

# MDMA-Assisted Psychotherapy in the Treatment of Posttraumatic Stress Disorder (PTSD): Protocol Submitted to FDA on October 1, 2001

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**I** am a psychiatrist in practice in the Charleston, South Carolina area, and am Clinical Assistant Professor of Psychiatry at the Medical University of South Carolina. I'm Board Certified in Psychiatry and was also board certified in Internal Medicine and Emergency Medicine. I'm also a Grof Certified Holotropic Breathwork Facilitator. A large part of my clinical practice consists of treating patients with posttraumatic stress disorder (PTSD).

On October 1, 2001, I submitted an Investigational New Drug Application (IND) to the U.S. Food and Drug Administration requesting permission to conduct a MAPS-sponsored study of MDMA-assisted psychotherapy for the treatment of PTSD. We are proposing a Phase 2 pilot study of twenty patients with chronic PTSD who have not responded to at least one attempt at therapy with a serotonin selective reuptake inhibitor (SSRI) such as Prozac or Zoloft, the only kind of medicine approved by the FDA in the treatment of PTSD. Phase 2 is the first level at which a drug is given to people with a diagnosed disorder to study the possible therapeutic effect. When this study is eventually approved in some form, it will become the first FDA-approved study of the therapeutic use of MDMA ever conducted.

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The treatment phase of the study, as we are proposing it, will consist of two MDMA sessions 3-4 weeks apart, using a single dose of 125 mg for each session. A male-female therapist team will be with the subjects continuously for the 6-8 hours of the session. The therapeutic method will be based on the model developed by Stanislav Grof, M.D., for LSD psychotherapy and Holotropic Breathwork, and recommended for MDMA-assisted therapy by Ralph Metzner, Ph.D., and George Greer, M.D., and Requa Tolbert, MSN.

In this model, particular attention is paid to set and setting. This will involve adequately preparing the subjects and helping them form clear intentions for the sessions, developing a strong therapeutic alliance, and providing a nurturing physical environment with appropriate music to support the MDMA-assisted psychotherapy session. In addition to the two MDMA sessions, there will be a total of twelve 90-minute sessions with the therapists. The first two of these will be devoted to preparation before

the drug sessions. The remaining ten will be to provide support and integration after the sessions.

This will be a “double blind” study in which 12 of the subjects will receive MDMA and 8 will receive an inactive

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placebo. Neither the investigators nor the subjects will know which has been administered. The nature of the treatment and follow-up sessions will be the same for each group. The reason for having a placebo group is to help us distinguish the effects of the intensive therapy sessions alone from the effects of the MDMA in conjunction with the therapy. After 3 months, if the subjects who received placebo are still having PTSD symptoms, they will have the option of having two MDMA-psychotherapy sessions and subsequent follow-up sessions.

At the beginning of the study and at several points after the MDMA-assisted psychotherapy sessions, independent raters will administer psychological rating scales to measure any changes in PTSD symptoms. Neuropsychological testing will also be done at the outset and the completion of the study. Careful medical monitoring will be performed throughout the study period. We recognize that in this small pilot study, we will not be able to prove the presence or absence of a statistically significant therapeutic effect from the MDMA. What we hope to do is to show a strong likelihood of efficacy so we can then apply for a larger Phase 3, trial which would be more definitive.

My fellow investigators on the application are, Mark Wagner, Ph.D. and Annie Mithoefer, BSN. Mark is Associate Professor of Neurology at The Medical University of South Carolina and Director of the Neuropsychology Section. He also has an extensive research background and many publications related to neuropsychology. Much of his clinical work has involved assessment of patient response to pharmacological agents. Annie is a registered nurse and is a Grof Certified Holotropic Breathwork Fa-

ilitator. She and I have had years of experience facilitating Holotropic Breathwork groups together and will be co-therapists for all the MDMA sessions. Matt Baggott, BA and Ilsa Jerome, Ph.D. have spent vast amounts of

time writing a literature review and several other sections that are part of our FDA application. I'm very grateful to have the opportunity

to collaborate with all of them.

Another aspect of this process that's been tremendously exciting and gratifying is the level of support we've received from MAPS and from many people who believe strongly in the importance of this kind of work. Rick Doblin's enthusiasm, encyclopedic knowledge of the issues involved and confidence that MAPS can raise the money for the study, are what allowed me to realize this could be accomplished in the first place. Since then we've received an amazing flow of invaluable advice and encouragement from many experienced clinicians and researchers from across the U.S. and Europe. All their generous help has brought us to this point with the application. Accompanying the application will be letters of support from: Charles Grob, M.D., Chief of Child Psychiatry at UCLA and principal investigator in one of the phase 1 MDMA trials in the U.S., Euphrosyne Gouzoulis-Mayfrank, M.D., one of the leading world authorities on the neuropsychological effects of MDMA, and Franz Vollenweider, M.D., Ph.D., Head of Behavioral Pharmacology at the Psychiatric University Hospital in Zurich, who has done very sophisticated prospective studies using PET scans and psychological testing before and after MDMA. In addition to his letter of support, he is allowing us to include his data, which shows no evidence of adverse effects from MDMA at the doses we will be using.

Now we're eagerly awaiting a response from the FDA, and hope to get started with the study in the near future.

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