

## MDMA-ASSISTED PSYCHOTHERAPY IN THE TREATMENT OF POSTTRAUMATIC STRESS DISORDER (PTSD): A SECOND UPDATE ON THE APPROVAL PROCESS.



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About a year and a half ago, on November 2, 2001, we received FDA approval to conduct a MAPS-sponsored study of MDMA-assisted psychotherapy for the treatment of posttraumatic stress disorder (PTSD). This is the first Phase 2 MDMA study approved in the U.S. In the last issue of the MAPS Bulletin (volume XI number 3), I reported that the FDA was on the verge of granting permission for us to change the proposed study location from a university inpatient unit to an outpatient office setting with extensive emergency equipment and additional back-up medical personnel. On June 14, 2002 we did receive approval for that change. The FDA Division of Neuropharmacological Drug Products, in consultation with the

Division of Cardioresenal Drugs, concluded that with the agreed upon provisions, we would be able to respond to any medical emergency in this setting at least as effectively as in a hospital. We were impressed by the FDA's careful attention to patient safety and their professional approach to discussing and evaluating modifications in our protocol.

The next step was to submit an application for protocol review to a private institutional review board (IRB), as well as applications to the U.S. Drug Enforcement Agency (DEA) and the South Carolina Bureau of Drug Control (SCBDC) for a Schedule I research registration. The chronology of events has been as follows:

**June 19, 2002:** We submitted an application with accompanying copies of our protocol and literature review to The Western IRB (WIRB) in Olympia, Washington, one of the best known private IRBs in the U.S.

**July 3, 2002:** I submitted Schedule I applications to DEA and the South Carolina Board of Drug Control.

**July 10, 2002:** We received notification that our protocol had been approved by the WIRB with some modifications to the informed consent form but no other changes.

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We were pleased to have received IRB approval, and we started to work actively to track, and hopefully expedite, the processing of my DEA application. I had a number of helpful conversations with the DEA field office in Columbia, SC about the security requirements for storing MDMA. In preparation for a site inspection by the DEA field officers we have made arrangements

to have a safe and an alarm system installed in the office. However, before the DEA field office or the SCBDC can act, they need approval from the DEA central office in Washington. The only information we have been able to get from that office, now nine months after my application was submitted, is that it is still under review and that the DEA has enlisted the involvement of a consultant outside the DEA. In phone conversations with DEA officials on January 14 I was told that they had concerns about “safety” but that the review should be finished “soon” and on February 19 that it “should not be long” before they come to a decision. It is my understanding that the DEA’s mission is to guard against drug diversion in pharmacological research, whereas the FDA is the agency with responsibility and expertise regarding safety. It therefore seems inappropriate that safety concerns are holding up my DEA application. Rick Doblin wrote the DEA in January to remind them of this.

#### **A more troublesome series of events occurred with the WIRB:**

- **September 5, 2002:** I received a phone call followed by a letter stating that the WIRB had decided to withdraw their approval of the protocol. At the request of “a WIRB affiliated physician” the board had met to reconsider our application. We were not informed of this meeting until after the fact. The physician (who remains unidentified to us) reportedly raised concerns based largely on telephone conversations with three scientists. We prepared a very thorough response to the WIRB addressing each of the concerns and including additional letters of support from prominent researchers (details available at <http://www.maps.org/research/mdma>). During this process, MAPS president Rick Doblin spoke to two of these scientists and to a co-author of the third in order to foster as much open discussion as possible. We informed the FDA and in-

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vited their input. The FDA, has not, as of yet, requested any changes in the protocol.

- **October 3, 2002:** Rick Doblin had a detailed discussion with the Executive Director of the WIRB. Rick requested that he and I have the opportunity to address the board at their October 30 meeting, when, we were told, they would consider our appeal.

- **October 15, 2002:** We submitted our formal, detailed appeal to the WIRB, addressing all the concerns they had raised in their letter.

- **October 17, 2002:** Rick was informed by phone that the WIRB would not be reviewing the scientific aspects of our appeal on October 30. Instead, the WIRB’s Executive Policy Committee would decide whether there would even be a scientific review at all, at a November 19, 2002 meeting which would address their general policy on “this kind of research,” presumably Schedule I drug research.

- **November 20, 2002:** I received a letter from the WIRB stating that, “Western Institutional Review Board, Inc. (WIRB) has made the decision to not provide institutional review board services for the Multidisciplinary Association for Psychedelic Studies (MAPS). Please find enclosed a refund of your previously paid fees, along with the material you submitted for review.” There was no explanation for their unusual behavior: first approving our protocol, then two months

**“We feel confident that, with persistence and responsiveness, we will be able to secure the approvals we need to move ahead with the study by Summer 2003.”**

later withdrawing approval for alleged scientific reasons, and, when we exercised our right to appeal, declining to review our response to their stated concerns, instead making the decision to terminate their involvement. Not only did they waste a lot of our time, their actions do not appear to be consistent with the responsibility of an IRB to review research protocols based on scientific and safety considerations. This is another disturbing example of non-scientific influences constraining academic and scientific freedom of inquiry.

• **December 17, 2002:** Less than a month after the WIRB returned our application, MAPS submitted the MDMA/PTSD protocol for review to a new IRB in California, Independent Review Consulting, Inc. (IRC-IRB). The IRC-IRB has read the entire correspondence between MAPS and the Western IRB and has indicated its willingness to carefully review the protocol on its merits without bias due to the controversial nature of MDMA-assisted psychotherapy research. Their review of our protocol on January 3 resulted in a long list of questions and concerns. We submitted a thorough written response on January 21, and on January 28 Rick Doblin and I attended the weekly meeting of the review board to respond to their questions and discuss any concerns in person. The board told us they appreciated the thoroughness of our written response, and the meeting had a tone of mutual respect. They asked challenging questions and we had the impression that we had come to agreement on most of the issues raised.

To our surprise, what followed was an eight page letter which, while it indicated a willingness to continue to work toward possible approval, raised two major new obstacles: 1) The idea that we must hire an outside “Contract Re-

search Organization” (for which we got an estimate of \$ 178,000) to monitor data collection, and 2) That we start with a multi-site trial. We feel strongly that neither of these measures would be appropriate at this stage of our research (an initial pilot study). The first is unnecessary and very expensive. The second is impossible because before a multi-site study can be done, the treatment must be standardized in pilot studies. Although subsequent communications with the IRC-IRB has have indicated that the board may not insist on these measures, they have thus far been unable to reach a decision about either of these issues and have tabled discussion, pending a request that MAPS pay for consultants to address some unrelated questions about study design.

MAPS is understandably reluctant to spend this additional money when the board cannot tell us how or when it might reach a decision about the other two major outstanding issues. Therefore, in late February we discussed the study with a third IRB, fully informed them about what has transpired thus far, and were told they would be willing accept our application for review. We submitted that application on March 7, having after two weeks not received anything from the IRC-IRB regarding the promised estimate for the costs of the consultants. We then waited an additional two and half weeks without receiving the estimate before notifying the IRC-IRB on March 25 of our decision to pursue other options.

I am optimistic that our persistence will result in both IRB and DEA approval within the next few months. We appreciate the continued support and hard work from MAPS that makes this persistence possible, and we’re looking forward to moving beyond this application phase and to beginning subject recruitment and the experimental sessions themselves. ■