

## MAPS-Sponsored MDMA/PTSD Research in Israel: An Update

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THE MAPS CLINICAL RESEARCH MONITORING TEAM, consisting of me and MAPS Clinical Program Manager Amy Emerson, along with MAPS President Rick Doblin, met with researchers at Beer Yaakov Menial Health Center on March 7, 2006 and again on March 12. We conducted an initial prestudy site visit to prepare for the MAPS-sponsored MDMA study that will take place in Israel with survivors of war- and terrorism-related PTSD. Moshe Kotler, M.D., Chair of the Department of Psychiatry at the Sackler School of Medicine at Tel Aviv University and former chief psychiatrist of the Israeli Defense Forces, will be the principal investigator for this study. Rael Strous, M.D., and Rakefet Rodriguez, M.D., will act as co-therapists.

This study was approved by the ethics committee at Beer Yaakov Menial Health Center and has also been approved by the Israel Ministry of Health. Later this spring, Dr. Strous and Dr. Rodriguez will observe an experimental session conducted by the Mithoefer's at the site of the MAPS-sponsored MDMA/PTSD study in Charleston, SC, and will participate in an accompanying training session on the specifics of conducting MAPS' MDMA-assisted psychotherapy research. This is a necessary step of preparing the therapists to conduct this type of therapy, and a useful practice as MAPS begins to develop a formal training program for psychedelic therapists. Once this training session has been completed and after MAPS clinical research monitoring team has launched the MDMA/PTSD study in Switzerland, we will begin the logistical preparations for this study. We aim to begin treating patients in Israel later this year.

We are now working to submit supplementary documents to the Israel Ministry of Health and to the US Food and Drug Administration (FDA). This study, although conducted in Israel, will be submitted to FDA under MAPS' Investigational New Drug (IND) application for MDMA in the treatment of PTSD and therefore fits into MAPS' mission of developing MDMA as a prescription medicine approved by both the FDA and the European Medicines Agency.

There are three phases in investigating a drug as a prescription medicine. Phase I involves collecting safety data in animals and humans. Phase II involves several pilot studies administering the drug to human subjects to treat a common indication under slightly different treatment protocols. The current MAPS study in Charleston, SC, the approved studies in Switzerland and Israel, and a proposed study in Spain fall under Phase II. When these Phase II studies are completed, MAPS will submit the data to the FDA and the regulatory agencies in the other countries. We will then apply to begin Phase III, where we will expand to multi-site studies under a shared protocol to test MDMA therapy in the treatment of PTSD on a large sample of subjects. These Phase III multi-site studies, one protocol conducted throughout multiple sites in the US and one protocol conducted throughout multiple sites in Europe and Israel, will each involve about 280 total subjects, cost in the range of \$2.5 million, and take two to three years.

The Israeli study differs from MAPS' original MDMA/PTSD study conducted by Dr. Michael Mithoefer in the US in that it has supplemental dosing halfway through each of the sessions. The Israel study also uses an active placebo of low dose MDMA, rather than an inactive placebo. This will make it more difficult for the therapist and subject to be able to tell whether the subject received an active dose of MDMA or not, increasing the success of the double-blind. In this study we will also collect long-term follow-up data for one year after the second experimental session. The study in Israel also tests the efficacy of using slightly less staff time, since only one therapist is present during some of the non-drug therapy sessions, rather than both therapists. Both therapists are present during all of the experimental sessions where MDMA is administered, and at some of the non-drug therapy sessions.

MAPS Clinical Program Manager Amy Emerson has been of tremendous help in volunteering her time to implement the rigorous standards required by the US FDA and the European Medicines Agency in conducting these clinical trials with MDMA. MAPS Patron Donor Ami Shmitzky has also been very generous in donating \$10,000 to this study and raising an additional \$25,000 of the total of \$100,000 needed to conduct this research. We are now seeking an additional \$65,000 for this study. Please contact the MAPS office if you are interested in making a donation. •

## MAPS-Sponsored Cancer Anxiety Research Dr. John Halpern's Study of MDMA-Assisted Psychotherapy in Subjects with Anxiety Associated with Advanced-Stage Cancer

Rick Doblin, Ph.D.



OVER the last five years, MAPS has donated over \$94,000 to Harvard Medical School-affiliated McLean Hospital in a long-term effort to sponsor Dr. John Halpern's proposed research into the use of MDMA-assisted psychotherapy in advanced-stage cancer patients. This MDMA-assisted psychotherapy study is part of MAPS' overall strategy to become the leader in sponsoring research into both the risks and the benefits of MDMA (Ecstasy). In terms of studies into the risks of Ecstasy, one fruit of MAPS support of Dr. Halpern over the years has been the initiation of the most methodologically well-designed study of the neurocognitive effects of MDMA, to take place in a population of subjects who had used Ecstasy numerous times with minimal use of other drugs. MAPS had brought information about and access to this population to the attention of Dr. Halpern and had donated in excess of \$15,000 to McLean Hospital for an initial pilot study in these subjects. The results of the pilot study were so promising that Dr. Halpern applied for and received a \$1.8 million, five-year grant from the National Institute on Drug Abuse (NIDA), with the grant application containing an acknowledgement of MAPS' support for the pilot study.

On January 19, 2006, we learned that the Drug Enforcement Administration (DEA) had issued the necessary license for Dr. Halpern's study of MDMA-assisted psychotherapy in advanced-stage cancer patients. This meant that final regulatory approval was in hand and the study could begin since additional approvals had previously been obtained in December 2004 from the Food and Drug Administration (FDA) and prior to that from the McLean Hospital's Institutional Review

Board (IRB), the IRB at the Lahey Clinic (where Dr. Todd Shuster, the oncologist who will refer subjects to the study, works) and the Massachusetts Department of Public Health. Yet just when it seemed that MAPS had achieved its long-sought goal of starting this study, it became necessary for MAPS to withdraw from further direct sponsorship of Dr. Halpern's research and from MAPS' parallel effort to sponsor research at McLean Hospital into the use of LSD and psilocybin in the treatment of people suffering from cluster headaches.

Immediately after DEA approval was obtained, I learned that the McLean Hospital administration felt that MAPS' long-term advocacy for MDMA psychotherapy research and general opposition to Prohibition would cause the results of the study to be challenged as biased if MAPS were to sponsor the study and that they did not want McLean to be involved in a study funded by MAPS. Therefore, I decided that it would be best for MAPS to offer to withdraw from further direct financial sponsorship of Dr. Halpern's research so that the study, which we had all labored so long to start, could proceed. Sacrifices sometimes need to be made.

Instead of funding the study, MAPS plans to assist Dr. Halpern in contacting donors interested in giving support directly to McLean Hospital. We believe that this financial distance from MAPS, and more so the rigor of the methodological design of the study itself, will enable the results of the research to be viewed by skeptics as more objective. If the results of the pilot study are promising, MAPS will again explore options for the support of research at McLean Hospital. •

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