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A Time of Tests

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MAPS HAS BEEN experiencing growing pains since the last newsletter was mailed to members. MAPS has been successful in enlarging its membership base, several research projects that MAPS is coordinating are coming to fruition, and the field of psychedelic research in general is experiencing a renaissance. The flow of mail, phone calls, and e-mail messages has increased (MAPS now has an internet address on America On Line: RICKMAPS@aol.com), as has the number of requests from the media for information (see article on drug trends in Newsweek, December 6, p. 62). MAPS' expanding opportunities and responsibilities have also coincided with a very personal and joyous but time-consuming series of celebrations, namely my marriage. ■ This MAPS newsletter is written almost entirely by myself, unlike the last issue which was more like a journal. MAPS has so many projects underway that I wanted to let you know about them in some detail. I should have more time to put out a lengthier newsletter with the next issue. Very fortunately, MAPS has recently obtained the part-time assistance of Sylvia Thyssen, a bilingual University of North Carolina at Chapel Hill liberal arts graduate (page 12). If contributions to MAPS are sufficient, it is our hope that Sylvia will be able to work full-time for MAPS in the not too distant future. ■ MAPS' growing pains are primarily a result of the recent developments in MDMA and marijuana research. After eight years of effort, FDA-approved Phase 1 human studies with MDMA are commencing at UCLA's Harbor Hospital under the direction of Dr. Charles Grob (page 2). MAPS recently donated $2,700 to pay for high-tech brain scans for two of Dr. Grob's experimental subjects. Research into the use of MDMA in the treatment of pain and distress in cancer patients will follow after the Phase 1 study. ■ During the last several months, three additional MAPS-coordinated research projects have cleared most of the hurdles required prior to actual implementation. Dr. Donald Abrams' marijuana project exploring the use of smoked marijuana in the treatment of the HIV-related wasting syndrome has been approved by the FDA (page 5). The MAPS-California NORML project to investigate the effectiveness of water pipes in filtering marijuana smoke will begin in early 1994. The necessary $28,800 has been obtained, due in part to the generous gift of $18,000 from a MAPS member who gave $14,000 and also bid $2,000 each for the two original Doonesberry cartoon strips donated to MAPS by Garry Trudeau (page 10). An exciting new MDMA research project, not previously discussed in any MAPS newsletter, will explore the use of MDMA-assisted psychotherapy in the treatment of post-traumatic stress related to war trauma. This study will take place at the Military Hospital in Managua, Nicaragua. Permission for the study has been granted by the Nicaraguan Minister of Health (page 3). ■ After enormous and sustained effort by advocates, the FDA has approved Phase 1 human trials designed to explore the physiological and psychological effects of the African psychedelic root, ibogaine. Phase 2 trials examining the use of ibogaine in the treatment of cocaine addiction will follow (page 4). ■ Your previous support of MAPS has nurtured the infant field of psychedelic research. Your continued support will help enable the field to continue its long, slow walk toward scientific maturity and social sanction. ■ Rick Doblin, *MAPS President*

We Begin! — The First FDA-Approved Study of the Effects of MDMA on Human Volunteers

ALL THE NECESSARY permissions, approvals, sign-offs, shipping forms, and scientific protocols are in place for the first ever FDA-approved human research with MDMA. Around New Years' Day, 1994, Dr. Charles Grob's pharmacy at Harbor UCLA Medical Center will receive a supply of legal MDMA from Dr. David Nichols of the Department of Medicinal Chemistry at Purdue University. Dr. Nichols, who under DEA license also manufactured Dr. Rick Strassman's DMT and psilocybin, originally made MDMA for research purposes in 1985. At the time, we weren't sure if we would ever be able to administer the MDMA to humans instead of just to research animals. Though it took eight long years to reach this point, it was well worth the effort.

Dr. Grob's original FDA-approved protocol involved the administration of two doses of MDMA and one dose of placebo to six people, along with a limited variety of physiological and psychological tests. However, in the intervening time between FDA-approval and all the other required approvals, Dr. Grob developed a collaboration with Russell Poland, Ph.D., a fellow UCLA faculty member who is an expert in the assessment of the effect of drugs on brain neurochemistry. As a consequence, the phase one study has been substantially expanded to clarify more exhaustively MDMA's physiological effects. MDMA pharmacokinetic studies will also be added to the study, as will fenfluramine challenge tests designed to probe the function of the subjects' serotonin system. Since serotonin is involved with the regulation of sleep, special sleep EEG studies will be conducted. Subjects in the study will also receive high-tech brain scans (Magnetic Resonance Imaging) and computer-enhanced analysis of brain wave patterns (SPECT). These tests will permit a more thorough evaluation of MDMA's short and long term effects on the serotonin system and its functional correlates. MAPS' donation of $2,700 towards the expenses of this study will cover the cost of these scans for two subjects.

Seekng Government Funding

Drs. Grob and Poland are also interested in conducting a separate study similar in design to Dr. George Ricaurte and Dr. Una McCann's multi-year investigation of the physiological and psychological differences between a group of MDMA users and a group of matched controls. Drs. Grob and Poland will thankfully substitute high-tech brain scans for spinal taps. Due to the substantially increased complexity and cost of Dr. Grob and Poland's Phase 1 MDMA study, and also to their plan to conduct another study involving matched controls, they are planning to apply to the National Institute on Drug Abuse (NIDA) for a grant for their MDMA research. The grant application is due February 1,1994 with the awards being announced about December, 1994. From now until February 1, Drs. Grob and Poland will be testing several subjects so as to gather preliminary pilot data to support their grant application.

MAPS' donation ($2,000 of which was raised from the conference commemorating the 50th anniversary of LSD and the remaining $700 from membership donations) will be used to help gather pilot data for the NIDA grant application. In this way, MAPS is using its relatively limited resources strategically, allowing Drs. Grob and Poland to use a small donation from MAPS in ways which enhance their efforts to secure a large grant from NIDA. This strategy has worked well in the past when MAPS offered some early assistance to Dr. Ricaurte so that he could gather preliminary MDMA neurotoxicity data from primates and MDMA users who volunteered for spinal taps. With the help of skilled researchers and a little luck, the strategy has an excellent chance of working again.

the phase one study has been substantially expanded

From February 1, 1994 until about the end of the year, when NIDA is supposed to decide whether or not to support their enlarged study, Drs. Grob and Poland will proceed with their Phase 1 study as far as their funds allow. In other words, donations are still needed to facilitate this project. (If interested in volunteering for the experiment, call Carla Edwards at Harbor UCLA Medical Center: (310) 222-1663. Subjects from southern California preferred; the study requires subjects to go the lab from 7–10 different days and/or nights.)

MDMA Cancer Study

It is our hope that enough basic Phase 1 safety data will be gathered by the fall of 1994 so that the FDA will permit Dr. Grob to initiate the Phase 2 study of the efficacy of MDMA in the reduction of pain and distress in terminal cancer patients. This MDMA study will focus on one of the most important areas of research in modern medicine, namely the mind-body connection. Dr. Grob and co-researchers will seek to determine whether MDMA-assisted psychotherapy and guided imagery can help patients reduce their sensitivity to pain and lessen the number of deadening narcotic painkillers they need, stimulate their immune system to fight their cancer, and help people deal more effectively with the emotions surrounding terminal illness. ■

The Nicaragua Project: MDMA in the Treatment of Post-Traumatic Stress Disorder Related to War Trauma

I AM ESPECIALLY PROUD to be able to announce a new MAPS project that has not previously been mentioned in the MAPS newsletter. This project will help evaluate the safety and effectiveness of MDMA-assisted psychotherapy in the treatment of patients suffering from post-traumatic stress disorder (PTSD) caused by war-related trauma. The project is being carried out under the direction of Dr. Manuel Marin Madriz, chief psychiatrist at the Military Hospital in Managua. Permission for the study has been obtained from the Nicaraguan Minister of Health, as well as from all the relevant hospital authorities. PTSD is a profound psychological disorder. Many therapists experienced with the use of MDMA believe that it can be especially effective in treating PTSD, even if patients have failed to find relief from more conventional therapies. MDMA-assisted psychotherapy proportedly has the potential to enable people to process difficult emotions more effectively than they might otherwise do, and can help patients move beyond being tormented by their past trauma. Though LSD has very different subjective qualities than MDMA, Dutch psychiatrist Dr. Hans Bastiaans' use of LSD for decades in the treatment of concentration camp survivors is an inspiring example of the beneficial use of psychedelics in the treatment of people with severe trauma.

When I founded MAPS in 1986, it was precisely to help facilitate research projects like this one. It gives me great satisfaction that MAPS is helping to coordinate the training of the Nicaraguan therapeutic team, the development of the scientific protocol, the implementation of the study, and is also assuming primary responsibility for funding the project. This project is what MAPS' members make possible.

The Advisory Team

MAPS has obtained the help of a remarkable group of psychiatric and psychotherapeutic advisors for this project. Experts who will share their approach to the therapeutic use of MDMA with the Nicaraguan researchers include Dr. Claudio Naranjo, the pioneering psychiatrist from Chile who first researched the therapeutic uses of MDA and MMDA; Richard Yensen,Ph.D., a psychedelic researcher whose dissertation was on the therapeutic use of MDA (and who also speaks Spanish); and Dr. George Greer, author of a paper on his therapeutic use of MDMA in 28 patients before MDMA was placed in Schedule 1.

When I founded MAPS in 1986, it was precisely to help facilitate research projects like this one.

MAPS is also assembling an outstanding team of experts in the study of post-traumatic stress who will help in the design of the study. MAPS has been very fortunate to obtain the help of Sylvia Garma, Ph.D., who works at the San Francisco VA Medical Center. She is originally from Argentina and was recently part of a State Department -coordinated visit to El Salvador designed to assist the Salvadoran Health Authorities in studying and improving their treatments for post-traumatic stress. MAPS is also seeking to obtain the assistance of one of the foremost academic experts on PTSD who previously studied under Dr. Hans Bastiaans, as well as a psychiatrist who specializes in treating PTSD patients.

The next issue of the MAPS newsletter will report more fully on this project. It is possible that some of MAPS' therapeutic experts will visit Nicaragua in February or March to begin sharing their expertise with the Nicaraguan researchers. The study should take about a year or so to conduct, and will cost about $30,000. Contributions earmarked for this project are most welcome. ■

MDMA Neurotoxicity Update – New Data from Drs. Ricaurte and McCann to Consider

THE RESULTS of Dr. Ricaurte and Dr. McCann's multi-year study were first presented at a neurosciences conference in mid-November,1993 and will be reported on in more detail in the next issue of the MAPS newsletter. The study found that the MDMA-experienced group (of which I was a member) had on average 30% lower levels of a serotonin metabolite in their spinal fluid than did the control group. Interestingly enough, the only functional and behavioral differences between the MDMA group and the controls were that the MDMA users "reported less impulsive and hostile personality traits, and greater constraint and control". As Drs. Ricaurte and McCann point out, these differences are generally considered positive. Furthermore, these findings are perplexing in that the generally held view is that lower serotonin levels lead to more hostile and impulsive behavior, not less. As with most MDMA neurotoxicity studies so far, this one raises more questions than it resolves. More research is required to sort out the findings.

One difficulty in interpreting the results of this study is that comparing people to matched controls is as much art as science. People are wonderfully unique, especially so when it comes to serotonin. Finding a perfectly matched control is almost impossible since the normal level of brain neurotransmitters varies enormously between individuals. Nevertheless, comparing people who have used MDMA many times in the past to matched controls who have not used MDMA does have some advantages over a controlled study administering only a few doses of MDMA to its subjects. In a matched control study, people who have used MDMA a substantial number of times can be evaluated (Dr. Ricaurte's group averaged over 50 doses), making any serotonin changes caused by MDMA more likely to be noticed. Data from both sorts of studies, with matched controls or subjects as their own control, will be needed to assess more fully MDMA's complex and fascinating effects.

Neurotoxicity Potential is Optional

If someone were seriously concerned about neutralizing the possibility of serotonin changes (though I think the evidence doesn't justify the effort), animal research has shown that combining the prescription drug Prozac with MDMA prevents neurotoxicity, even when Prozac is taken up to six hours after the MDMA. This works because Prozac binds to the same serotonin re-uptake sites which can be damaged by MDMA metabolites (though only when MDMA is administered at doses higher than the standard therapeutic or non-medical amount). The presence of Prozac at the re-uptake sites prevents the neurotoxic MDMA metabolites from binding, eliminating its potential effect on the re-uptake sites. An interesting paper by Dr. McCann and Dr. Ricaurte discusses the effects of the MDMA/Prozac combination (Journal of Clinical Psychopharmacology, 13 (3): pp. 214-217, 1993.) ■

FDA Approves Human Studies with Ibogaine

THE FIRST FDA-approved studies into the physiological and psychological effects of ibogaine in humans will take place at the University of Miami under the direction of Dr. Juan Sanchez-Ramos and Deborah Mash, Ph.D. The ibogaine study is intended primarily to gather data about safety, leaving studies of efficacy for the next stage of research (assuming the drug is considered safe enough for further trials).

These trials are designed as classic dose-response studies in which the effects of very small doses of a drug are thoroughly monitored before increasingly larger doses are tested. Generally, the doses range from "too little" to "too much". Dose levels often include placebo, below any noticeable threshold, barely noticeable, less than standard, average, large, and somewhat more than is comfortable. This study design is basically the same as that used by Dr. Rick Strassman in his research with DMT, and that he will soon use in his upcoming studies of psilocybin. Dr. Charles Grob's Phase 1 MDMA protocol is also a dose-response study. Even the medical marijuana study may also be conducted with this design.

After the Phase 1 trials with ibogaine are complete, perhaps a year or so after they begin, Phase 2 trials will start to explore the use of ibogaine in the treatment of cocaine addiction. MAPS made a small donation of $1,000 to support Drs. Sanchez-Ramos and Mash in their efforts to secure FDA-approval for the ibogaine protocol. It was a pleasure to direct some of MAPS ' limited resources to the ibogaine project .The study of the use of psychedelics in the treatment of substance abuse is one of the most powerful ways of contributing to a cultural shift away from demonizing drug addicts, and psychedelic drugs. Perhaps in time we will see a popular recognition that both drug addicts and psychedelic drugs may yet have positive contributions to make to society when given the option of supportive cultural contexts. ■

Medical Marijuana Research

AFTER about a decade's hiatus in the research into smoked marijuana's medical uses, the FDA has approved a study comparing smoked marijuana to the oral THC pill in the treatment of weight loss caused by the HIV-related wasting syndrome. The principle investigator in the study is Dr. Donald Abrams of the San Francisco Community Consortium. Previous editions of the MAPS newsletter have reported on this project, and on the $50,000 pledge that MAPS received for the study from an individual in the Netherlands.

As a result of my work assisting Dr. Abrams with protocol development, I was asked by officials at the FDA to draft a Clinical Plan suggesting a comprehensive research agenda for the development of the medical uses of marijuana (this plan will be more fully discussed in the next issue of the MAPS newsletter). This Clinical Plan formed the basis for further discussions with the FDA. These discussions focused on the sequence, size and design of the studies that the FDA will require to be successfully carried out prior to any approval of the prescription availability of marijuana for one or more medical indications.

Protocol Design Issues

The discussions with the FDA led to some very helpful suggestions about how to design the marijuana research protocol. Unfortunately, there are still some major obstacles in the road ahead. As a result of the work on the Clinical Plan, a major protocol design issue has arisen which involves the clash of differing sets of concerns, all of which have some validity. The FDA requires at least two "adequate and well-controlled trials" demonstrating safety and efficacy before it will approve a drug for prescription use. Traditionally, these studies are designed in the standard double-blind placebo-controlled manner. If a study is not double-blind, the FDA is not inclined to consider it "well-controlled." Given that a single medical marijuana study will probably take over a year to conduct and cost over $150,000, it is essential that the FDA will seriously consider the data it generates.

Though the FDA has approved Dr. Abrams' study comparing smoked marijuana to Marinol, it considered it a pilot study that was not "well-controlled." The rationale was that since the study design compares smoked marijuana to oral THC capsules, all the patients could easily determine which experimental treatment they were receiving simply by noticing if their medicine is smoked or swallowed. This knowledge in turn compromises the double-blind. As a result, bias can be consciously or unconsciously introduced into the experiment by either the subjects, the researchers, or both. Limiting the potential for bias to influence the results of the study is the fact that patients suffering from the wasting syndrome are by definition not able to control their weight at will (if they could they wouldn't be in the study). Nevertheless, subjects would be able to alter their reports concerning their appetite, an outcome variable that was going to be measured through patient self-reports.

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Despite everyone's best intentions, there is no known way to conduct successfully a double-blind study with the two psychoactive drugs, marijuana and the oral THC capsule. The best way to attempt to create a double-blind experiment with these two drugs is to give patients either active marijuana and placebo THC, or placebo marijuana and an active THC capsule. Since the pill takes about 45 minutes to take effect, the subjects would be asked to first take the pill, wait about 45 minutes, and then smoke some marijuana.

Even with the attempt to confuse the patient about which drug was active, patients would still be able to tell which active drug they received. The rapid, almost instantaneous onset of the psychoactive effects of smoked marijuana differs dramatically from the slow onset of the THC capsule. Even the nature of the subjective experience is different. Furthermore, the oral THC pill's absorption into the body is quite variable from day to day depending on diet and other factors. The pill's actual time of onset could never be perfectly corre-

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PUBLICATIONS AVAILABLE FROM MAPS

(Simply circle the ones you want and enclose payment)

1. Exploring Ecstasy: A Description of MDMA Users. Final Report to the National Institute on Drug Abuse. Marsha Rosenbaum, & Patricia Morgan, Co-Principle Investigators, Jerome Beck, Project Director. 253 pages. Cost - $30.
2. The MDMA Controversy: Contexts of Use and Social Control, Jerry Beck's Ph.D thesis for a Doctor of Public Health from the U. of Cal., Berkeley. 271 pages. Cost - $30.
3. E for Ecstasy, by Nicholas Saunders, — $16 postpaid.
4. Through the Gateway of the Heart, signed by Ralph Metzner, $11.50 postpaid.
5. Marijuana – The Forbidden Medicine, by Lester Grinspoon and James Bakalar – $25.75 postpaid
6. LSD in the Treatment of Substance Abuse Protocol, by Kurland, Yensen and Dryer, 20 pages, & Smoked Marijuana vs Oral THC in the Treatment of the HIV-related Wasting Syndrome Protocol, by Abrams, 8 pages; both $8.
7. MDMA Psychotherapy in End-Stage Cancer Patients–The Protocol - 49 pages, $10.
8. The Good Friday Experiment Follow-Up, the article on psychedelics and experimental mysticism by Rick Doblin, published in the August, 1991 *Journal of Transpersonal Psychology*, $8.
9. Against Excess: Drug Policy for Results, Mark A. R. Kleiman - $26.
10. Journal of Nervous and Mental Disease paper analyzing self-reports of 20 psychiatrists about their own MDMA experiences, *ReVision Magazine* article on MDMA, and December 1992 *High Times* interview with Rick Doblin, 23 pages, $8.
11. Complete set of MAPS Newsletter back issues, 1988–1p., 1989–4p., 1990–10p., 1991–12p., 1991–4p., 1991–12p., 1992–16p., 1992–24p., 1992–36p., 1993–48p, 1993–56p; $35.

Now Available – A Complete Set of Back Issues of the MAPS Newsletter

AUDIOTAPES AND VIDEOTAPES AVAILABLE FROM MAPS

(Simply circle the ones you want and enclose payment)

Audiotape: **Prague, June, 1992**–3 hour audiotape of MAPS discussion on working with the terminally ill with psychedelics, Ram Dass, Ken Ring, and Richard Yensen, $20.

AUDIO & VIDEO – TAPES FROM 50TH ANNIVERSARY OF LSD EVENTS:
Videos are $35 each, postpaid. Audiotapes: $10 each, postpaid

Video

1. Complete Santa Cruz: LSD
2. Highlights from San Francisco

Audio

1. & 2. Complete Santa Cruz: LSD (2-tape set)
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4. San Francisco: MDMA

For additional video and audio tapes of the San Francisco 50th anniversary of LSD event, contact:
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❑ YES! I would like to join the Multidisciplinary Association for Psychedelic Studies.
Enclosed is my tax-deductible contribution of: ❑ **$30** ❑ **$100** ❑ **$250** or more ❑ $ other____
❑ If outside the US, add $10 for postage. **NOTE: Your donation *will not* be spent on animal studies.**

Name

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City State Zip Country

PATRONS ONLY: CHECK THE MEMBERSHIP BENEFIT YOU PREFER...
❑ Santa Cruz: LSD Video
❑ San Francisco: Highlights Video

MAPS is a membership-based organization working to assist psychedelic researchers around the world design, obtain governmental approval, fund, conduct and report on psychedelic research in humans. Founded in 1986, MAPS is an IRS approved 501 (c)(3) non-profit corporation funded by tax deductible donations from about 700 members. MAPS' founder and current president, Rick Doblin, is on leave of absence from the Ph.D. program in Public Policy at Harvard's Kennedy School of Government and has previously graduated from Stan and Christina Grof's Holotropic Breathwork 3 year training program.

MAPS has previously funded basic scientific research in both humans and animals into the safety of MDMA (methylenedioxymethamphetamine, Ecstasy) and has opened a Drug Master File for MDMA at the U.S. Food and Drug Administration. MAPS is now focused primarily on assisting scientists to conduct human studies to generate essential information about the risks and psycho-therapeutic benefits of MDMA, other psychedelics, and marijuana, with the goal of eventually gaining governmental approval for their medical uses.

Albert Einstein wrote that *"Imagination is more important than knowledge."* If you can even faintly imagine a cultural reintegration of the use of psychedelics and the states of mind they engender, please consider joining MAPS in supporting the expansion of scientific knowledge in this area. Progress is possible with the support of individuals who care enough to take individual and collective action. In addition to supporting research, your contributions will return to you the following benefits:

The MAPS Newsletter:

Each quarterly newsletter will report on MAPS research in progress. In addition to reporting on our own studies, the newsletter may focus on psychedelic research both in the US and abroad and on conferences, books and articles of interest. Issues raised in letters and calls from members may be addressed, as may political developments that effect psychedelic research and usage.

General Membership: $30.
(If outside US add $10 postage.)
General members will receive the newsletter and a copy of Drs. Kurland, Yensen and Dryer's *LSD in the Treatment of Substance Abuse Protocol* as well as Dr. Abrams' *Study of smoked marijuana and oral THC in the treatment of the HIV-related Wasting Syndrome*

Supporting Membership: $100.
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Supporting members will receive all the benefits sent to the General Members plus the audiotape from the 50th Anniversary of LSD event in Santa Cruz, April 16, 1993

Patron: $250 or more.
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Patrons will receive all the benefits sent to Supporting Members plus one item of your choice from among the videotapes from the 50th Anniversary of LSD events. Patrons may also request research updates at any time on matters of personal interest and will receive advance information and discounts to MAPS events.

MAPS Membership Information

Rick Doblin, MAPS President

"We must free science and medicine from the grasp of politics and give all Americans access to the very latest and best medical treatments."

President W. J. Clinton, January 22, 1993

MEDICAL MARIJUANA... *continued from page 5*

lated with any standardized time suggested to the patient about when to smoke the marijuana. After several days in the study, at the longest, all the patients would know which drug they received, the active marijuana or the active pill.

After some discussion, the FDA officials and I agreed that a design involving high dose marijuana (10% THC), medium dose marijuana (3-5% THC) and placebo marijuana (less than 1% THC) would come the closest to being a true double-blind study. Such a study would be considered as one of the two required "adequate and well-controlled" studies. I therefore suggested to Dr. Abrams that we redesign the study by dropping the use of Marinol and adding a medium dose group and a placebo marijuana group. Dr. Abrams agreed to present the new study design to the Scientific Advisory Board (SAC) of the Community Consortium at its December 2, 1993 meeting.

No To Placebo Marijuana

To my surprise, the SAC rejected the proposed protocol design. The reasons for its decision are valid, as is the FDA's competing need for a "well-controlled" study. Some mutual accommodation will need to be developed. While the SAC approved of the use of high- and medium-dose marijuana, it refused to administer placebo marijuana to its patients. The rationale was that the subjects would be exposed to the potentially harmful effects of smoking without receiving any benefits. Furthermore, after a few days in the study, they would certainly be able to determine whether they were smoking active marijuana or not, thereby compromising the double-blind. Since the double-blind would not be effective anyway, the SAC saw no reason to go through with an empty formality that carried even a slight degree of risk.

I had also thought that patients in the study would indeed be able to tell if they had active or placebo marijuana. However, I thought a good-faith effort at the double-blind would be worth it in order for the study as a whole to be considered "well-controlled". Furthermore, I considered the risk of harm to the subjects from the smoke from the placebo marijuana to be minimal, especially since there are simple ways to reduce the risk of smoking, for example with a water pipe. In deciding to recommend this design, I tried to weigh the risk/benefit ratio for the subjects who would be randomly assigned to the placebo marijuana group. While I recognized that they would not benefit from their three months in the study, and would also be exposed to smoke without therapeutic value, I thought that their opportunity to obtain legal access to smoked marijuana after the conclusion of the three month study period might adequately compensate them for participating in the study in the placebo marijuana group.

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The SAC had one additional concern that even I could see was compelling. The SAC pointed out the ethical problem of not providing patients suffering from the life-threatening wasting syndrome with some active treatment, especially since there already are two drugs approved by the FDA for this indication — Marinol and a new drug called Megace. When there are no FDA-approved drugs for an illness, having a placebo group is easily justified since there are no proven alternatives that have been demonstrated to be safe and effective. Indeed, given that all drugs have some side-effects, administering a drug of unknown safety and efficacy is probably harder to justify than giving a placebo.

Though there are FDA-approved drugs for the wasting syndrome, the SAC was not enthusiastic about the therapeutic value of either Marinol or Megace. Marinol has only been demonstrated to increase appetite but not weight. While Megace has a small effect on weight gain, this may primarily be water weight of little consequence to overall health. Despite their shortcomings, the SAC preferred to administer one of these drugs to the control group instead of placebo marijuana. Using either of these drugs, however, would still not result in a double-blind study. Furthermore, using an active placebo with some therapeutic potential creates another problem. When the data from standard double-blind studies are analyzed, the important variable is the difference between the effect of the treatment and the effect of the placebo. The statistical probability that the observed effect of the treatment is due to the treatment and not to chance depends in part on how large the difference is between the two groups. However, when the drug used as a placebo has some therapeutic effectiveness of its own, the true effect of the treatment is more difficult to determine.

One Possible Solution

Dr. Abrams, the SAC, the FDA and I are all still trying to develop an appropriate protocol design. My preference is to use low-THC marijuana that still has some therapeutic effect, perhaps 2% marijuana. The study design would

then be patterned on a standard dose-response study, though without an inactive placebo. Using three groups with high-, medium- or low-THC content at least maximizes the chance that patients and researchers will be blind as to which treatment group the patients are in. The problem of comparing the results of the high and medium doses to an active placebo remains to be addressed, but there seems to be no way to avoid this. In any case, isn't this why some people become statisticians?

Some progress has resulted from all this struggle to craft the best design for the experiment. The SAC decided that it would be a good idea to conduct a small pilot study with whatever design we come up with, rather than enter into a big trial without first testing out the methodology with a smaller group of patients. Since we have already been pledged $50,000, we do have enough funding for a pilot study. As soon as the protocol design is finalized and all the regulatory permissions are in hand, we can begin the experiment instead of waiting until larger sums are available. It should be much easier to raise the remaining funds once the pilot study is underway. At that time we would have actually demonstrated that this project was not just another pipe dream but instead was an actual study that could have dramatic implications for the medical treatment of the wasting syndrome, and for medical marijuana research in general.

FDA Grant Program

In a good-faith attempt to help the medical marijuana debate be resolved on the scientific merits of research data, an FDA official who did not have to do so nevertheless informed me about a grant program that I did not know existed. This grant program had the potential to provide substantial funding for the wasting syndrome study. This gesture convinced me more than ever that working with the FDA to conduct scientific research is an essential part of breaking the logjam concerning the medical use of marijuana.

The grant I was shown was from FDA's Office of Orphan Products Development. These grants are for research into the therapeutic potential of drugs intended for diseases which afflict 200,000 people per year or less, such as the AIDS-related wasting syndrome. I had erroneously assumed that marijuana would first need to be formally approved by the FDA as an Orphan Drug before any funding proposals would be considered. I was told instead that researchers need only have an approved protocol, which Dr. Abrams already had. The grant application deadline was December 27, 1993, about a month and a half after I was informed about the program. If there were no unexpected problems, it seemed that there just might be enough lead time for Dr. Abrams and the Community Consortium to prepare a grant application for the research study, and possibly obtain funding support for the study directly from the FDA.

working with the FDA to conduct scientific research is an essential part of breaking the logjam concerning the medical use of marijuana.

The SAC's decision to reject the proposed protocol design with the placebo marijuana group had one major unfortunate side-effect. In the absence of a protocol design that the SAC was willing to implement and the FDA was willing to consider well-controlled, Dr. Abrams was not able to prepare an application for FDA funding for the study in time for the December 27, 1993 application date. Since this grant program is on an annual cycle, the opportunity for FDA funding for medical marijuana research slipped through our fingers for at least a year. While other sources of funding will probably become available eventually, FDA funding would have been particularly appropriate for such a controversial drug at this stage in its development.

National Medical Marijuana Day

Another idea to help raise funds for medical marijuana research is to initiate a National Medical Marijuana Day, perhaps in April or May of 1994. The idea would be to catalyze hundreds of small, local fundraising events all synchronized to take place on the same day. The events would ideally be co-sponsored by local medical marijuana groups, NORML chapters, and the Cannabis Action Network, some of the same groups that helped with the symposium commemorating the 50th anniversary of LSD. In addition, we would advise the local organizers to seek co-sponsorship of the events with their local AIDS groups. If each local event raised $500 and there were 100 events, $50,000 would be generated.

The central organizers would need to assemble a "Local Organizers Starter Packet" composed of a video about the issue, some informational material, and organizational tips. This kit could be sold at a price that covers costs, perhaps $25. It should also be possible to arrange a benefit concert to take place in San Francisco on the same day with some very popular bands. More on this idea later. If you would be interested in sponsoring a local event, please contact MAPS. ■

Marijuana Water Pipe Study

INCLUDED in the Medical Marijuana Clinical Plan is a study of the effectiveness of water pipes in filtering marijuana smoke. This project has been mentioned in previous MAPS newsletters. The study is designed to determine if there are safer ways than a standard marijuana cigarette to administer the therapeutic components of marijuana, while at the same time still retaining the advantages of smoking over the oral THC pill. These advantages include smoked marijuana's rapid onset of effects, the patients' ability to self-titrate their dose, and the delivery of a complex set of constituents of the marijuana plant which may work more effectively than THC alone. If we can demonstrate that a specific water pipe does indeed have a beneficial advantage over a standard marijuana cigarette, we will distribute the pipe to all AIDS patients in the wasting syndrome study.

Good news – all the funds needed for this study, $28,800, have been pledged.

Good news – all the funds needed for this study, $28,800, have been pledged. The study will take place under the direction of Dr. Hoffman at the Institute for Smoking and Health in New York. This study is possible primarily because MAPS received a grant for this project of $18,000 from a single donor who gave $14,000 outright, and also submitted the winning bid of $2,000 each in the MAPS auction of the two original art Doonesberry cartoons donated to MAPS by Garry Trudeau. The remaining funds for the study were obtained from two donors, both of whom pledged $5,000 each. Rounding out the sum, an additional $800 is coming from numerous small donations to MAPS.

Sending The Wrong Message?

Some medical marijuana advocates have cautioned that this study could "send the wrong message" that smoked marijuana is too risky to use as is, thus slowing down or preventing altogether FDA-approval of smoked marijuana in rolled cigarette form. To the contrary, I feel that we should be able to acknowledge that for some patients, smoking marijuana carries certain risks which are nevertheless exceeded by its therapeutic benefits. Studying ways to possibly improve the delivery of marijuana should not undercut the effort to secure prescription availability of marijuana as rapidly as possible. On the contrary, this study might even hasten the day that the FDA approves medical marijuana by reducing the efficacy of arguments against it. Demonstrating scientifically that there is a way to reduce the risks of smoking favorably alters marijuana's risk/benefit ratio, improving its chances of securing FDA-approval. More compelling reasons for this study are that we are exploring the use of marijuana in AIDS patients whose immune systems are already compromised. For some of marijuana's other medical applications, like spasticity, patients may need to smoke marijuana every day of their life. It simply makes good sense to see if the ratio of marijuana's therapeutic components to tars and particulate matter can be increased through some simple sort of water pipe.

Water Pipe Patent Search

In preparation for this study, MAPS had a patent attorney conduct a patent search of water pipes. The search indicated that more pipes than one might have imagined had been patented. Some of the patented pipes were very humorous. One was a combination water pipe/drink holder with separate liquid containers for the drink and the water that would filter the smoke (perhaps for those who can't decide if they prefer alcohol or marijuana). Other designs were made to be more difficult to spill (a not uncommon and messy problem), or involved an efficient way to refill the bowl through the use of a separate chute filled with "expensive tobacco" that deposited a measured amount into the bowl when a knob was rotated.

Only two of the pipes made health claims. One inventor installed a filter in the inhalation tube between the water bowl and the mouthpiece. No evidence was presented indicating that the filter selectively filtered out particulate matter as opposed to simply reducing both particulate matter and THC. The other designer placed stones in the water to lengthen the path of the smoke through the water. Once again, there was no evidence that this actually increased the amount of filtering done by the water.

Putting Pipes To The Test

Previous studies, reported by Nick Cozzi in the last issue of the MAPS newsletter, have demonstrated that water pipes do filter some of the potentially harmful constituents of marijuana smoke. Dr. Hoffman's study will be the first to quantify the specific components that various smoking devices filter out of marijuana smoke. What we seek to determine are the exact differences, if any, in the amounts of THC and other cannabinoids, and tars and particulate matter contained in water-filtered smoke compared to unfiltered smoke.

The study has two phases. First, smoke from three different types of pipes will be tested in a rough, quick way to determine their relative amounts of THC and one representative tar. Second, the water pipe that delivers the highest THC/tar ratio will then be run through a very comprehensive analysis comparing the materials in the smoke from the water pipe to the materials in the smoke from a standard unfiltered marijuana cigarette.

The three pipes to be tested in the first phase of the study are quite different from each other. The first is a rather interesting water pipe with a small battery operated fan blade immersed in the water. The fan blade creates turbulence in the water in order to increase the mixing of the smoke with the water. Theoretically, this should result in more filtering action than if the water was still. The second water pipe is being designed by Nick Cozzi and a MAPS member who was inspired by Nick's article to see if he could design an efficient water pipe that would incorporate various filters. Nick will suggest the filters (a gas diffusion frit and a cigarette-type particulate filter) and the MAPS member will build the prototype.

The third pipe that will be tested is not a water pipe. This pipe exploits the fact that THC and other cannabinoids will vaporize at a temperature below that of the burning point of marijuana. The pipe enables people to inhale marijuana vapor containing THC and other cannabinoids rather than marijuana smoke containing THC along with all sorts of particulate matter, tars, and some gaseous products of combustion. This pipe is likely to produce very little particulate matter and deliver little or no undesirable gas combustion products.

The pipe uses an electric heating plate rather than matches. It works by heating the marijuana enough to vaporize the THC. It then gathers the vapor in an enclosed space and delivers the vaporized smoke to the smoker through a standard mouthpiece. While this pipe is likely to be the best from a health standpoint, it will probably take some further refinement before it can be made easy to use, reliable, and efficient in terms of getting as much of the THC out of the marijuana as possible. Because of the more practical nature of the water pipes compared to the vaporization device, we will conduct the comprehensive test with whichever water pipe performs the best in the initial trial.

Harm Reduction

This water pipe study is a classic example of the harm reduction approach to drug use. If water pipes really reduce the harm associated with marijuana smoking, non-medical users can be educated about the benefits of water pipes and encouraged to use them whenever possible. Since smoking is one of the main harms associated with the use of marijuana (accidents are another), this simple water pipe study may help lay the groundwork for significantly reducing the harmfulness of marijuana smoke. If US drug policy ever moves to a harm-reduction approach to marijuana, studies such as this one will play an important role in helping users to identify and minimize the health risks of marijuana. The shift to prevention rather than treatment is consistent with the current health care debate and seems likely to reduce costs in the long run.

After over a year of effort, the MAPS study of the effectiveness of water pipes in filtering marijuana smoke is about to begin. I would like to express my deep appreciation for the generosity of the MAPS member who believed in the importance of this study, and in putting this matter to a scientific test. ■

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Dr. Albert Hofmann receiving a poster from MAPS' 50th Anniversary of LSD Symposium.

Swiss Academy of Medical Sciences Commemorates the 50th Anniversary of Dr. Albert Hofmann's Discovery of LSD

ON October 22 and 23, 1993, the Swiss Academy of Medical Sciences held its LSD conference in Lugano -Agno, Switzerland amidst mountain lakes near the Italian border. By the end of the conference, I felt that the consensus of the participants was that LSD should indeed be the subject of renewed scientific inquiry. This conclusion seemed to be echoed by all concerned including experts in the treatment of drug abuse, therapists, brain neurochemists, and even government regulators from several countries. While the renewal of psychedelic research is still in its infancy, the Swiss Academy of Medical Sciences conference made an important contribution toward strengthening the scientific arguments and political consensus for its continued growth. Perhaps Albert Hofmann's problem child, like so many of us whose path to adulthood was turbulent and troubled, may yet grow into a responsible citizen. Much hangs in the balance.

At its heart, the Swiss Academy conference was a tribute to the very important scientific and medical contributions made by Dr. Albert Hofmann. In his wonderful synthesis of the science of chemistry, the art of living, and the spirituality of the psychedelic experience, Dr. Hofmann has been a profound inspiration to many people all over the globe. For those who know the value of LSD, the world seems doubly gifted, first by LSD's discovery and second by the fact that it was Dr. Albert Hofmann who discovered it. ■

Hello from Sylvia Thyssen – MAPS' New Staff Member

Dear MAPS Members;

"Who is this person who has begun to answer our MAPS mail?" you ask. For years, my career passion has been museum studies, though now, I'm not so sure, and I'm exploring other interests. Upon graduation, I was far from committing to a graduate program, so fortune returned me to my hometown of Charlotte, where I met Rick. Though what I first found compelling about MAPS was the full 19-syllable name, what has kept me committed is its multi-disciplinary imperative, weaving together the varied threads of thought and deed that cross paths with the MAPS office. This approach can only enhance research projects, heal minds and bodies, and inspire us to understand more deeply our right to joy and freedom. Ignore the interplay of culture, medicine, and politics, and you're missing the point.

This is why I am here! I look forward to working with you.

Sylvia Thyssen

Sylvia surrounded by MAPS newsletters.