THE MDMA PHASE 1 PROTOCOL: EXPERIMENTAL DESIGN AND METHODS

This is a Phase 1 safety and tolerance study designed to determine the psychological and analgesic threshold level for MDMA.

Type of Study

This is a Phase 1 safety and tolerance study designed to determine the psychological and analgesic threshold level for MDMA. We will gather preliminary data on MDMA's effect on vital signs and, through blood analysis, on organ and immunological systems. Pharmacokinetic and neuropsychological studies will also be conducted.

Number of Subjects

There will be six subjects in this study.

Inclusion Criteria

Subjects must work full-time in the health care industry in professions such as physician, psychologist or nurse. Subjects must have previously self-administered MDMA and be between the ages of 25 and 55 years. Subjects must be willing to receive two doses of MDMA and a placebo as well as several blood, urine, and psychological tests. In addition, subjects must be willing to refrain from taking any psychiatric drugs during the experiment. Female subjects of child-bearing potential must have a negative pregnancy test and agree to use an effective form of birth control.

Exclusion Criteria

Subjects who have a history of schizophrenia, bipolar affective disorder, delusional disorder, paranoid disorder, or schizoaffective disorder will be excluded, as will any subjects who exhibit psychotic symptoms or have a history of epileptic seizures. Subjects who currently have a substance abuse disorder, or who have severe cardiovascular problems will also be excluded. Female subjects who are pregnant or who are not utilizing effective means of birth control will be excluded.

Dosing Plan

All subjects will participate in three experimental sessions. The experimental sessions will be separated by at least two weeks and at most four weeks from the previous session. All six subjects will be expected to gather together for all the sessions. Subjects will be permitted to skip only one session due to scheduling conflicts. A fourth make-up session will be scheduled if needed.

Each session will involve the oral administration of one capsule to each subject. In the course of the experiment, each subject will receive two different doses of MDMA and an inactive placebo. In the two MDMA sessions, the capsules will contain MDMA in the amounts of .15 and .75 mg/kg. These amounts are intended to produce the following effects:

1) a predicted below threshold dose (.15mg/kg)
2) a predicted threshold dose (.75 mg/kg)

The order in which the capsules will be presented will be randomized on a per subject basis with each subject receiving each of the three possible doses only once. All subjects, investigators, and independent raters will be blind as to which capsule was presented during any specific session.

All experimental sessions will begin at 10:00 am and will take place in the UCI Medical Center. The investigator/psychotherapist and a research assistant will be present and available throughout the session to tend to each subject's needs and handle any difficulties that might arise. Sessions will last four and a half hours. Automobile rides home will be prearranged so that subjects will not have to drive after the sessions. A psychiatrist will be on call 24-hours a day, seven days a week to handle any concerns or emergencies related to the protocol.

METHODS OF ANALYSIS

Organ Function and Vital Signs

Subjects will have blood drawn immediately before the first session begins and two weeks after the last treatment session. Complete blood workups will be conducted including hematologic, hepatic and renal analysis. Immunological

MDMA RESEARCH - REGULATORY STATUS

We have begun our final set of applications and expect to receive approvals fairly soon. Though the FDA has approved this Phase 1 study, the California Research Advisory Panel must also approve the experiment and the Drug Enforcement Administration must approve the experimenters. Furthermore, the UC Irvine Human Subjects Committee has to approve this specific protocol, even though it previously approved a much larger and more delicate study of the use of MDMA to treat pain and distress in end-stage cancer patients. This experiment will hopefully begin in early 1993. The cancer patient study will probably start after the Phase 1 research is well underway, hopefully in mid 1993.

parameters will also be analyzed. Vital signs and temperature will be monitored every half an hour.

Acute Psychological Effects

The acute psychological effects of the treatments will be measured through the use of the Brief Profile of Mood States-SR (POMS-SR) (McNair et al, 1971) and the State-Trait Anxiety Inventory (STAI) (Spielberger, 1983). These tests will be administered to all subjects before the experimental sessions begin and at the first, second, third and fourth hours of the session. The Hallucinogenic Rating Scale (HRS), currently under development by Dr. R. J. Strassman, will be administered at the fourth hour immediately after the POMS and the STAI.

Pain

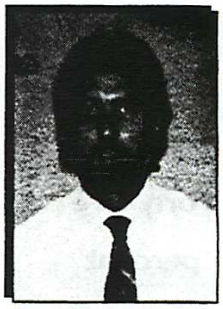
All subjects will have a cold-pressor pain test administered thirty minutes before each experimental session begins and again at a half hour, an hour and a half, two and a half, three and a half, and four and a half hours post-treatment.

Neuropsychological Effects

A battery of neuropsychological tests to include the Verbal Selective Reminding Test with delayed free and multiple choice recall, Wechsler Adult Intelligence Scale (WAIS-R) Digit Span, WAIS-R Arithmetic, WAIS-R Digit Symbol, Trail Making Tests A &B, Controlled Oral Word Association Test, a series of 20-point Likert-type scales with endpoints of "Extreme Decrease"/-10 to "Extreme Increase"/+10 for four groups of subjective effects; hallucinogen-associated symptoms, amphetamine-like symptoms, acute psychosis and mood, and other symptoms, and the Profile of Mood States, will be administered one week before the first and one week after the last session.

Pharmacokinetics

Blood for pharmacokinetic analysis will be drawn from each subject once during each session at the time of peak blood level concentrations, as determined by Swiss researcher Dr. Helmlin. ■



Dr. Charles Grob

Dr. Gary Bravo

Human studies with MDMA are now possible. To support this study see MAPS membership information on page 34 – 35.

PSYCHEDELICS AND THE AMERICAN PSYCHIATRIC ASSOCIATION

Charles Grob, M.D. of the University of California, Irvine and Rick Strassman, M.D. of the University of New Mexico have recently been informed by the American Psychiatric Association (APA) that their workshop submission on "Human Research with Hallucinogens" has been accepted for presentation at the APA's annual meeting in May, 1993 in San Francisco. Drs. Grob and Strassman plan to review the history of psychiatric research with hallucinogens, including an update on recent developments in the field. The progress and current status of human research protocols with N,N-dimethyltryptamine (DMT), psilocybin, 3,4-methylenedioxymethamphetamine (MDMA) and ayahuasca will be presented. This will be the first presentation at the APA in many years of human research and clinical potentials of hallucinogens.