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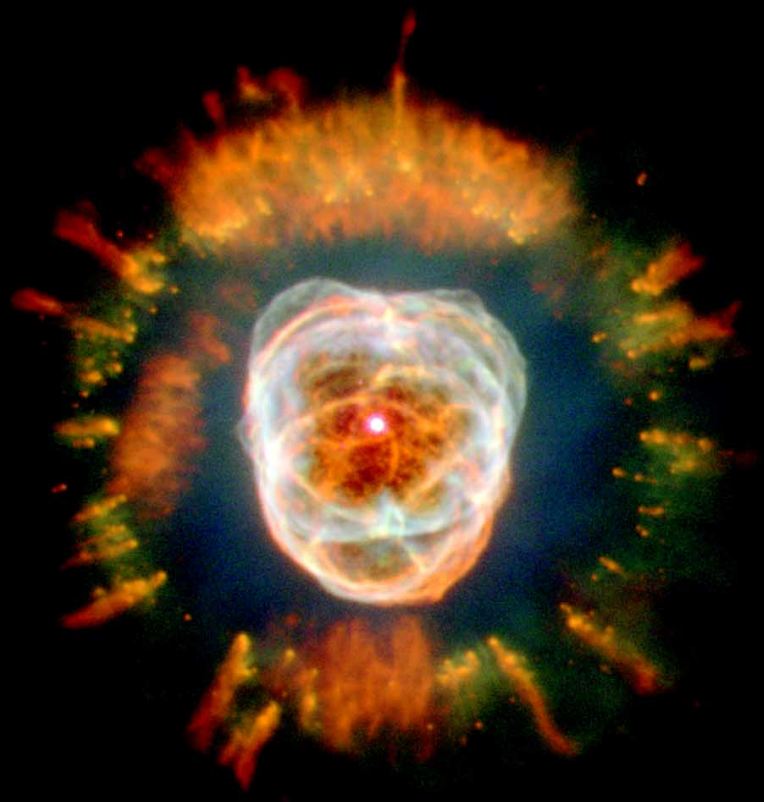

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Brittle Star Scavenging on an Alcyonarian Coral
J. Rottman

MAPS (Multidisciplinary Association for Psychedelic Studies) 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. MAPS is now focused primarily on assisting scientists to conduct human studies to generate essential information about the risks and psychotherapeutic benefits of MDMA, other psychedelics, and marijuana, with the goal of eventually gaining government approval for their medical uses. Interested parties wishing to copy any portion of this publication are encouraged to do so and are kindly requested to credit MAPS including name and address. The MAPS Bulletin is produced by a small group of dedicated staff and volunteers. Your participation, financial or otherwise, is welcome.

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Image of "Peace Protecting Genius" used on page 25 from *The Apotheosis of Democracy, 1908-1916 : The Pediment for the House Wing of the United States Capitol,* by Thomas B. Somma © 1995 University of Delaware Press

Special thanks to Johnathan Steelman for assistance locating image of "Peace Protecting Genius", page 25.

Correction: In the previous issue, in the story on Ayahuasca Tourism, it was erroneously reported that Alan Shoemaker was imprisoned in Peru for distributing ayahuasca. In fact, Alan was accused of distributing ayahuasca but the product seized turned out not to be ayahuasca.

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Letter from Rick Doblin, Ph.D., MAPS President

Visions are sustaining and guiding forces, pulling us through the darkest nights and most difficult days by virtue of their power to generate inspiration and hope. Yet visions need to become more than just intuitions or dreams in order to become fully realized. For MAPS, our central vision is of the tremendous value that can flow to individuals and cultures from the creation of legal contexts for the full range of beneficial uses of psychedelics and marijuana. This vision, however, is so far-reaching that it can't by itself serve as a plan for action nor is it self-evident why this vision is so compelling or worth sacrificing to bring about.

In order to explain more fully MAPS' vision, we've created this special "Vision" issue of the MAPS Bulletin with just two relatively long articles. The first article offers a strategic rationale and an implementation sequence for the relatively limited and circumscribed vision of the transformation of MDMA into a prescription medicine for the treatment of posttraumatic stress disorder (PTSD). This drug development plan is where most of MAPS' staff time and financial resources are directed. As a result, MAPS is on the verge of becoming, in practice as well as in theory, a non-profit psychedelic pharmaceutical company. Therefore, it's both appropriate and necessary to offer to MAPS members a detailed justification and specific plan for evaluation, comment and, hopefully, endorsement and support. This article was originally intended to become the final chapter of my dissertation but as it developed it became clear that the content had crossed the line from analysis into advocacy, and thus needed to be a separate document. A similar plan for the transformation of marijuana into an FDA-approved medicine is in the early stages of development.

The second and final article in this issue is a sweeping discussion of the mystical experience illuminated by science, informed by politics, and endowed with a compassionate and courageous call to action. The article is actually the text of a speech by U.S. Congressional Representative Kucinich (D-OH) that focuses on the political implications of the mystical experience of unity. It's not at all intended to be a psychedelic manifesto but it provides one of the clearest explanations that I've ever read of why MAPS' broad vision of helping to create legal contexts for psychedelic experiences is potentially so transformative and life-affirming. Psychedelics are arguably the most powerful and reliable catalysts of mystical experiences and, as such, offer the potential to facilitate healing transformations of individual personality and collective culture. It's not an accident of history that that oldest and most continuous use of psychedelics has been in religious/spiritual contexts. Yet as Prof. Huston Smith has astutely written, spiritual experiences aren't the same as a spiritual life, which requires constant work grounding the insights of the mystical experiences into daily practice. Rep. Kucinich's speech is a rare attempt to trace the

While this issue is focused on vision, the next issue of the Bulletin will be focused in large part on mundane details, offering a comprehensive explanation of MAPS' income and expenses over the last two years, linked to a discussion of MAPS' myriad research and educational projects and the costs of operating the organization. To lay the groundwork for the upcoming issue, I'll now briefly review the current status of MAPS' most important projects. Because we have encountered substantial obstructions and reversals in almost every project, this review will also highlight the essential contribution of MAPS' vision in providing motivation that enables this organization to persevere despite a challenging environment.

To begin with, for the last several years MAPS has been sponsoring Jose Carlos Bouso's efforts to conduct a pilot study in Madrid, Spain, exploring the use of MDMA-assisted psychotherapy in the treatment of PTSD. This has been the first double-blind, placebo- controlled study of the

therapeutic use of MDMA ever approved and conducted and has also been the world's only ongoing study of any kind into any therapeutic use of MDMA. In May 2002, a series of favorable media articles appeared in Spain about the study. Shortly afterwards, the Spanish Anti-Drug Agency and drug police intimidated the hospital where the study was taking place into shutting down the experiment. The Ministry of Health has not withdrawn approval, so we hope to resume this project, but for now we are engaged in a classic struggle of scientific freedom v. entrenched interests.

For the US MDMA/PTSD project, to be directed by Dr. Michael Mithoefer of Charleston, South Carolina, we've previously reported that we had an application in process with an independent Institutional Review Board (IRB) called the Western IRB (WIRB). On July 10, 2002, we were informed that the WIRB had approved the study. On September 6, 2002, we were totally shocked to hear from the IRB that approval had been revoked, based on conversations (not on data!) that an WIRB staff person had sought out with some outside experts. We weren't even given a chance to respond to the opinions before a decision had been made to revoke the approval! Fortunately, there is a good chance that we can reverse the reversal, but only after a meeting in person with the IRB that is tentatively scheduled for the end of October. In addition to IRB approval, Dr. Mithoefer still needs to obtain a DEA Schedule 1 license prior to our being fully approved to start the study. Dr. Mithoefer applied to the DEA in early July, but for two and a half months, DEA did nothing with the application, telling us that processing it "wasn't a high priority." After frequent complaints, DEA finally entered the application into its computer system and now tells us maybe it will be approved before the end of November.

The Israeli MDMA/PTSD study is contingent on the US MDMA/PTSD being fully approved first. MAPS has organized a seminar about MDMA/PTSD research for the Israeli Ministry of Health and the Israeli Society of Addiction Medicine, to take place near Tel Aviv on November 14, with a smaller protocol design meeting on November 17.

In Russia, MAPS has for many years been funding Dr. Krupitsky's research into the use of ketamine-assisted psychotherapy in the treatment of heroin addiction and alcoholism. Early in 2002, Russia tightened the regulations controlling ketamine and withdrew permission for Dr. Krupitsky's research. Dr. Krupitsky was told that permission would almost certainly be restored around the end of 2002, but this has not yet taken place.

Regarding medical marijuana research, the Drug Enforcement Administration is still considering the application by Prof. Lyle Craker, UMass Amherst Dept. of Plant and Soil Sciences, Medicinal Plant program, for a license to grow high-potency marijuana only in federally-approved research. The marijuana would be grown under a grant from MAPS. DEA Administrator Asa Hutchinson has previously indicated that DEA can't grant the license due to US international treaty obligations. Complicating matters for the DEA is that along with the license application, Prof. Craker submitted a legal analysis by Washington DC law firm Covington & Burling and the ACLU, working for MAPS and Prof. Craker on a pro-bono basis. The legal analysis made a persuasive case that DEA's interpretation of the treaty is mistaken. It seems clear that DEA opposition to unhindered medical marijuana research is what is actually blocking approval of the license.

Tragically, as you will note on the back cover, Bob Wallace, one of MAPS' most generous supporters, has died an untimely death from pneumonia. In order to honor Bob's memory, and to remain true to the visions that have animated MAPS since its founding in 1986, we will continue to persevere. I hope you continue to journey with us to bring shared visions into being.

– Rick Doblin, Ph.D. MAPS President.

A Clinical Plan for MDMA (Ecstasy) in the Treatment of Post-Traumatic Stress Disorder (PTSD): Partnering with the FDA

Rick Doblin, Ph.D.

The following article was originally published in the April-June 2002 special MDMA issue of the Journal of Psychoactive Drugs *(www.hafci.org). The article presents the rationale behind MAPS' efforts to sponsor research in Spain, the US and Israel investigating MDMA's potential in treating patients suffering from posttraumatic stress disorder (PTSD). This document is the clearest expression to date of MAPS' role as a membership-based non-profit pharmaceutical company, as distinct from MAPS' other research and educational functions. We are reprinting this article in order to explain in detail to MAPS' membership the vision and strategy animating MAPS' MDMA/PTSD research projects and associated fundraising efforts. A mission statement in a way, this article should help to explain why MAPS has chosen the ambitious goal of developing MDMA into an FDA-approved prescription medicine in the treatment of PTSD. Since this article was written, the Spain MDMA/PTSD research project has been halted (hopefully temporarily) due to political pressure, and it has taken longer than expected to obtain DEA and IRB permission to start the US MDMA/PTSD project.*

The Multidisciplinary Association for Psychedelic Studies (MAPS, www.maps.org), a membership-based non-profit research and educational organization, is sponsoring a series of studies designed to develop MDMA into an FDA-approved prescription medicine, initially for the treatment of post-traumatic stress disorder (PTSD). MAPS is currently sponsoring a pilot MDMA dose-escalation study in Madrid, Spain with PTSD patients, conducted under the direction of Dr. Pedro Sopelana and Jose Carlos Bouso, Ph.D. candidate (Sopelana & Bouso 1999). This is the world's only ongoing study of the efficacy of MDMA-assisted psychotherapy. On November 2, 2001, a MAPS-sponsored study under the direction of Dr. Michael Mithoefer was approved by the FDA, with Institutional Review Board (IRB) approval in process (Mithoefer & Wagner 2001). MAPS is also working to sponsor an MDMA/PTSD study in Israel, under the direction of Dr. Moshe Kotler.

This paper elaborates a five-year, $5 million Clinical Plan outlining a proposed sequence of studies to investigate MDMA-assisted psychotherapy in the treatment of PTSD. This Clinical Plan starts with pilot studies and concludes with two FDA-required "adequate and well controlled investigations" of safety and efficacy. This discussion outlines a strategy for developing MDMA into an FDA-approved prescription medicine. A series of regulatory, ethical and methodological issues for the investigation of psychedelic psychotherapy in the context of FDA-approved clinical trials, which form the basis for the Clinical Plan, are discussed in detail in the context of my Public Policy dissertation (Doblin 2001).

Given the political and scientific hurdles, a rational analysis of the likely return on investment would probably not inspire any venture capitalists to invest their risk capital into the development of MDMA as a prescription medicine. MDMA is off patent, PTSD or any other psychological disorder for which MDMA might be effective affect more than 200,000 people so that patent protection under FDA's Orphan Drug program cannot be obtained, and the political hurdles due to MDMA's non-medical use may not be surmountable within any time frame that an investor

"This paper elaborates a five-year, $5 million Clinical Plan outlining a proposed sequence of studies to investigate MDMA-assisted psychotherapy in the treatment of PTSD, as part of a strategy for developing MDMA into an FDA-approved prescription medicine."

would consider realistic. Though the for-profit approach for the development of MDMA as a prescription medicine is of questionable viability, the non-profit approach is more likely to succeed. There are probably enough philanthropists who, from personal experiences or otherwise, appreciate the political, scientific and medical importance of supporting the struggle to develop MDMA into a legal prescription medicine.

This discussion begins by evaluating the strategic advantages associated with the conduct of FDA-approved research with MDMA for PTSD, as compared to other psychedelics that could be used for psychotherapy and other potential patient populations. Proposed protocol designs and sample sizes for the studies evaluating the potential use of MDMA in the treatment of PTSD are based in part on a review of documents pertaining to Pfizer's successful development of Zoloft into the first FDA-approved medicine for the treatment of PTSD. These documents were obtained from FDA by the author through Freedom of Information Act (FOIA) request. A FOIA request for FDA documents related to its approval of Paxil for PTSD is still pending.

Choosing Drug and Patient Population

The primary strategic issue in conducting psychedelic psychotherapy research is estimating the probabilities of success in the FDA drug development and approval process of the numerous combinations of any of the psychedelic drugs and patient populations. Psychedelic drugs, though each with a unique set of actions and side effects, all serve the generally similar function of increasing access to psychological, emotional processes. As a result, psychedelics can be used as general purpose adjuncts to psychotherapy, in the treatment of many conditions for which people seek out psychotherapy or psychiatric treatment. The limited resources available to fund psychedelic psychotherapy research make it essential to chose the best test case of a specific psychedelic drug used in treating a specific clinical indication.

Why MDMA?

On the one hand, the psychological safety profile of MDMA is superior to that of all the other psychedelics. MDMA is relatively short acting with primary effects lasting only about 4 hours with gradual return to baseline over the course of another 2 hours or so. MDMA rarely interferes with cognitive functioning or perception and usually produces a warm, emotionally grounded feeling with a sense of self-acceptance, and a reduction of fear and defensiveness. Subjects under the influence of MDMA can usually "negotiate" with their emergent psychological material and often retain the ability to move at will toward or away from certain thoughts or emotions. In contrast, LSD lasts 8 to 10 hours, interrupts rational cognitive processes, impacts perception, requires surrender to inner emotional processes rather than permitting negotiation, and can result in feelings of loss of control, fear and panic, as well as more positive emotions. All the major psychedelics such as psilocybin, mescaline, ibogaine, DMT, etc., resemble LSD

more so than they resemble MDMA. Even the effects of marijuana are more similar to the classic psychedelics than to MDMA.

In terms of therapeutic potential, MDMA is remarkable effective, gentle yet profound. Because it operates on emotions more so than cognitive processing, the MDMA state is only subtly different than normal. As a result, the thoughts and emotions of the MDMA state can be easily remembered after the effects of the drug have worn off, facilitating integration and long-term growth. Due to its relative short-acting duration and its gentle action, MDMA has the greatest opportunity of any psychedelic to be integrated into psychiatric practice. The classic psychedelics can be equally or even more therapeutic but in different ways and with greater personal struggles required of patients and therapists.

On the other hand, the physiological safety profile of all the classic psychedelics is superior to that of MDMA. The extreme position on risk is expressed by Dr. Alan Leshner, ex-Director of the National Institute on Drug Abuse (NIDA), who claims that "There is no safe way to use any of these drugs [such as MDMA]," (Mertl 2000) that "even experimenting with club drugs [such as MDMA] is an unpredictable and dangerous thing to do," and that chronic use of MDMA may cause long-term problems with emotion, memory, sleep and pain (Leshner 2001).

When used recreationally in dance clubs, some users of MDMA (mostly in combination with other drugs) have died from hyperthermia as a result of overheating from vigorous dancing in high ambient temperature environments with inadequate water or other fluid replacement. From 1994 through 1999, there have been a total of 68 MDMA-related deaths (may or may not be causal) reported to the Drug Abuse Warning Network (DAWN), though not all deaths were related to hyperthermia. Medical Examiner data reports 1 death associated with MDMA in 1994, 6 in 1995, 8 in 1996, 3 in 1997, 9 in 1998, 41 in 1999 (Office of Applied Studies, 2001a). Relatively few of the Medical Examiner cases were for MDMA alone. Most were associated with MDMA used in combination with one or more other drugs. The Medical Examiner numbers do not reflect national totals, which do not exist, but are simply the totals reported by the Medical Examiner offices that are included in the DAWN system. MDMA-related (though not necessarily causally related) hospital Emergency Room visits reported to DAWN (these are national estimates) totaled 247 in 1994, 422 in 1995, 319 in 1996, 637 in 1997, 1142 in 1998, 2850 in 1999, and 4511 in 2000. (Office of Applied Studies, 2001b).

Furthermore, with the exception of ibogaine, the classic psychedelics have not been claimed to be "neurotoxic," as has MDMA. In primates, at doses slightly higher than the amounts used in psychotherapy, MDMA has been linked to minor persisting reductions in serotonin levels in a few brain regions (Ricaurte et al. 1988), with the no-effect level for serotonin reductions in primates being 2.5 mg/kg, administered orally once every two weeks for four months (8X) (Ricaurte, unpublished, cited in Vollenweider et al. 1999a). Whether therapeutic doses of MDMA have any permanent impact on serotonin levels is a matter of substantial controversy (Lieberman & Aghajanian 1999). If high doses of MDMA are consumed frequently, a dosage pattern seen in some recreational users of MDMA, MDMA may reduce serotonin levels for extended periods of time (McCann et al. 1998). Though there is evidence of recovery of serotonin levels over time, serotonin does not reach initial levels in all brain regions while some brain regions recover to levels higher than baseline (Fischer et al. 1995). Some changes may be permanent (Hatzidimitriou, McCann & Ricaurte 1999). Fortunately for the heavy recreational users of MDMA, these changes in serotonin levels, if they do indeed occur in humans, seem largely asymptomatic. Evidence for any functional consequences in animals or humans resulting from even massive consumption of MDMA is

weak. Concern centers around a series of studies that show statistically significant but mostly clinically insignificant reductions in a few memory functions in heavy poly-drug users who have consumed large amounts of MDMA (Bolla, McCann and Ricaurte 1998; Reneman et al. 2001; Zakzanis & Young 2001; Croft et al. 2001; Gouzoulis-Mayfrank et al. 2000; Gamma 2001). Concerns that negative functional consequences associated with MDMA use will increase over time as MDMA users age are hypothetical, and are not evidence-based.

Research has shown that neurotoxicity is exacerbated by high body temperatures and can be eliminated by a slight cooling of body temperature (Malberg, Sabol & Seiden 1996; Malberg & Seiden 1998). The effect of temperature makes data about risk that is gathered from people who take MDMA at raves of limited predictive value for estimating the risk of subjects exposed to MDMA in clinical settings. MDMA's increased risk profile is a direct result of its use in recreational settings, with use in clinical research settings relatively non-problematic (Vollenweider et al. 1999a). In therapy, MDMA is not used on a daily basis but rather as an adjunct to psychotherapy administered a relatively few times, with several weeks between therapy sessions. The most sophisticated investigation of MDMA-neurotoxicity has been conducted by Dr. Franz Vollenweider at the U. of Zurich. Dr. Vollenweider found no evidence for serotonin reductions in MDMA-naive subjects who were given a PET scan shortly before and then again four weeks after receiving a moderate amount of MDMA in the therapeutic dose range (1.5-1.7 mg/kg) (Vollenweider 2001).

The combination of the remarkable therapeutic potential of MDMA, along with its substantial safety for use in clinical settings, makes it a very attractive choice for drug development. A comprehensive risk/benefit analysis that lent support to the case for clinical psychotherapy research with MDMA was funded by MAPS and submitted to FDA (Baggott, Jerome & Stuart, 2001). Politically, however, MDMA is not the easiest psychedelic to try to develop into a prescription medicine. Its non-medical use is increasing, especially among young people. In the 2001 Monitoring the Future survey, funded by NIDA, 11.7 % of high school seniors reported that they had tried Ecstasy at some point, up from 11.0 % in 2000 and 8.0 % in 1999 (Johnston, O'Malley & Bachman 2001). Police authorities are seizing increasingly large amounts. Customs officials have seized 9.3 million ecstasy pills in FY 2000, as compared to 3.5 million in FY 1999 and 750,000 in FY 1998 (Office of Public Affairs, US Customs Service, 2000; National Drug Intelligence Center, 2000). NIDA has called the increased use of MDMA an epidemic (NIDA 2000).

Yet the political controversy about MDMA offers one crucial advantage that makes MDMA much more likely to become the first psychedelic to be approved as a prescription medicine. As a result of the millions of non-medical users of MDMA around the world, health authorities, anti-drug authorities and research scientists have expended an amazing amount of time, energy and money trying to understand the risks of MDMA, its mechanisms of action, and the consequences of acute and long-term use.

The number of scientific papers in the peer-reviewed scientific literature reporting on research with MDMA in humans and animals, along with case reports discussing adverse events, exceeds 1240 according to a Medline search conducted by the author on May 1, 2002. Data in the peer-reviewed scientific literature can be submitted to FDA as evidence in the assessment of MDMA's risk profile and safety, with the only cost being the time it takes to systematically review the papers and organize the data for submission to FDA. FDA is willing to accept published papers for review and has even approved drugs "based primarily or exclusively on published reports (FDA 1998)." The costs of conducting these published MDMA studies is well over $20 million. The availability of data from

these studies dramatically reduces the amount of additional funding that will be required to argue a case before FDA for MDMA's safety and efficacy.

Several researchers have administered MDMA to human subjects in clinical studies of MDMA's safety, mechanism of action and physiological and psychological effects. More frequently, researchers have compared people who have used MDMA in non-medical contexts with controls. As of March 2002, more than 262 subjects had been administered MDMA in the context of legal research. There was also data in the scientific literature from more than 985 people who had used MDMA, sometimes in astonishingly large amounts, in non-medical recreational contexts. These MDMA users have been compared to more than 835 controls."

An MDMA Phase I study with 18 patients has been successful completed in the United States, though data on only the first 6 subjects have been published (Grob et al. 1996). Two other Phase I studies with MDMA focused on objectives other than safety have also been conducted in the United States. An MDMA pharmacokinetic study was conducted at UC San Francisco (Everhart et al. 1999) and a study is underway investigating which brain neurotransmitter receptor sites are involved in producing MDMA's subjective effects (Tancer & Johanson 2001). Studies in Switzerland have investigated MDMA's action on brain neurotransmitter receptor sites (Liechti et al. 2000), on information processing (Vollenweider et al. 1999b) and on the psychological and cardiovascular effects of a single dose of MDMA (Vollenweider 1998). Three MDMA pharmacokinetic studies have been conducted in Europe in England (Fallon et al. 1999), Spain (de la Torre et al. 2000), and Switzerland (Helmlin et al. 1996). A Phase I dose-response safety study has been completed place in Spain (Mas et al. 1999; Cami et al. 2000), as well as a study investigating MDMA/alcohol interactions (Hernandez-Lopez et al. 2002). A study investigating the hormonal effects of MDMA has taken place in England (Henry et al. 1998) and a study investigating the immunological effects has taken place in Spain (Pacifici et al. 1999). Yet with all this research, there is not one single paper reporting data from a controlled scientific study into the therapeutic use of MDMA.

MAPS' effort to initiate controlled, FDA-approved scientific research into the therapeutic potential of MDMA in patient populations began in 1986, and has taken 16 years to come to fruition. A Phase II dose-escalation pilot study of MDMA-assisted psychotherapy in the treatment of post-traumatic stress disorder (PTSD) has been approved in Spain. This is currently the only study into the therapeutic use of MDMA approved anywhere in the world. The existence of the Spain study, sponsored by MAPS, is an important practical factor behind the selection of MDMA as the initial psychedelic drug to focus on developing into an FDA-approved prescription medicine. The sixth patient in Spain, at the 75 mg. dose level, was treated on April 15, 2002. The researchers conducting the study will gather the data in a sufficiently rigorous manner so that it can be submitted to FDA for review. With the approval of this study, the chance to develop the therapeutic potential of MDMA is now more than a mirage.

"Psychedelic drugs, though each with a unique set of actions and side effects, all serve the generally similar function of increasing access to psychological, emotional processes. As a result, psychedelics can be used as general purpose adjuncts to psychotherapy."

Why Post-Traumatic Stress Disorder?

In choosing the patient population to study, one of the criteria was that the unique properties of MDMA-enhanced psychotherapy needed to be matched to a patient population in which MDMA therapy could offer a dramatic benefit. Ideally, this benefit would require only from one to three drug sessions to produce significant, measurable and long-lasting clinical progress. Alternative medications for this patient population should be relatively ineffective, at least in some subpopulation of patients. The patient population should also be a group that the general public feels compassion towards, in order to help overcome resistance to the idea of the therapeutic use of psychedelics.

The core of the MDMA experience has been described by one of the pioneering psychiatrists who worked with MDMA-assisted psychotherapy in terminal cancer patients as "reducing the fear response to a perceived emotional threat." When used therapeutically, MDMA is administered as an adjunct to psychotherapy on an intermittent basis within a larger therapeutic relationship, usually fewer than four times and frequently only once or twice. Numerous case histories and anecdotal reports testify to MDMA's ability to assist people struggling to come to terms with difficult life events (Stevens 1999/2000; Otalora 1984). These reports suggest that MDMA-assisted psychotherapy should initially be explored not in patients whose psychiatric symptoms originated with biological imbalances with possible genetic components, though MDMA might still be helpful in some ways with such patients, but rather in patients who need some assistance in processing difficult emotions that have a deep component of fear and/or anxiety. Two of the main categories of patients that fit this description are people suffering from PTSD and people facing terminal illness. People with these two types of clinical conditions have been treated with MDMA with some remarkable results in some patients.

The main advantage of working with a PTSD patient population instead of patients with terminal illness is that PTSD patients as a group are probably in better overall health than cancer patients and are taking fewer other medications, making it less complicated to work with them. Once the MDMA/PTSD study is underway in the US, MAPS will seek to obtain FDA approval for a study of MDMA-assisted psychotherapy in hospice patients.

In the US market, there are only two conventional pharmacological treatments that have been approved for patients with PTSD. On December 7, 1999, FDA approved the drug known as Zoloft (sertraline) for PTSD, on the basis of four small clinical trials (it was already on the market as an anti-depressant). Two of the clinical trials showed no efficacy, two showed some efficacy. These studies involved a total of 351 subjects. Subgroup analysis revealed that Zoloft was efficacious in female patients but not in male patients. According to Dr. Katz, Director of the Division of Neuropharmacological Drug Products, "The effect of the treatment appears to come essentially completely from women (Katz 1999)." On December 14, 2001, FDA approved the use of Paxil (paroxetine) in the treatment of PTSD. Unlike the Zoloft trials, studies with Paxil showed efficacy in both men and woman. Interestingly, Zoloft and Paxil's mechanism of action is to increase the amount in the synapse of the brain neurotransmitter serotonin, the same neurotransmitter that MDMA primarily impacts. The difference is that MDMA increases serotonin acutely for a period of 4-8 hours after a single dose while Zoloft increases serotonin chronically but must be taken on a daily basis.

The patient group that will be tested with MDMA in Spain is women survivors of sexual assault who suffer from chronic PTSD and who have already failed on at least one course of conventional treatment. The patient group that will be tested in the US will include men and women, survivors of sexual and/or criminal assault, who have failed on one course of treat-

ment with an SSRI such as Zoloft or Paxil. The patient group for the Israeli study will include patients who have PTSD as a result of war or terrorism, as well as sexual or criminal assault, and who have failed on one course of an SSRI. By choosing subjects who have already failed on one course of conventional treatment, the risk/benefit ratio is improved in favor of permitting the study to proceed.

We hypothesize that MDMA will prove helpful in resolving some of these subjects' difficult and painful memories so that they can move forward with some degree of resolution, not forgetting the past but not as burdened by it either. MDMA-assisted psychotherapy also has the potential advantage of being cost-effective, since it can be delivered within a relatively short time.

MDMA in the treatment of PTSD is probably the best combination of psychedelic drug and clinical indication that can most justify a focused drug development effort. What such a drug development plan might look like will be elaborated below, after a brief review of the discussion of the Psychopharmacologic Drugs Advisory Committee that recommended that Zoloft be approved for use in the treatment of PTSD.

FDA Review of Zoloft for PTSD

Pfizer's recent experience with its successful development of Zoloft for the treatment of PTSD offers the most direct window into FDA policies and procedures for the design of research protocols and the review of data for the pharmacological treatment of PTSD. There are many analogous issues and also important differences between the development of Zoloft, a medication that has been approved by FDA for daily use for the relief of symptoms associated with PTSD, and the development of MDMA, a drug that is meant to be administered from 1-3 times on an in-patient basis as an adjunct to psychotherapy for the relief of the underlying causes of PTSD. The public record related to FDA approval of Zoloft will be reviewed in order to understand FDA regulatory policy as it applies directly to the development of medications to treat PTSD. The most valuable documents in the public record include transcripts of the October 8, 1999 Psychopharmacologic Drugs Advisory Committee (Psychopharmacologic Drugs Advisory Committee 1999), a slide show delivered at that meeting by Dr. David Smith, Statistical Reviewer, FDA Office of Biostatistics (Smith 1999), and a complete file of the FDA approval package for Zoloft, NDA19839,SO26, obtained from FDA through Freedom of Information Act (FOIA) request. As of May 2002, FDA has not yet responded to a FOIA request for the Paxil approval package.

October 8, 1999 Psychopharmacologic Drugs Advisory Committee Meeting: Study Design Issues

Four clinical trials were reviewed on October 8, 1999 by FDA's Psychopharmacologic Drugs Advisory Committee, advising the Division of Neuropharmacological Drug Products. Outcome data was presented at the meeting by Pfizer and FDA representatives.

The Advisory Committee meeting began with an overview presented to the Committee by Dr. Tom Laughren, Team Leader for Psychopharmacology at FDA. He indicated that PTSD is a chronic disorder and FDA, "ordinarily uses parallel group studies although one might ask whether a crossover design might be appropriate even for a chronic condition, if the condition is very stable over time and there is a return to baseline if the treatment is stopped (Psychopharmacologic Drugs Advisory Committee 1999: 10)."

Dr. Laughren further noted that, "this is a chronic disorder and one may ask the question whether or not there is a need for long-term data and at what point in development should that information become available should that become an issue for approvability. Now, as an

"There are many analogous issues and also important differences between the development of Zoloft...and the development of MDMA."

aside, I should say that we never, up until now, made that a requirement for approving a new indication in psychiatric disorders (Psychopharmacologic Drugs Advisory Committee 1999: 11)."

Dr. Farfel, a Pfizer scientist, indicated that "subjects were dosed once daily beginning with 25 mg/dy in the first week [dosing was not initially based on mg/kg] and then continuing flexibly titrated between 50 and 200 mg/dy thereafter (Psychopharmacologic Drugs Advisory Committee 1999: 33)." FDA's Dr. Temple commented about the titration design, indicating that he would have preferred fixed doses. He said, "I would be curious as to why that design was chosen. If it was chosen to avoid adverse effect, that would make some sense, but ordinarily I think you would learn more from a randomization to fixed doses, even if you inched your way up to those doses...Now you could analyze this to see if there was a dose/response hidden in Psychopharmacologic Drugs Advisory Committee 1999: 127)." Dr. Hammer, Advisory Committee member, made the suggestion that one of the major studies should have been fixed dose and the other flexible, so as to have gained some information about dose/response relationships in one of the studies.

Dr. Laughlen said, "One thing that we like to see for an indication that is more mature in some sense than this is, from a regulatory standpoint, we like to see an active control arm in a trial to help us in interpreting it, so that if an active standard drug, which is believed to work, also fails, we are more inclined to discount that study. This is obviously not a strategy you can use early on in the development of a new indication (Psychopharmacologic Drugs Advisory Committee 1999: 145)."

This suggestion of an active control arm for subsequent treatments for PTSD should be adopted. In testing MDMA-assisted psychotherapy for PTSD, parallel groups are more appropriate than a crossover design since the hypothesis is that there will not be a return to baseline after the MDMA treatment is over. This is different for Zoloft, which offers mostly symptomatic relief with a significant number of subjects relapsing once the use of Zoloft is ended. From a financial perspective, this seems ideal for a pharmaceutical company since patients have a continued need to purchase the product or the symptoms will return. In contrast, MDMA-assisted psychotherapy has been helpful in some reported case histories after one to three sessions, with no additional MDMA sessions required to maintain clinical improvement.

The fact that the Zoloft design allowed titration suggests that it might also be possible to titrate the number of doses of MDMA-assisted psychotherapy a patient receives in one of the Phase III trials, to match the treatment to the depth and speed at which the patient is able to resolve issues related to the original trauma.

Sample Size for Efficacy

Dr. Gary Ryan, Group Director of Clinical Research, Pfizer, stated, "Our PTSD Clinical Trial program consisted of four placebo controlled trials enrolling a total of 757 patients (Psychopharmacologic Drugs Advisory Committee 1999: 16)." Though Dr. Ryan reported a total of 757 patients, the data presented in the slides by Dr. Smith indicated only 597 subjects, with the difference due to attrition. Pfizer's Dr. Farfel reported that, "the mean number of subjects in each treatment group was approximately 95, for a total of 376 subjects treated with sertraline and 381 treated with placebo (Psychopharmacologic Drugs Advisory Committee 1999: 32)."

In the two clinical trials that demonstrated efficacy, a total of 385 patients were enrolled, 191 who received Zoloft and 194 who received placebo (Smith Slide #9). Dr. Charles Marmar, Professor and Vice Chairman, Department of Psychiatry, UC San Francisco, spoke for Pfizer and noted that "you can see that for the most part the effects, while meaningful, have been modest (Psychopharmacologic Drugs Advisory Committee 1999: 29)," indicating that sample sizes may need to be fairly large, especially in a comparison study between MDMA and Zoloft or Paxil.

Dr. Katz, Director of the Division of Neuropharmacological Drug Products, stated, "There are conditions where we have considered studies positive or approved drugs on the basis of fairly small studies, but in which the treatment has been statistically significantly different from the control. Of course, the smaller the study, the more likelihood that there is some bias creeping in or that there is an imbalance is an important characteristic that you don't really know how to test for, you don't even know what they are necessarily. So we like to see larger studies but there is no specific requirement for numbers (Psychopharmacologic Drugs Advisory Committee 1999: 149)."

Sample Size for Safety

Dr. Laughren mentioned that "this program overall was relatively small, and so in making a judgement about the safety of Zoloft, we relied heavily on the safety experience on other populations. So, a question is, is that a reasonable extrapolation? (Psychopharmacologic Drugs Advisory Committee 1999: 14) " Dr. Farfel commented on safety reporting, "Safety was investigated in 757 subjects, and nothing that was found in this development program suggests a risk that has not already been identified in previous trials and indications, and is already not described in the labeling (Psychopharmacologic Drugs Advisory Committee 1999: 55)."

The minimal number of MDMA-assisted psychotherapy sessions that will be administered to subjects, along with all the safety data already gathered about MDMA from clinical trials around the world, may enable the safety of MDMA in PTSD patients to be investigated with as few subjects as were used in the studies of Zoloft in the treatment of PTSD. This is a reasonable assumption that would change depending on the strength and clarity of the data actually gathered in the clinical studies.

Estimates for Sample Sizes for the MDMA Phase III Trials

Based on FDA's review of research into the use of Zoloft in the treatment of PTSD, the power of Pfizer's studies as designed was considered inadequate for subgroup analysis but adequate for group comparisons. The studies as completed had roughly 75 subjects per group. According to Dr. Farfel, the groups had a mean initial enrollment of about 95 subjects, with about 75 per group completing the trial and included in final data analysis.

Until the effect size and variance of response to MDMA-assisted psychotherapy is determined, sample sizes cannot be estimated with accuracy. The more pronounced the treatment effect and the smaller the variation in outcomes, the smaller the sample size needs to be to generate significant results (Friedman, Furberg & Demets 1985). In order to reduce variance so as to reduce sample size, a homogenous patient population with a relatively uniform response should be selected. In the Zoloft studies, there was a substantial difference in response between men and women. The Phase III MDMA studies should be able to avoid this problem through the review of data gathered in the Phase II trials that will evaluate the effectiveness of MDMA in men and in women. The Phase III trials can then be designed either with all men, all women, or a combination. With an advantage in uniformity over the Zoloft designs, it will probably be possible to obtain adequate power with 80 sub-

jects in each of the three treatment groups and 40 in the psychotherapy-alone sub-threshold dose condition. It might even be possible to use only 70 subjects per group, since Dr. Kazdin has estimated, "for comparing two treatments [for superiority, not equivalence, making this a high estimate for a test of equivalence]...a sample size of 71 per group would be needed to retain power at the desired level for the median ES [effect size]." (Kazdin & Bass 1989).

"Yet the political controversy about MDMA offers one crucial advantage that makes MDMA much more likely to become the first psychedelic to be approved as a prescription medicine."

Duration of Studies

The studies of Zoloft that Pfizer submitted for review were designed as 12-week trials. Dr. Marmar noted that "suicide rates are an important issue both in the acute and chronic form (Psychopharmacologic Drugs Advisory Committee 1999: 27)," suggesting caution in the use of placebo groups in PTSD patients with a risk factor for suicide. Relatively short treatment courses should be employed to minimize the amount of time patients are receiving placebo, or instead psychotherapy-alone with a sub-threshold dose of MDMA, which will maximize suggestion without providing a direct pharmacological effect of MDMA.

Dr. Domingez, Advisory Committee Member, suggested that 12 weeks was sufficient for the study since most people respond by then. She noted that there was a trade-off between the desire to extend treatment in order to give enough time to find an effect and the desire not to keep people on placebo for an unnecessarily long period of time (Psychopharmacologic Drugs Advisory Committee 1999: 129).

This discussion supports limiting the length of MDMA treatment in the clinical trials to 12 weeks, though longer-term follow-up data should also be gathered.

Orphan Drug Designation: Not Possible

Dr. Marmar stated that the lifetime prevalence for PTSD in the American adult population is 7.8%. Dr. Bonnie Green, Professor of Psychiatry at Georgetown University Medical School, President Elect of the International Society for Traumatic Stress Studies (ISTSS) commented that any one time, 5% of women and 2-3% of men have PTSD (Psychopharmacologic Drugs Advisory Committee 1999: 22). Since the adult population of the United States is greater than 170 million, PTSD clearly does not qualify as an Orphan disease since there are more than 200,000 potential patients in any given year.

MAPS' Clinical Plan for MDMA for PTSD

The following outline is of a sequence of studies designed to evaluate the risks and benefits of the use of MDMA-assisted psychotherapy in the treatment of post traumatic stress disorder (PTSD). This plan includes only studies focused on the safety and efficacy of the use of one to four sessions of MDMA-assisted psychotherapy in patients with PTSD. The Clinical Plan begins with a Phase II study since Phase I MDMA safety studies have already been conducted in the United States, Spain and Switzerland.

As the studies of MDMA in patients with PTSD are conducted, additional safety issues may become apparent. Further research addressing specific issues related to the safety of MDMA may be required by FDA before there will be sufficient information to justify a New Drug Application (NDA). These additional studies, if needed, may involve issues that will be addressed by gov-

ernment-funded research teams around the world already working to assess questions of safety and mechanisms of action. Alternatively, these issues may need to become the subject of research by MAPS-funded scientific teams. However, based on what is already known about MDMA, it is likely that any safety issues related to the use of MDMA in PTSD patients can be adequately addressed by the proposed studies in PTSD patients.

Phase II Spain Dose-Finding Pilot Study in Women Survivors of Sexual Assault

This study, being conducted by Dr. Pedro Sopelano and Jose Carlos Bouso, Ph.D. candidate, U. Autonoma de Madrid, is currently the only MDMA psychotherapy study underway anywhere in the world in which MDMA is being administered to patients. The goals of this study are, 1) to evaluate whether a single dose of MDMA can be administered safely to 29 female survivors of sexual assault with chronic PTSD, 2) to gather preliminary evidence about therapeutic efficacy and, 3) to determine which dose or doses should be used in subsequent larger-scale studies. This study treated the sixth subject on April 15, 2002 and is scheduled to complete the testing of all 29 subjects by May 2003.

The Phase II dose/response study in Spain will cost $65,000, or $2,240 per subject. The Spain study involves just one treatment session per subject. The study is being coordinated by Jose Carlos Bouso, a Ph.D. candidate working on the study for his dissertation. Under these circumstances, a cost of $2,240 per subject can be obtained. This is the lower limit for the cost-per-patient of any MDMA protocol.

Phase II United States Full-Dose Pilot Study in Male and Female PTSD patients

A research team under the director of Dr. Michael Mithoefer has worked with MAPS to design and obtain FDA-approval to conduct an MDMA/PTSD pilot study in the United States. The protocol was approved by the FDA on November 2, 2001. As of May 2002, the protocol is still in the midst of the IRB approval process. The study should begin Summer 2002. The protocol will involve 20 subjects with PTSD, both male and female. All 20 subjects will receive about 12 hours of non-drug psychotherapy. Twelve subjects will also receive two sessions of MDMA-assisted psychotherapy scheduled three to five weeks apart, with a dose of 125 mgs at each session, while 8 subjects will receive 2 placebo sessions. The goals of this study are 1) to evaluate whether MDMA can be safely administered to PTSD patients and 2) to determine whether there is any preliminary evidence of therapeutic efficacy and, if so, to develop an estimate of the effect size.

The entire treatment course will be conducted in 12 weeks or less, in accordance with the recommendations made in the FDA Pharmacologic Drugs Advisory Committee meeting that reviewed the data from the trials of Zoloft in the treatment of PTSD,

If the study does begin in Summer 2002, the research team should be able to complete both sessions in all 20 patients by Summer 2003. The analysis of initial data can be completed by Fall 2003, with six month follow-up data analysis completed by Winter 2003. The final report can be completed by Spring 2004.

The cost of the study is estimated to be $12,000 per subject or $240,000. The costs of this study include non-drug psychotherapy hours as well as thorough neuropsychological evaluations, and quite a substantial cost for administrative work on the FDA and IRB approval process. Subsequent studies will probably require fewer non-drug psychotherapy hours and may not require any neuropsychological evaluations, depending on the results from this initial pilot study. Since administrative costs have been averaged over a small number of subjects, subsequent studies with much larger subject populations, at least 10 times the size of this pilot

study, can be conducted with significantly less cost per patient.

Phase III Trials - 4 -Arm Multi-Site Study, United States

The goal of this study is to be one of the two primary FDA-required "adequate and well-controlled investigations" demonstrating safety and efficacy of the use of MDMA in patients with PTSD. Depending on the data from the pilot studies, the study will focus either on women, on men, or on both. The study will be designed with a psychotherapy-alone group receiving a subthreshold (placebo) dose of MDMA, a medium dose group, a full dose group and a Zoloft or Paxil comparison group.

The number of sessions will be titrated by agreement of patient and therapeutic team, with a maximum of 4 sessions within a 12 week period. This study will hopefully start in Spring 2004 and will take three years to conduct. The study will enroll approximately 280 subjects, 80 in each drug treatment group and 40 in the psychotherapy-alone group. Due to economies of scale, the study should be able to be conducted for about $8,000 per subject, for a total cost of $2,240,000.

Phase III Trials- 4-Arm Study Spain or Israel

The second large-scale trial will be conducted outside of the United States, in Spain or possibly in Israel. FDA will accept data gathered outside of the United States, if it is gathered according to standards set by FDA. With one study conducted in the United States and one in Spain or Israel, it should be possible to obtain marketing approval in both the United States and the European Community.

The goal of this study is to be one of the two primary "adequate and well-controlled investigations" demonstrating safety and efficacy. Depending on the data from the pilot studies, the study will focus either on women, on men, or on both. The study will be designed with a psychotherapy-alone group receiving a subthreshold (placebo) dose of MDMA, a medium dose group, a full dose group and a Zoloft or Paxil comparison group. The study will enroll approximately 280 subjects, 80 in each drug treatment group and 40 in the psychotherapy-alone group. This study will involve a fixed number of sessions administered within a 12 week period. This study will involve three sessions for each subject, once every four weeks, with no titration permitted. The use of two different designs for the two different Phase III studies, with the US study using a variable number of treatment sessions depending upon patient and therapist decision and the foreign study employing a fixed number of three sessions, is based on the recommendation made by Dr. Hammer during the October 8, 1999 meeting of FDA's Pharmacologic Drugs Advisory Committee.

This study will hopefully start in Spring 2004 and will take three years to conduct. The study will enroll 280 subjects, should cost in the range of $8,000 per subject, for $2,240,000.

Total Cost

The total cost of the sequence of studies enumerated above amounts to $4,720,000. Additional animal or human toxicity studies may be needed, though it is likely that these studies will have already been government-funded with the data in the public domain.

The Clinical Plan elaborated above suggests that a rough estimate of about $5 million will need to be expended over a five-year period to develop MDMA into a prescription medicine for just one clinical indication, PTSD. After MDMA is approved initially for PTSD, only one adequate and well controlled multi-site investigation might be sufficient for the approval of subsequent uses of MDMA in closely related disorders, such as in the psychotherapeutic treatment of anxiety and depression in cancer patients. ■

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Spirit and Stardust

A speech delivered by U.S. Rep. Dennis Kucinich (D-OH) at the Praxis Peace Institute Conference in Dubrovnik, Croatia on June 9, 2002


Eagle Nebula (M16)
NASA/STScI

This speech by Rep. Dennis Kucinich (D-OH), though definitely not written as a psychedelic manifesto, is one of the clearest examples in print of the political implications of the mystical experience. Over the past few months, this speech by Rep. Kucinich has been posted to numerous Internet sites and e-mail lists devoted to peace and social justice. We thought it remarkably appropriate for this issue of the MAPS Bulletin, in which we reflect on our vision for the future.

There is an idealism at the core of the psychedelic community that is difficult to explain. It's based in part on the conviction that even partial unitive mystical experiences, whether or not catalyzed by psychedelics, can have a transformative effect. The hope is that the lasting effects of these experiences include more tolerance and appreciation of diversity of all kinds, enhanced environmental awareness, solidarity with the poor and oppressed, and a willingness to work through difficult emotions rather than project them onto an external enemy or scapegoat. This vision/hypothesis of the social value of psychedelic mystical experiences is supported by the findings of Rick Doblin's 25+ year follow-up study to Dr. Walter Pahnke's classic Good Friday experiment (http://druglibrary.org/schaffer/lsd/doblin.htm).

Rep. Kucinich beautifully voices the possibility of translating the experience of unity and transcendence into action and change. We agree with Rep. Kucinich that when "spiritual principles form the basis of active citizenship," small groups of people can create positive change against great odds. We are pleased to share his inspirational message with MAPS members.

As one studies the images of the Eagle Nebula, brought back by the Hubble Telescope from that place in deep space where stars are born, one can imagine the interplay of cosmic forces across space and time, of matter and spirit dancing to the music of the spheres, atop an infinite sea of numbers.

Spirit merges with matter to sanctify the universe. Matter transcends to return to spirit. The interchangeability of matter and spirit means the starlit magic of the outermost life of our uni-

verse becomes the soul-light magic of the innermost life of our self. The energy of the stars becomes us.

We become the energy of the stars. Stardust and spirit unite and we begin: One with the universe. Whole and holy. From one source, endless creative energy, bursting forth, kinetic, elemental. We, the earth, air, water and fire-source of nearly fifteen billion years of cosmic spiraling.

We begin as a perfect union of matter and spirit. We receive the blessings of the Eternal from sky and earth. In our outstretched hands we can feel the energy of the universe. We receive the blessings of the Eternal from water, which nourishes and sanctifies life. We receive the blessings of the Eternal from the primal fire, the pulsating heart of creation. We experience the wonder of life multidimensional and transcendent. We extend our hands upwards and we are showered with abundance. We ask and we receive. A universe of plenty flows to us, through us. It is in us. We become filled with endless possibilities.

We need to remember where we came from; to know that we are one. To understand that we are of an undivided whole: race, color, nationality, creed, gender are beams of light, refracted through one great prism. We begin as perfect and journey through life to become more perfect in the singularity of "I" and in the multiplicity of "we"; a more perfect union of matter and spirit. — This is human striving. This is where, in Shelley's words, "...hope creates from its own wreck the thing it contemplates."

This is what Browning spoke of: Our 'reach exceeding [our] grasp'. This is a search for heaven within, a quest for our eternal home. In our soul's Magnificat, we become conscious of the cosmos within us. We hear the music of peace, we hear the music of cooperation, we hear music of love. We hear harmony, a celestial symphony. In our soul's forgetting, we become unconscious of our cosmic birthright, plighted with disharmony, disunity, torn asunder from the stars in a disaster well-described by Matthew Arnold in Dover Beach: "...the world, which seems to lie before us like a land of dreams, so various, so beautiful, so new, hath really neither joy, nor love, nor light, nor certitude nor peace, nor help for pain. And we are here, as on a darkling plain, swept with confused alarms of struggle and flight, where ignorant armies clash by night."

Today Dover Beach is upon the shores of the Potomac River in Washington, D.C. Our leaders think the unthinkable and speak of the unspeakable inevitability of nuclear war; of a nuclear attack on New York City, of terrorist attacks throughout our nation; of war against Iraq using nuclear weapons; of biological and chemi-

cal weapon attacks on civilian populations; of catastrophic global climate change; of war in outer space.

When death (not life) becomes inevitable, we are presented with an opportunity for great clarity, for a great awakening, to rescue the human spirit from the arms of Morpheus through love, through compassion and through integrating spiritual vision and active citizenship to restore peace to our world. The moment that one world is about to end, a new world is about to begin. We need to remember where we came from. Because the path home is also the way to the future.

Fountain of Eternal Life
Marshall A. Fredricks
Cleveland, Ohio

In the city I represent in the United States Congress, there is a memorial to Peace, named by its sculptor, Marshall A. Fredericks the "Fountain of Eternal Life." A figure rises from the flames, his gaze fixed to the stars, his hands positioned sextant-like, as if measuring the distance. Though flames of war from the millions of hearts and the dozens of places wherein it rages, may lick at our consciousness, our gaze must be fixed upward to invoke universal principles of unity, of co-operation, of compassion, to infuse our world with peace, to ask for the active presence of peace, to expand our capacity to receive it and to express it in our everyday life. We must do this fearlessly and courageously and not breathe in the poison gas of terror. As we receive, so shall we give.

As citizen-diplomats of the world, we send peace as conscious expression where ever, whenever and to whomever it is needed: to the Middle East, to the Israelis and the Palestinians, to the Pakistanis and the Indians, to Americans and Al-Qaeda, and to the people of Iraq, and to all those locked in deadly combat. And we fly to be with the bereft, with those on the brink, to lis-

U.S. Department of Energy

ten compassionately, setting aside judgment and malice to become peacemakers, to intervene, to mediate, to bring ourselves back from the abyss, to bind up the world's wounds.

As we aspire to universal brotherhood and sisterhood, we harken to the cry from the heart of the world and respond affirmatively to address through thought, word and deed conditions which give rise to conflict: Economic exploitation, empire building, political oppression, religious intolerance, poverty, disease, famine, homelessness, struggles over control of water, land, minerals, and oil.

We realize that what affects anyone, anywhere affects everyone, everywhere.

As we help others to heal, we heal ourselves. Our vision of interconnectedness resonates with new networks of world citizens in nongovernmental organizations linking from numberless centers of energy, expressing the emergence of a new organic whole, seeking unity within and across national lines. New transnational web-based email and telecommunications systems transcend governments and carry within them the power of qualitative transformation of social and politica structures and a new sense of creative intelligence. If governments and their leaders, bound by hierarchy and patriarchy, wedded to military might for legitimacy, fail to grasp the implications of an emerging world consciousness for cooperation, for peace and for sustainability, they may become irrelevant.

As citizen-activists the world over merge, they can become an irresistible force to create peace and protect the planet. From here will come a new movement to abolish nuclear weapons and all weapons of mass destruction. From here will come the demand for sustainable communities, for new systems of energy, transportation and commerce. From here comes the future rushing in on us.

How does one acquire the capacity for active citizenship? The opportunities exist every day. In Cleveland, citizens have developed the ability to intercede when schools are scheduled to be closed, and have kept the schools open; to rally to keep hospitals open; to save industries which provide jobs; to protect neighborhood libraries from curtailment of service, to improve community policing; to meet racial, ethnic and religious intolerance openly and directly.

Active citizenship begins with an envisioning of the desired outcome and a conscious application of spiritual principles. I know. I have worked with the people in my own community. I have seen the dynamic of faith in self, faith in one's ability to change things, faith in one's ability to prevail against the odds through an

Crinoids
J. Rottman

appeal to the spirit of the world for help, through an appeal to the spirit of community for participation, through an appeal to the spirit of cooperation, which multiplies energy. I have seen citizens challenge condition without condemning anyone, while invoking principles of non-opposition and inclusion of those who disagree.

I have seen groups of people overcome incredible odds as they become aware they are participating in a cause beyond self and sense the movement of the inexorable which comes from unity. When you feel this principle at work, when you see spiritual principles form the basis of active citizenship, you are reminded once again of the merging of stardust and spirit. There is creativity. There is magic. There is alchemy.

Citizens across the United States are now uniting in a great cause to establish a Department of Peace, seeking nothing less than the transformation of our society, to make non-violence an organizing principle, to make war archaic through creating a paradigm shift in our culture for human development, for economic and political justice and for violence control. Its work in violence control will be to support disarmament, treaties, peaceful coexistence and peaceful consensus building. Its focus on economic and political justice will examine and enhance resource distribution, human and economic rights and strengthen democratic values.

Domestically, the Department of Peace would address violence in the home, spousal abuse, child abuse, gangs, police-community relations conflicts and work with individuals and groups to achieve changes in attitudes that examine the mythologies of cherished world views, such as 'violence is inevitable' or 'war is inevitable'. Thus it will help with the discovery of new selves and new paths toward peaceful consensus.

The Department of Peace will also address human development and the unique concerns of women and children. It will envision and seek to implement plans for peace education, not simply as a course of study, but as a template for

Cup Coral
J. Rottman

all pursuits of knowledge within formal educational settings.

Violence is not inevitable. War is not inevitable. Non-violence and peace are inevitable. We can make of this world a gift of peace which will confirm the presence of universal spirit in our lives. We can send into the future the gift which will protect our children from fear, from harm, from destruction.

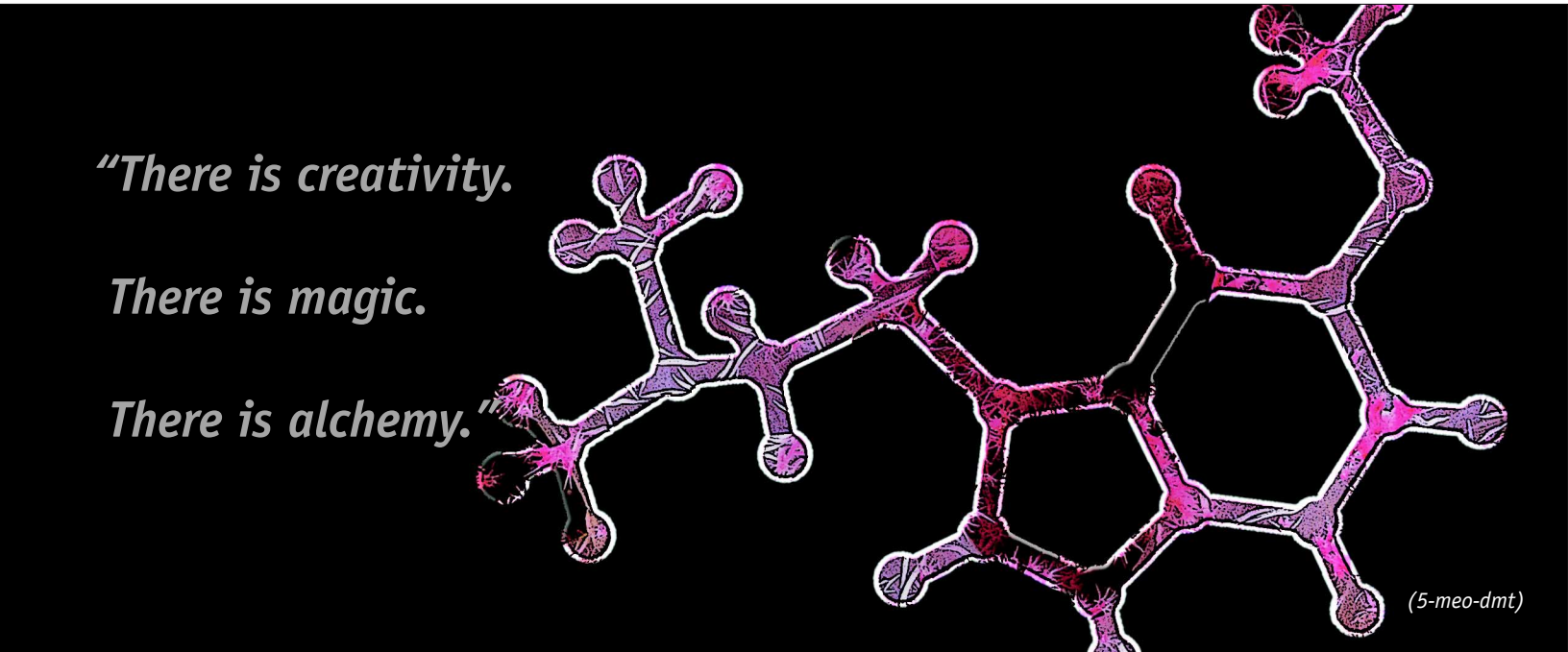
Peace Protecting Genius
Paul Wayland-Bartlett

Carved inside the pediment which sits atop the marble columns is a sentinel at the entrance to the United States House of Representatives. Standing resolutely inside this "Apotheosis of Democracy" is a woman, a shield by her left side, with her outstretched right arm protecting a child happily sitting at her feet. The child holds the lamp of knowledge under the protection of this patroness.

This wondrous sculpture by Paul Wayland Bartlett, is entitled "Peace Protecting Genius." Not with nuclear arms, but with a loving maternal arm is the knowing child Genius shielded from harm. This is the promise of hope over fear. This is the promise of love which overcomes all. This is the promise of faith which overcomes doubt. This is the promise of light which overcomes darkness. This is the promise of peace which overcomes war.

Thank You.

Email responses to info@thespiritoffreedom.com or Dkucinich@AOL.com



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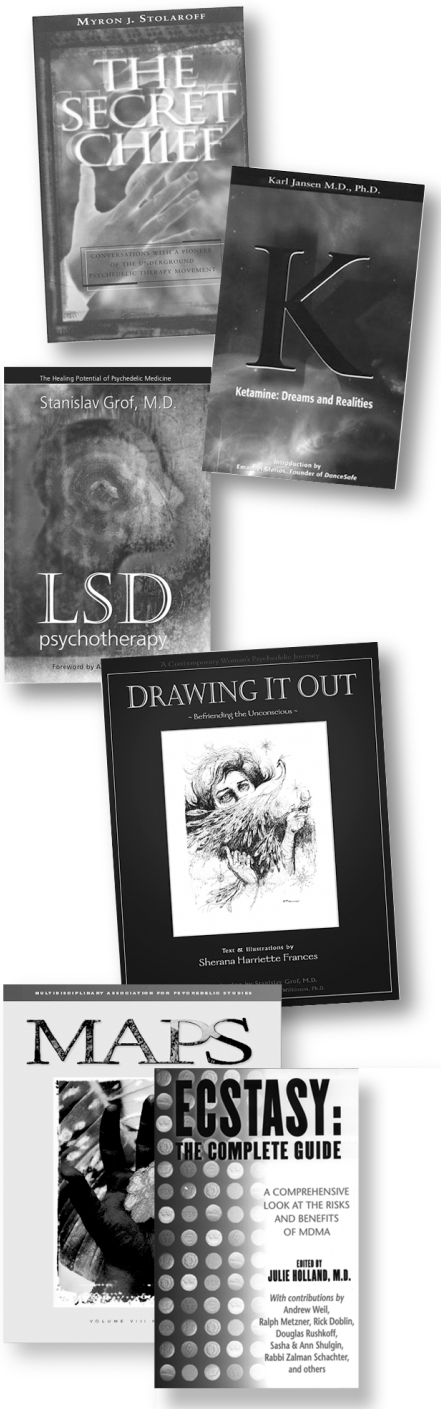

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MAPS MEMBERSHIP INFORMATION

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 1,800 members.

MAPS has previously funded basic scientific research in both humans and animals into the safety of MDMA (3,4-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 psychotherapeutic benefits of MDMA, other psychedelics, and marijuana, with the goal of eventually gaining governmental approval for their medical uses.

ALBERT EINSTEIN WROTE: "**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 join 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.

The MAPS Bulletin

Each Bulletin will report on MAPS research in progress. In addition to reporting on research both in the United States and abroad, the Bulletin can include feature articles, reports on conferences, book reviews, Heffter Research Institute updates, and the Hofmann Report. Issues raised in letters, calls and e-mail from MAPS members may also be addressed, as may political developments that affect psychedelic research and usage.

MAPS' founder and President Rick Doblin earned his Ph.D. in Public Policy from the Kennedy School of Government at Harvard University. Doblin was also in Stan and Christina Grof's first training group to receive certification as a Holotropic Breathwork practitioner.

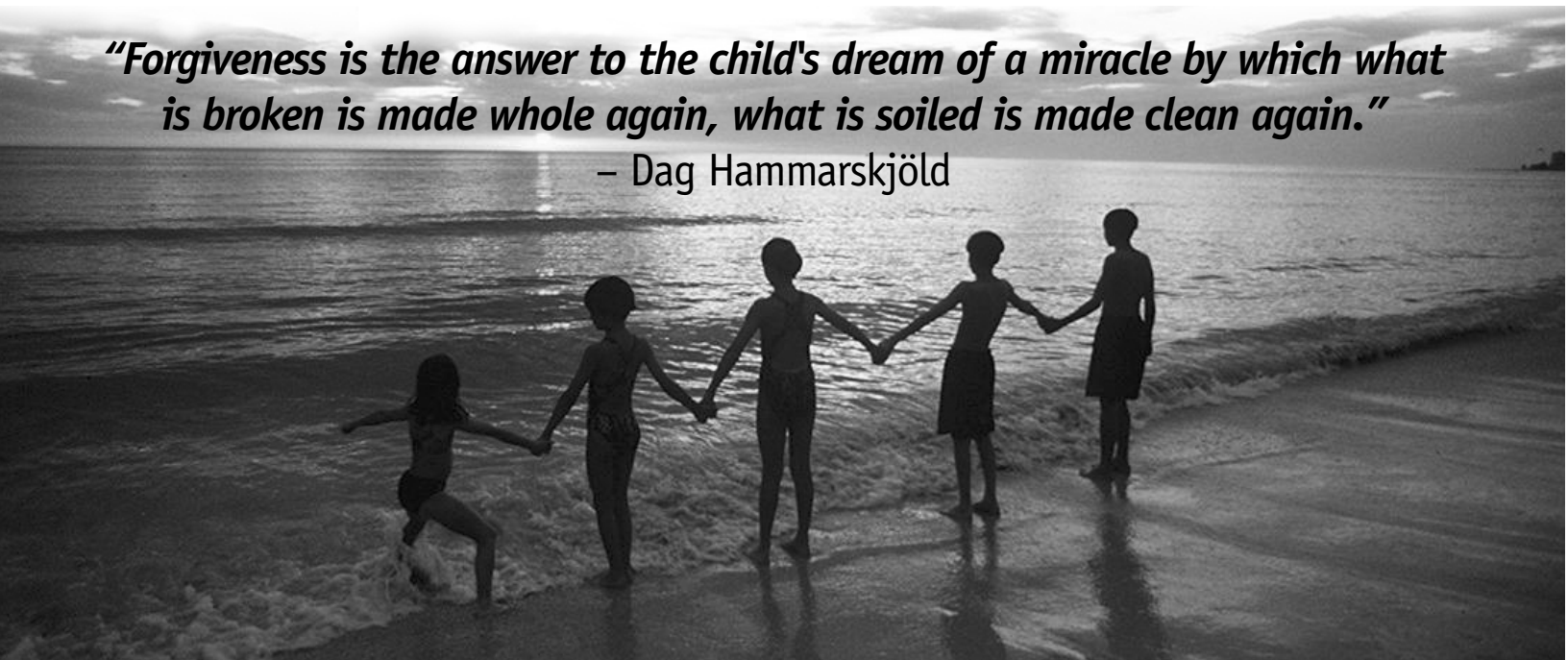
Nicole Tavernier, Director of Operations, has a background in various fields of business and is currently working on her degree in Business Administration.

Mercedes Paulino, Director of Electronic Media, an electro-anthro-bricolier, has become a connoisseur of Deceased Culture, weird hieroglyphs, a frequenter of forgotten systems of Mysterious Statue Chambers and Pyramids, sole witness to Polyhedral Phenomenon of alarming scale in the night sky and Sudden Unexplained Stellar Reconfiguration.

Brandy Doyle, Director of Special Projects, is pleased to add bulletin editing and member correspondence to her responsibilities at MAPS. She enjoys the way MAPS is situated at the intersection of research and action, consciousness and public policy, understanding the mind and changing the world.

Marissa Vaudo, Membership and Sales Coordinator, is grateful to psychedelics as guides and teachers that strive for health and awareness. In her eyes, MAPS is researching so that this help can be available to all who want to heal and challenge themselves.

Maggie Hall, Director of Development, is interested in broadening the scope of MAPS' research and educational activities by developing more financial resources for the organization. She sees the incredible benefits available to the global community by providing the full range of therapies that every person has a right to have access to when necessary, believing strongly in personal freedom and choice.

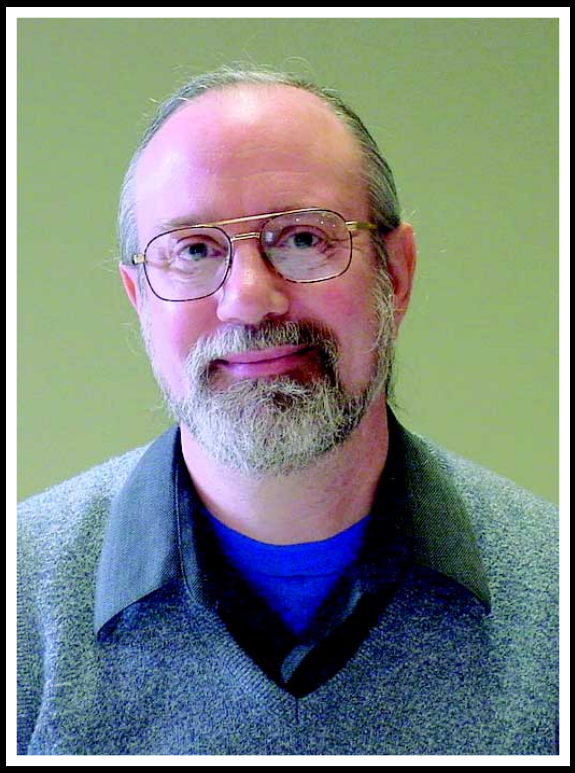


In this 1978 photo are the 11 people who started Microsoft. Shown, top row from left, are Steve Wood, Bob Wallace and Jim Lane; second row, Bob O'Rear, Bob Greenberg, March McDonald and Gordon Letwin; and front row, Bill Gates, Andrea Lewis, Marla Wood and Paul Allen.

***Seattle Times* obituary, September 24, 2002**
http://www.maps.org/media/bobwallace9.24.02.html

***New York Times* obituary, September 26, 2002**
hhttp://www.maps.org/media/bobwallace-nyt9.26.02.html

***Seattle Post-Intelligencer* obituary, September 26, 2002**
http://www.maps.org/media/bobwallace9.26.02.html



In Honor and Memory of Bob Wallace
Software Pioneer and Psychedelic Philanthropist

Photo Credit: Dave Racette/Heffter