the national institute on drug abuse and the may 16,1994 **ibogaine** protocol development meeting

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A MOST REMARKABLE DISCUSSION about scientific research into ibogaine, a psychoactive alkaloid derived from a root found in Africa, took place on May 16, 1994 under the auspices of the Medications Development Division (MDD) of the National Institute on Drug Abuse (NIDA). The meeting was the second in a series (the first was on October 28,1993) whose purpose is to assist MDD in choosing the most appropriate methodological design for an initial ibogaine safety study. What made the meeting all the more remarkable is that NIDA intends to provide all the necessary funding for the safety study.

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Furthermore, if the results of the safety study are encouraging, NIDA might fund subsequent efficacy studies into the use of ibogaine to treat cocaine abusers. NIDA's efforts concerning ibogaine have come about as a result of a long-term campaign by Howard Lotsof of NDA International, Inc., Bob Sisko of the International Coalition for Addict Self-Help (ICASH) and a growing number of other people who have seen first-hand the therapeutic potential of ibogaine. The development of new treatments for drug abuse is a national priority.

Now that NIDA has decided to enter the field of ibogaine research, it is sparing no expense in gathering the required data. Its leisurely timetable, however, leaves something to be desired. NIDA's ibogaine protocol development meeting involved about 60 invited participants from around the country. Among the participants familiar to readers of past issues of the MAPS newsletter were Dr. Rick Strassman, DMT and psilocybin researcher from the University of New Mexico; Dr. J. Sanchez-Ramos and Dr. Deborah Mash, ibogaine researchers from the University of Miami; Howard Lotsof and Bob Sisko; Richard Yensen, Ph.D. and Dr. Donna Dryer, LSD researchers; and Dr. Curtis Wright of the FDA. Also present were representatives of the Drug Enforcement Administration, the National Institute of Mental Health, the White House Office of National Drug Control Policy, and MAPS.

Protocol Design

The protocol design proposed by MDD is called a double-blind dose run-up study. In a design of this type, small doses are tested for safety in one group of subjects before higher doses are administered to another group. This study will involve four different groups of fifteen people each. Twelve of the people in each group will receive the same dose of ibogaine, and three will receive a placebo. The first group will be administered 150 milligrams of ibogaine, about one-sixth of a full therapeutic dose. If all goes well, subsequent groups will receive 300 mg, 600 mg, and 900 mg. The final dose of 900 mg is on the low end of the therapeutic range. After 12 subjects have received the same initial dose of ibogaine and 3 people have received the placebo, the data will be evaluated to determine whether it is safe to administer the next highest dose (or placebo) to another group of 15 people. Due to the complexity of the study, scientists at two or three different research centers will simultaneously conduct the research, pooling their data. Subjects will be evaluated for acute and long-term psychological and physiological effects. Various data will be collected prior to

the administration of the ibogaine or placebo, during the time of administration, within the next two days, and at one week, one month, three month, six month, nine month, and one year intervals. The effects to be measured are grouped into three distinct categories; neurological, cardiovascular and general bodily functions. The neurological evaluation will include a battery of tests of cognitive function, psychiatric state of mind, and neuro-psychological functioning. Special attention will be devoted to motor control, since very high doses of ibogaine given to rats demonstrated some neurotoxicity in an area of the brain that influences motor control.

This was not evident in primates. Acute psychological effects will be measured by Dr. Strassman's Hallucinogen Rating Scale as well as the Psychosis Scale of the Brief Psychiatric Rating Scale. The cardiovascular evaluation will include measurement of pulse and blood pressure, and electrocardiographs. The general bodily function tests will include measures of temperature and respiration, and multiple blood tests and urinanalysis. Pharmacokinetics tests will also be conducted.

NIDA's study is not intended to prove or disprove the efficacy of ibogaine in treating patients with a cocaine-related substance abuse problem. In fact, many of the tests designed to gather safety data may interfere with the efficacy of the treatment. Nevertheless, preliminary data will be gathered about efficacy using urine tests, measures of the intensity of craving for cocaine, and reports from subjects and counselors.

"Go- No Go" Rules

From my perspective, there was one defining moment of the entire meeting. This revealing moment took place during a discussion of the proposed "go- no go" rules. These rules would govern the review of the safety data from one dose level and guide FDA and NIDA in determining if it was appropriate to administer the next higher dosage level (or placebo) to fifteen more subjects. Dr. Sanchez-Ramos volunteered that perhaps it might be wise to stop the study if any evidence of neurotoxicity were to be determined, even if there were no significant functional or behavioral consequences at that dose level. In response, Dr. Curtis Wright of FDA made the point that substance abuse is a very serious problem with an often fatal outcome. Dr. Wright reminded everyone that the drug approval process involves weighing risks against benefits, and that some risk of neurotoxicity could be accepted if a counterbalancing benefit of ibogaine was the elimination or significant reduction of episodes of drug abuse. This interchange revealed that a generation of repression has sometimes made psychedelic researchers act more cautious than good medicine requires. It also showed that the winds of change at the FDA (begun in the Bush administration) have resulted in sensible and helpful regulators who are willing to give psychedelics a fair review.

Single or multiple dosing

The main concern I have about the protocol is that it involves only one administration of ibogaine to each subject. Unfortunately, this ensures that the data will not be completely relevant to the most likely use of ibogaine in therapy. Ibogaine is not a miracle cure, as the proponents of the therapeutic use of ibogaine all now admit. Most drug abusers will probably need to receive several doses over the course of one or two years, along with a great deal of other non-drug therapy and support. NIDA's protocol could be revised at this point to include multiple administrations. A "go- no go" rule could easily be prepared to determine whether it was safe to administer a second dose to a subject. If the design is not revised before the study is initiated, it will take much longer to get this necessary data.

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The fact that NIDA is planning to conduct and fund this safety study is remarkably good news, and represents significant progress. NIDA deserves a great deal of credit for going ahead with this study. Nevertheless, a more rapid timetable need not result in any lowering of the quality of data that will be gathered. Given the seriousness of the problem of cocaine abuse, too slowly developing a useful medicine can be as bad as approving a useless or harmful medicine. Still, NIDA needs time to develop its expertise in psychedelic research. Those of us who support ibogaine research should apreciate NIDA's effort. With some luck, NIDA will add "respected psychedelic research agency" to the list of things it can be. ■