RESEARCH AGENDA

ibogaine research

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IN NOVEMBER 1995, MAPS donated $25,000 to the FDA-approved Phase 1 ibogaine dose-response safety study being conducted by Juan Sanchez-Ramos, M.D. and Deborah Mash, Ph.D. at the University of Miami. This represents the single largest donation to date that MAPS has ever made to a specific research project. (MAPS' donations to MDMA research have exceeded that amount in total but have been disbursed to several different projects.) Funds for this donation came from two sources, $21,000 from the bequest of Eric Bass and $4,000 from a person in the music business in Seattle who has seen the detrimental effects on musicians of heroin and cocaine addiction and wanted to support MAPS' efforts to find a treatment.

MAPS' $25,000 donation covered the costs to analyze the effects of ibogaine on six subjects administered a dose of 2 mg/kg, the second dose level in the dose-response study. The information gathered as a result of MAPS' donation will be used as pilot data to support a grant application to the National Institute on Drug Abuse (NIDA) for the approximately $200,000 that is needed to complete the Phase 1 study. This safety study is a prerequisite to the crucial Phase 2 study into the use of ibogaine in the treatment of heroin and cocaine addiction. The Phase 2 study will address whether or not ibogaine has efficacy in the treatment of substance abuse disorders.

In 1996, MAPS will work to find additional resources for the Phase 1 ibogaine safety study if the NIDA grant application is not successful. It would be a tragic shame if all the necessary regulatory approvals to conduct ibogaine research were obtained yet the research came to an end due to a lack of funds.

What is Ibogaine?

Ibogaine is derived from the *Tabernanthe iboga* plant which is used for religious purposes in western Africa, principally Gabon. Iboga is used in a manner somewhat similar to the religious and traditional medical use of peyote by the Native American Church in the United States and the use of ayahuasca tea by the União do Vegetal and the Santo Daime churches in Brazil. Ibogaine is, however, generally administered only a few times during a person's lifetime.

Interest in ibogaine's therapeutic use as a treatment of heroin and cocaine addiction is primarily the result of the efforts of several ex-addicts who were able to break their patterns of addiction after some fortuitous experiences with ibogaine. In some cases, they formed addict self-help groups to administer ibogaine to other addicts and in one case established a corporation, NDA International Inc., to pursue formal development of ibogaine within the context of FDA regulations. Ibogaine is somewhat similar to LSD and the other classic psychedelics but has unique effects. The two preeminent therapists who worked with ibogaine, Dr. Claudia Naranjo and "Jacob" (see p.15), treated about 700 patients between them and considered it to have exceptional therapeutic potential.

The Phase 1 Safety Study

The FDA-approved Phase 1 ibogaine safety study is proceeding very cautiously. The therapeutic dose of ibogaine is in the range of 15 to 20 mg/kg, yet the FDA has only given permission for the researchers to administer ibogaine to three subjects at the 1 mg/kg dose level and to six subjects at each of the four following dose levels; 2 mg/kg, 4 mg/kg, 6 mg/kg, and 8 mg/kg. After the current 2 mg/kg

dose level has been administered to six subjects, the data must be analyzed and submitted to an external committee for review. After evaluation of all the available data to assess safety is completed and reviewed by a team of experts, then the researchers may proceed to the next higher dose. Once all the data has been gathered from the 1 mg/kg, 2 mg/kg, 4 mg/kg, 6 mg/kg, and 8 mg/kg dose levels, a more comprehensive review will take place to determine if the research can proceed into the testing of doses that will approach the therapeutic dose range. All of these data will be presented to the FDA for the next evaluation prior to protocol revision.

Only male subjects are being permitted to volunteer for this initial safety study because of the reported deaths of two women that were associated with, but perhaps not solely caused by, the administration of ibogaine outside of hospital settings. While a matter of the utmost concern, these deaths have not stopped all research with ibogaine because their causes are uncertain, thousands of people have taken ibogaine without incident, drug addiction itself is often fatal and the available treatments for addiction have a relatively low success rate. The acceptable level of risk for potentially fatal diseases such as addiction and cancer is higher than that for treatments of diseases with less severe consequences or more effective treatments. For example, drugs used for the treatment of cancer can sometimes themselves be fatal, a situation which occasionally does occur without causing physicians to abandon the therapeutic uses of these medications.

According to Howard Lotsof, President of NDA International, both screening for possible ibogaine sensitivity and an antidote for idiosyncratic toxicity will most likely be available within six months. These developments will allow the treatment of female subjects at full therapeutic doses outside of the United States in NDA's ongoing ibogaine treatment program in the Republic of Panama.

NIDA and Ibogaine Research

Over the course of the last five years, NIDA's Medications Development Division (MDD) has taken an interest in ibogaine's therapeutic potential and has invested several million dollars into ibogaine-related preclinical animal research. These studies have demonstrated that ibogaine can reduce the self-administration of addictive substances as well as the symptoms of withdrawal. Some evidence of neurotoxicity has been discovered in animal models at doses well in excess of the human therapeutic dose range but not at therapeutic dose levels. The clinical significance of these findings to the use of therapeutic doses in humans is unclear.

Since October 1993, MDD has explored the possibility of funding human trials with ibogaine in a series of protocol development meetings that involved the convening of many experts in the fields of ibogaine pre-clinical research, basic human clinical research, and human psychedelic research. These meetings alone probably cost in excess of $100,000.

In late 1994, MAPS helped arrange a direct donation of $25,000 to Drs. Sanchez-Ramos and Mash's ibogaine research from an anonymous philanthropist. This funding paid for the costs of administering 1 mg/kg to several subjects and for gathering some data about neurotoxicity. Drs. Sanchez-Ramos and Mash reported on these findings at NIDA's protocol development meetings and used the data to support their request for NIDA funding for the human testing of ibogaine.

By the end of 1995, it was clear that MDD was not convinced of ibogaine's potential and was not imminently planning to fund human research. Although the FDA had approved research on the safety of ibogaine, Drs.Sanchez-Ramos and Mash were left without a source of private or federal funding. As a result, all human research with ibogaine was in danger of ending. Rather than see all the preliminary work go to waste and lose the chance to evaluate the therapeutic potential of ibogaine in the treatment of addiction, MAPS allocated $25,000 to the ibogaine safety study. The pilot data gathered will keep the project alive and will be used as the basis for a NIDA RO1 peer reviewed grant application to fully fund the Phase 1 safety study. The application is due February 21, 1996, with a decision expected several months later.

MAPS' $25,000 Investment

The decision to invest $25,000 in the ibogaine study was not made lightly. It is quite possible that NIDA's peer review process will decide not to support the remainder of the safety study and that alternative sources of funding will not be found. If the ibogaine research is halted for lack of funds, perhaps the $25,000 could have done more good if it had been invested elsewhere.

The donation was made after consultations with Howard Lotsof, who felt that a donation to the Miami project was the most

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important support that could be offered to ibogaine research, and with the members of the Heffter Research Institute's Board of Directors, who felt that the donation compared favorably with alternative investments in psychedelic research.

The decision to make the investment was based on several factors. Foremost among them was that the ibogaine project provides an excellent opportunity to demonstrate that the psychedelic community cares about the problem of addiction and indeed may have something very valuable to offer. MAPS' donation of a substantial portion of its precious resources to the ibogaine project was the best way I could see to try to build common cause with the larger community of people involved in the prevention and treatment of drug abuse. By focusing such a substantial portion of MAPS' resources on the ibogaine project, it will perhaps become evident that while strategies toward reducing the costs of drug abuse may differ, concern over the pain of drug abuse is shared equally by those who support the therapeutic uses of psychedelics and those who fear that possibility. When supporters of the view that drugs are not good or bad in themselves but have good and bad uses depending on a variety of factors are no longer characterized as "the enemy within," perhaps then we can begin to heal the modern day civil war over drug use.

One Door Closes, One Door Opens

Another factor that contributed to MAPS' $25,000 donation to ibogaine research is that MAPS had pledged $25,000 out of the bequest of Eric Bass to Dr. Rick Strassman for his proposed pilot study of the use of psilocybin in the psychotherapeutic treatment of AIDS and cancer patients. This Phase 2 efficacy study is exactly the kind of experiment that MAPS seeks to support in that it stood an excellent chance of generating promising results that could have attracted larger amounts of funding from more traditional sources. The psilocybin project would also have complemented Dr. Grob's proposed study into the use of MDMA in the treatment of cancer patients. However, Dr. Strassman's decision to end the first phase of his career in psychedelic research and move to Canada for personal and family reasons meant that his proposed study would not take place. In addition to freeing $25,000 for other purposes, the ending of Dr. Strassman's psilocybin and DMT research made it even more important for the field of psychedelic research that MAPS try to keep the ibogaine project from prematurely closing down as well.

Time will tell if NIDA or some other funding source will support the ibogaine research that MAPS has enabled to continue for a few more months. In any case, all of MAPS' projects are just small steps on a path for which all the required resources are not in hand or even within sight. As the saying goes, while we are not required to complete the task of making the world a better place, neither are we permitted to do nothing.•