MDMA-Assisted Psychotherapy in the Treatment of Posttraumatic Stress Disorder (PTSD): A Third Update on the Approval Process

Michael Mithoefer, M.D. (mmit@bellsouth.net)

I have several encouraging developments to report, including the exciting news that we just received Institutional Review Board (IRB) approval for the study on September 23, 2003! I will start with a very brief summary of events that I have described in more detail in previous Bulletin updates.

October 1, 2001	Protocol submitted to FDA
November 2, 2001	FDA approved study to be conducted in inpatient setting
June 14, 2002	FDA approved protocol change to allow study to be conducted in office setting, allowing us to proceed with seeking IRB approval and my DEA Schedule I license
June 19, 2002	Application submitted to Western Institutional Review Board (WIRB)
July 8, 2002	Application for Schedule I research license submitted to DEA
July 10, 2002	Approval by WIRB
September 5, 2002	WIRB withdrew approval citing safety concerns, which we responded to in writing and by scheduling a meeting with the board
November 19, 2002	WIRB notified us they had made an administrative decision to terminate involvement with our study rather than hold the previously scheduled meeting to discuss our response to safety concerns
December 17, 2002	Application submitted to Independent Review Consultants (IRC), another independent IRB which agreed to review our protocol

In my last Bulletin update I reported that we'd had extensive correspondence and discussions (including a meeting Rick Doblin and I had with them in person) with the IRC IRB. As I also reported, our dealings with them seemed very promising for some time, but to our surprise they suddenly came up with a number of new demands that we did not feel were reasonable. On March 25, 2003 we notified them that we no longer desired their services because of the impasse created by their unusual demands. Interestingly, we later learned that the IRC had been receiving a lot of pressure (from a source they would not name) not to approve our protocol. This was reminiscent of the sudden reversal we'd experienced from the WIRB. While we still don't have an explanation for the unconventional behavior of the WIRB, in light of recent events it is interesting to look back at the sequence of events surrounding their decisions. The WIRB told us that one of the scientists who had raised safety concerns to them was Dr. Una McCann from Johns Hopkins. She and her husband George Ricaurte are both authors of a paper that came out in *Science* on September 25, 2002, claiming that MDMA caused dopamine toxicity and death in primates. This was six days after the WIRB had terminated working with us. As Rick Doblin discusses in detail elsewhere in this issue, Ricaurte and McCann have recently retracted this paper because it turns out they mistakenly administered methamphetamine, not MDMA, to the primates in

this and apparently in some other studies.

For a couple of months after the IRC IRB didn't work out, Rick continued to search for an IRB that would be willing to take on this controversial project. We submitted extensive information to an IRB in Canada and another in the US who indicated they might be interested, but both ultimately declined to formally review the protocol. In May and June of 2003 we began to seriously explore the possibility of forming a MAPS IRB. Rick had extensive talks with the FDA and learned that there are many precedents for doing so, and it would be perfectly acceptable for MAPS to have its own IRB. We were gratified to find a panel of very experienced and distinguished scientists and lay people who agreed to volunteer their time to serve on a MAPS IRB.

"The DEA agents were interested in helping us understand and follow their rules, and were quite reasonable."

During this time we also heard from one more independent IRB in the US, to which Rick had previously sent an inquiry. They said they would accept the protocol for review. Although we felt confident that the MAPS IRB would certainly have the expertise to evaluate and oversee our research, and that the reputations of the individuals on the board would make their objectivity difficult for anyone to question, we decided that it was worth one more try to work with an independent IRB.

This final IRB, which prefers to remain anonymous in the media, has proved to be very thorough and exacting, but is also thoughtful and reasonable. We submitted our initial application to them on June 17, 2003. Over the next three months they held three meetings to review the protocol, and we responded to the various questions, suggestions and revisions that arose from our extensive correspondence and phone discussions with them. In addition to their own board members, they hired an independent posttraumatic stress disorder expert to advise them. All this resulted in a successful collaborative process that led to improvements in the protocol and to IRB approval of the study on September 23, 2003. A complete list of the protocol changes that resulted is posted on the MAPS website. The most significant of these is that now subjects will stay in the clinic overnight following each MDMA or placebo session. A registered nurse of the same gender as the subject will be hired to stay with them from the time Annie and I (the co-therapists for the study) leave in the evening until we return for the follow-up therapy session the next morning. We will give these nurses specific training about how to be present with subjects after an MDMA session in a supportive but non-intrusive manner. Using an RN rather than a less highly paid attendant is a compromise we agreed upon to satisfy the board. Requiring subjects to spend the night, however, is a change we are enthusiastic about. This will provide the advantage of a longer period of integration in a quiet, supportive setting without the distractions of the outside world.

The only remaining regulatory hurdle is my DEA Schedule I license. On October 28, agents from both the regional DEA office and the South Carolina Bureau of Drug Control inspected my office. The inspection, which is a routine step in the processing of a Schedule I license, went very well. The inspectors focused on issues of diversion control and checked out the safe, the alarm system and the forms and procedures that will be used to track all of the MDMA and placebo capsules. The DEA agents were interested in helping us understand and follow their rules, and were quite reasonable. I expect to receive my license in several weeks to several months. If so, we should be able to start recruiting subjects in early 2004. I realize I've made overoptimistic predictions before about when we'll start, but one of these times I'm going to be right. ■