Plan for External Evaluation:
MDMA-Assisted Psychotherapy for the Treatment of Posttraumatic Stress Disorder

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The following elements form our plan for external evaluation of the procedures, data collection and analysis and safety monitoring of the proposed study of MDMA-assisted psychotherapy for the treatment of posttraumatic stress disorder (PTSD).

Informed Consent

- Any potential subjects who are or have been patients of Dr. Mithoefer within the last three years must have a 30 minute meeting with another psychiatrist at the sponsor's expense, to discuss the decision about whether or not to participate before signing the informed consent. This psychiatrist will have veto power over a patient's participation, to be exercised if the psychiatrist thinks there is undue influence. In addition, any subjects from Dr. Mithoefer's patient base will meet a second time with this psychiatrist between the first and second MDMA/placebo sessions to ensure that they remain unencumbered by undue influence over whether or not to continue in the study.

Communication with Outside Therapists

Potential subjects who are in treatment will be required to discuss the study with their therapist before agreeing to take part in the study. Dr. Mithoefer will be required to contact their therapist and prescribing physician (if they are on medications) to discuss issues of safety before accepting a patient into the study. If a subject is not currently in treatment, Dr. Mithoefer will be required to talk to their former therapist and physician (this last requirement will be waived only if the therapist or physician is no longer reachable for a reason such as no longer being in practice).

- Dr. Mithoefer will contact each subject's therapist after each MDMA/placebo session to inform them about the patient's experience and any therapeutic gains or potential problems. He will also let them know that he will call them about any significant developments between MDMA/placebo sessions.

- Dr. Mithoefer will give each outside therapist his emergency number and ask the therapist to call if they are aware of any problems developing, have any questions about what we're doing, or have any insights they think would be helpful to us.

Additional Safety Team for Experimental Sessions

There will be a currently practicing, board certified, emergency physician and emergency nurse present in the adjacent room for the first 5 hours of each MDMA/placebo session.

Significant Other to Monitor Patient After Each Experimental Session

All subjects will be required to have a partner, family member or friend who will be with them for at least 24 hours after each treatment session.

External Screening, Outcome Measures and Data Analysis

All assessments will be performed by Mark Wagner, Ph.D. He is a hired consultant, is not involved in any interventions, and is blind to what occurs during therapy and to which subjects are in either the experimental or control groups. Dr. Wagner, though a clinical psychologist, rather than solely a statistician, is very experienced in statistical analysis, as a review of his CV will demonstrate. He is the external statistician who will be hired to analyze and review the results.

Data Safety Monitoring Committee (DSMC)

We propose to add to the DSMC a third physician who is not otherwise associated with the study. We believe there is an advantage to Dr. Mithoefer's remaining on the DSMC because he will have first hand information about what transpires during study sessions. The two other physicians would, together or independently, have a mandate to report any concerns to the IRB and to the FDA even if Dr. Mithoefer were not in agreement.