D6. Furthermore, it is a sensitive substrate of CYPD26. Thus, MDMA significantly inhibits its own metabolism. Patients who require treatment with a drug that is a CYP2D6 inhibitor must be excluded from the study. Patients requiring treatment with a drug primarily metabolized through CYP2D6 must also be excluded from the study. Patients who are CYP2D6 poor metabolizers must be excluded from the study. The protocol must be amended to include these requirements.

4. Patients with cardiac valvular disease should be excluded from the study. During screening, the examining physician must assess for a history of cardiac valvular disease and signs and symptoms of cardiac valvular disease.

As sponsor of this IND, you are responsible for compliance with the FDCA (21 U.S.C. §§ 301 et. seq.) as well as the implementing regulations [Title 21 of the Code of Federal Regulations (CFR)]. A searchable version of these regulations is available at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm. Your responsibilities include:

- Reporting any unexpected fatal or life-threatening suspected adverse reactions to this Division no later than 7 calendar days after initial receipt of the information [21 CFR 312.32(c)(2)]. If your IND is in eCTD format, submit 7-day reports electronically in eCTD format. If your IND is not in eCTD format, you may submit 7-day reports by telephone or fax;

- Reporting any (1) serious, unexpected suspected adverse reactions, (2) findings from other clinical, animal, or in-vitro studies that suggest significant human risk, and (3) a clinically important increase in the rate of a serious suspected adverse reaction to this Division and to all investigators no later than 15 calendar days after determining that the information qualifies for reporting [21 CFR 312.32(c)(1)]. If your IND is in eCTD format, submit 15-day reports to FDA electronically in eCTD format. If your IND is not in eCTD format, you may submit 15-day reports in paper format; and

- Submitting annual progress reports within 60 days of the anniversary of the date that the IND went into effect (the date clinical studies were permitted to begin) [21 CFR 312.33].

If you have any questions, please contact Ann Sohn, Regulatory Project Manager, at ann.sohn@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Mitchell V. Mathis, M.D.
CAPT, USPHS
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 and this page is the manifestation of the electronic signature.

/s/

MITCHELL V Mathis
04/30/2013