MDMA's ability to assist people struggling to come to terms with difficult life events.[37] 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. Another advantage is that for males with PTSD, there is still no approved pharmacological treatment. This lack of alternative treatments favorably changes the risk/benefit ratio for the use of MDMA

In the US market, there is only one conventional pharmacological treatment that has been approved for the treatment of PTSD. On December 7, 1999, FDA approved the drug known as Zoloft 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."[38] Interestingly, Zoloft's mechanism of action is to increase the amount 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. By choosing subjects who have already failed on one course of conventional treatment, the risk/benefit ratio is changed in favor of permitting the study to proceed. Most importantly, MDMA is likely to 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 may be able to prove helpful to these patients to some extent within a relatively short time.

MDMA in the treatment of PTSD is probably the best combination of 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 Pharmacologic Drugs Advisory Committee that recommended that Zoloft be approved for use in the treatment of PTSD.

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[37] Sue and Shane. Speaking the silence: MDMA in a couple dealing with cancer. MAPS 9 (Winter 1999/2000) 4: 31-34. http://www.maps.org/news-letters/v09n4/09431sue.html

[38] Memorandum, December 6, 1999 from Director of Division of Neuropharmacological Drug Products to File, NDA 19-839/S-026. Obtained from FDA through FOIA request, along with entire approval package for Zoloft. FOIA Request filed January 20, 2000. Package arrived 4/15/00.

FDA Review of Zoloft for PTSD

Pfizer's recent experience with its successful development of Zoloft (sertraline) 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 the development of medications to treat PTSD. The most valuable documents in the public record include transcripts of the October 8, 1999 Pharmacologic Drugs Advisory Committee,[39] a slide show delivered at that meeting by Dr.David Smith, Statistical Reviewer, FDA Office of Biostatistics,[40] and a complete file of the FDA approval package for Zoloft, obtained from FDA through Freedom of Information Act (FOIA) request.[41]

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

Four clinical trials were reviewed on October 8, 1999 by FDA's Pharmacologic Drugs Advisory Committee, advising the Division of Neuropharmacological Drug Products.[42] 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."[43]

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 aside, I should say that we never, up until now, made that a requirement for approving a new indication in psychiatric disorders."[44]

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

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[39]Transcript of the October 8. 1999 meeting of the Pharmacologic Drugs Advisory Committee. Page 10
http://www.fda.gov/ohrms/dockets/ac/cder99t.htm#Psychopharmacologic%20Drugs 3556t1a.pdf

[40]http://www.fda.gov/ohrms/dockets/ac/99/slides/3556s1a/sld001.htm

[41]Approval Package NDA 19839, S026. (about 200 pages)

[42]Transcript of the October 8. 1999 meeting of the Pharmacologic Drugs Advisory Committee. Page 10
http://www.fda.gov/ohrms/dockets/ac/cder99t.htm#Psychopharmacologic%20Drugs 3556t1a.pdf

[43]Transcript of the October 8. 1999 meeting of the Pharmacologic Drugs Advisory Committee, 10.

[44]Transcript of the October 8. 1999 meeting of the Pharmacologic Drugs Advisory Committee, 11.

then continuing flexibly titrated between 50 and 200 mg/dy thereafter."[45] 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 there."[46] 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."[47]

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.[48]

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 3 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."[49] 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."[50]

In the two clinical trials that demonstrated efficacy, a total of 385 patients were enrolled, 191 who received Zoloft and 194 who received placebo.[51] Dr. Marmar noted

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[45]Ibid, 33.

[46]Ibid, 127.

[47]Ibid, 145.

[48]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.

[49]Ibid, 16.

[50]Ibid, 32.

[51]These numbers come from Slide # 9, http://www.fda.gov/ohrms/dockets/ac/99/slides/3556s1a/sld009.htm However, Slide #16 shows that there were 306 subjects in the two clinical trials that showed efficacy, 149 who received Zoloft and 157 who received placebo. I have chosen to use the higher numbers for the cost estimates.

that "you can see that for the most part the effects, while meaningful, have been modest,"[52] indicating that sample sizes may need to be fairly large, especially in a comparison study between MDMA and Zoloft.

Dr. Katz, Director of 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."[53]

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?"[54] 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."[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.

Duration of Studies

The studies of Zoloft that Pfizer submitted for review were designed as 12 week trials.[56] Dr. Marmar noted that "suicide rates are an important issue both in the acute and chronic form,"[57] 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 even psychotherapy-alone with sub-threshold dose of MDMA.[58]

Dr. Domingez 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

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[52]Ibid, 29.
[53]Ibid, 147.
[54]Ibid, 14.
[55]Ibid, 55.
[56]Transcript of the October 8. 1999 meeting of the Pharmacologic Drugs Advisory Committee. Page 10
http://www.fda.gov/ohrms/dockets/ac/cder99t.htm#Psychopharmacologic%20Drugs .3556t1a.pdf .
[57]Ibid, 27.
[58]The sub-threshold dose of MDMA was previously recommended in the methodology chapters as the ideal choice for "placebo."

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.[59]

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. Charles Marmar, Professor and Vice Chairman, Department of Psychiatry, UC San Francisco, spoke for Pfizer and stated that the lifetime prevalence for PTSD in the American adult population is 7.8%.[60] 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.[61]

PTSD does not qualify as an Orphan disease since there are more than 200,000 potential patients in any given year.[62]

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).[63] 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 2 study since Phase 1 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 government-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

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[59]Ibid, 129.

[60]Ibid, 22.

[61]Ibid, 103.

[62]If the adult population is 170 million, 7.8% is 13.3 million people with PTSD during their adult lifetime. Since PTSD is chronic, many of these people have the disease across multiple years.

[63]To review a Clinical Plan that was not implemented for the development of the medical use of marijuana in the treatment of AIDS wasting, see: Doblin R. A Comprehensive Clinical Plan for the Investigation of Marijuana's Medical Use in the Treatment of the HIV-Related Wasting Syndrome. Bull MAPS 5 (Summer 1994) 1:16-18. The Plan was developed in consultation with FDA's Dr. Dan Spyker, when he was at Pilot Drug. The plan has not been implemented due to the inability to obtain marijuana for research from NIDA. The timeline on the plan suggests how the research effort might have developed if it had been possible to obtain permission from NIDA to use its marijuana in FDA-approved studies. Since the plan was written, the disease of AIDS Wasting has largely disappeared as a result of advances in the use of protease inhibitors. However, many HIV+ people still use marijuana for the control of nausea associated with their protease inhibitors and other medications. http://www.maps.org/news-letters/v05n1/05116cli.html

safety issues related to the use of MDMA in PTSD patients can be adequately addressed by the studies in PTSD patients.

Phase 2 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 approved 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 will start treating patients in November 2000 and is scheduled to complete the testing of all 29 subjects by December 2001.

The Phase 2 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 2 United States Full-Dose Pilot Study in Male and Female PTSD patients

A research team at the Medical University of South Carolina, under the director of Dr. Michael Mithoefer, is working with MAPS to design and obtain FDA-approval to conduct an MDMA/PTSD pilot study in the United States. The protocol will be submitted to FDA for review in March, 2001. The protocol will involve 20 subjects with PTSD, both male and female, each receiving three sessions of MDMA-assisted psychotherapy (placebo, low/medium and medium doses), scheduled several weeks apart,. 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 and estimate of the effect size.

This study will investigate whether MDMA shows preliminary signs of efficacy in treating a subgroup of PTSD patients (males) that Zoloft was not effective in treating. The evaluation of the use of MDMA in male PTSD patients is an important exploration since at present there is no treatment for PTSD with proven efficacy for males.

This study will involve three treatment sessions administered in a randomized double-blind procedure, two with MDMA and one with either a sub-threshold dose of MDMA serving as a placebo session, or an completely inactive placedo. 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,

This study will hopefully be approved by June, 2001. If that milestone is reached, the research team should be able to complete all three sessions in all 20 patients by February, 2002. The analysis of initial data can be completed by March 2002, with six month follow-up data analysis completed by August 2002. Twelve month follow-up data can be analyzed by March 2003. The final report can be completed by April 2003.

The cost of the study is estimated to be $6,000 per subject or $120,000.

Phase 3 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 sub-threshold group, a medium dose group, a full dose group and a Zoloft 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 June 2002 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, (see below for rationale for this estimate). The study will cost $6,000 per subject, for a total cost of $1,680,000.

Phase 3 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 sub-threshold group, a medium dose group, a full dose group and a Zoloft comparison group. The study will enroll approximately 280 subjects, 80 in each drug treatment group and 40 in the psychotherapy-alone group, (see below for rationale for this estimate). 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 3 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 June 2002 and will take three years to conduct. The study will enroll 280 subjects (see below for rationale for this estimate), may cost $5,500 per subject, for $1,540,000.

Estimates for Sample Sizes for the Phase 3 Four-Arm 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.[64] 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 3 MDMA studies should be able to avoid this problem through the review of data gathered in the Phase 2 trials that will evaluate the effectiveness of MDMA in men and in women. The Phase 3 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 subjects 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]."[65] Despite the possible use of sample sizes in the range of 70, these estimates have been prepared based on sample sizes of 80.

Total Cost

The total cost of the sequence of studies enumerated above amounts to $3,405,000. Additional animal or human toxicity studies costing about $350,000 may be needed, though it is also possible that these studies will be government-funded with the data in the public domain. Legal and consultant fees are estimated to be about $250,000.

The Clinical Plan elaborated above suggests that a rough estimate of about $4,000,000 will need to be expended over a five-year period to develop MDMA into a prescription medicine for just one clinical indication, PTSD.[66]

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[64]Friedman L, Furberg C and Demets D. The Fundamentals of Clinical Trials.2nd Edition. St Loius: Mosby-Year Book. 1985. 96-97.

[65]Kazdin A, Bass D. Power to detect differences between alternative treatments in comparative psychotherapy outcome research. J Consult and Clin Psych 57 (Feb 1989) 1:144.

[66] 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, such as in the psychotherapeutic treatment of cancer patients, FDA Guidance document, Clinical Evidence for Effectiveness, 10. "(2) Demonstration of Effectiveness by a Single Study of a New Use with Independent Substantiation from Related Study Data, (e) Studies in a closely related disease, (f) Studies in less closely related diseases, but where the general purpose of therapy is similar. " However, the Guidance also states, "reliance on only a single study will generally be limited to situations in which a trial has demonstrated a clinically meaningful effect on mortality, irreversible morbidity, or prevention of a disease with potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible." 13.

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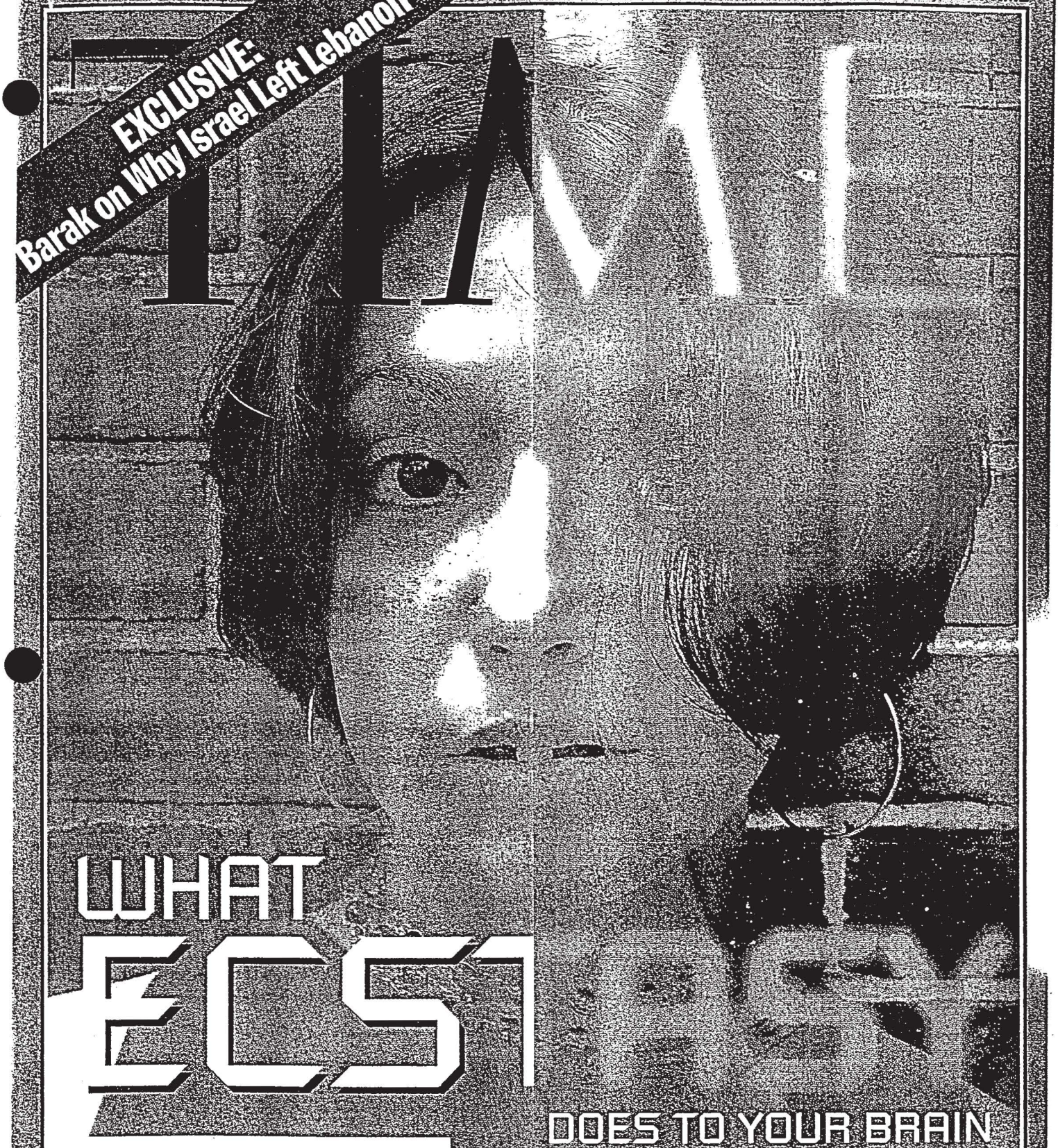

WHAT ECSTASY DOES TO YOUR BRAIN

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- The Rave Scene
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January 2001

Due to the errors of one of the reporters who helped research the June 5, 2000, article "The Lure of Ecstasy," Time printed several mistakes:

1. "In November [1999], [George] Ricaurte recorded for the first time the effects of ecstasy the human brain." Actually, the first study was conducted in the 1980s and published in 1992, and Ricaurte was a contributing researcher, not the only one.

2. "[The Multidisciplinary Association for Psychedelic Studies] has funded important MDMA studies, including Ricaurte's first work on the drug." Actually, MAPS contributed to Ricaurte's first studies in primates and humans, but not the very first ones, which were in rodents.

3. "In [the United States], the FDA has approved only one study [using MDMA]." The FDA has approved three studies with MDMA.

4. "In 1995 Dr. Charles Grob, a UCLA psychiatrist, used [MDMA] as a pain reliever for end-stage cancer patients." Wrong. Dr. Grob completed a phase I safety study for MDMA in 1995, but he did not give the drug to cancer patients.

I regret these errors and take responsibility for not fixing them before publication.

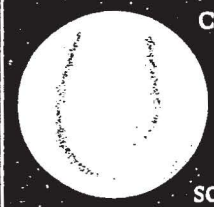
John Cloud
Staff Writer
Time

ECSTASY | HAPPINESS IS ... A PILL?

the lure of ecstasy

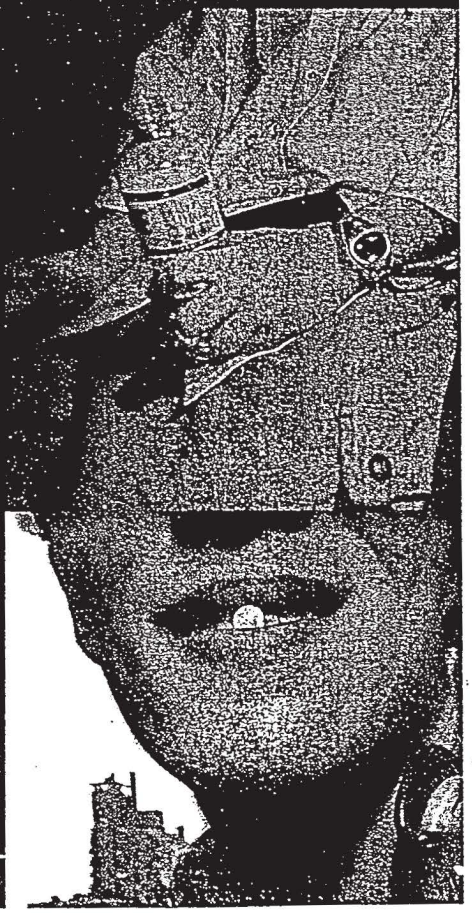
THE ELIXIR BEST KNOWN FOR POWERING RAVES IS AN 80-YEAR-OLD ILLEGAL DRUG. BUT IT'S SHOWING UP OUTSIDE CLUBS TOO, AND ADVOCATES CLAIM IT EVEN HAS THERAPEUTIC BENEFITS. JUST HOW DANGEROUS IS IT?

By JOHN CLOUD



COBB COUNTY, GA., MAY 11, 2000. IT'S A THURSDAY MORNING, and 18-year-old "Karen" and five friends decide to go for it. They skip first period and sneak into the woods near their upscale high school. One of them takes out six rolls—six ecstasy pills—and they each swallow one. Then back to school, flying on a drug they once used only on weekends. Now they smile stupid gelatinous smiles at one another, even as high school passes them by. That night they will all go out and drop more ecstasy, rolling into the early hours of another school day. It's rare that anyone would take ecstasy so often—it's not physically addictive—but teenagers everywhere have begun experimenting with it. "The cliques are pretty big in my school," Karen says, "and every clique does it."

Grand Rapids, Mich., May 1997. Sue and Shane Stevens have sent the three kids away for the weekend. They have locked the doors and hidden the car so no one will bug them. Tonight they hope to talk about Shane's cancer, a topic they have mostly avoided for years. It has eaten away at their marriage just as it corrodes his kidney. A friend has recommended that they take ecstasy, except he calls it MDMA and says therapists used it 20 years ago to get people to discuss difficult topics. And, in fact, after tonight, Sue and Shane will open up, and Sue will come to believe MDMA is prolonging her marriage—and perhaps Shane's life.



Photographs for TIME by Scott Houston—Corbis Sygma

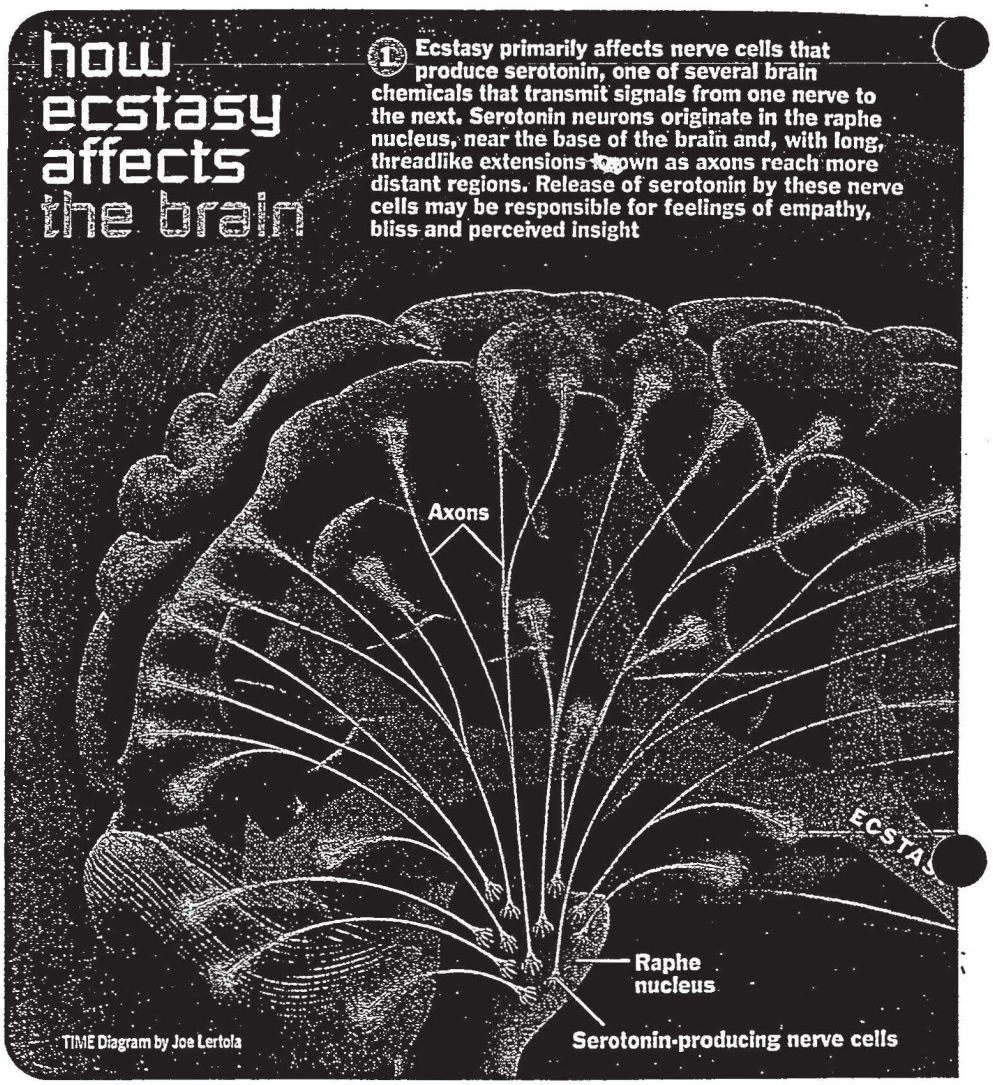
So we know that ecstasy is versatile. Actually, that's one of the first things we knew about it. Alexander Shulgin, 74, the biochemist who in 1978 published the first scientific article about the drug's effect on humans, noticed this panacea quality back then. The drug "could be all things to all people," he recalled later, a cure for one student's speech impediment and for one's bad LSD trip, and a way for Shulgin to have fun at cocktail parties without martinis.

The ready availability of ecstasy, from Cobb County to Grand Rapids, is a newer phenomenon. Ecstasy—or "e"—enjoyed a brief spurt of mainstream use in the '80s, before the government outlawed it in 1985. Until recently, it remained common only on the margins of society—in clubland, in gay America, in lower Manhattan. But in the past year or so, ecstasy has returned to the heartland. Established drug dealers and mobsters have taken over the trade, and they are meeting the astonishing demand in places like Flagstaff, Ariz., where "Katrina," a student at Northern Arizona University who first took it last summer, can now buy it easily; or San Marcos, Texas, a town of 39,000 where authorities found 500 pills last month; or Richmond, Va., where a police investigation led to the arrest this year of a man thought to have sold tens of thousands of hits of e. On May 12, authorities seized half a million pills at San Francisco's airport—the biggest e bust ever. Each pill costs pennies to make but sells for between $20 and $40, so someone missed a big payday.

Ecstasy remains a niche drug. The number of people who use it once a month remains so small—less than 1% of the population—that ecstasy use doesn't register in the government's drug survey. (By comparison, 5% of Americans older than 12 say they use marijuana once a month, and 1.8% use cocaine.) But ecstasy use is growing. Eight percent of U.S. high school seniors say they have tried it at least once, up from 5.8% in 1997; teen use of most other drugs declined in the late '90s. Nationwide, customs officers have already seized more ecstasy this fiscal year, more than 5.4 million hits, than in all of last year. In 1998 they seized just 750,000 hits.

The drug's appeal has never been limited to ravers. Today it can be found for sale on Bourbon Street in New Orleans along with the 24-hour booze; a group of lawyers in Little Rock, Ark., takes it occasionally, as does a cheerleading captain at a Miami high school. The drug is also showing up in hip-hop circles. Bone Thugs-N-Harmony raps a paean to it on its latest album: "Oh, man, I don't even f___ with the weed no more."

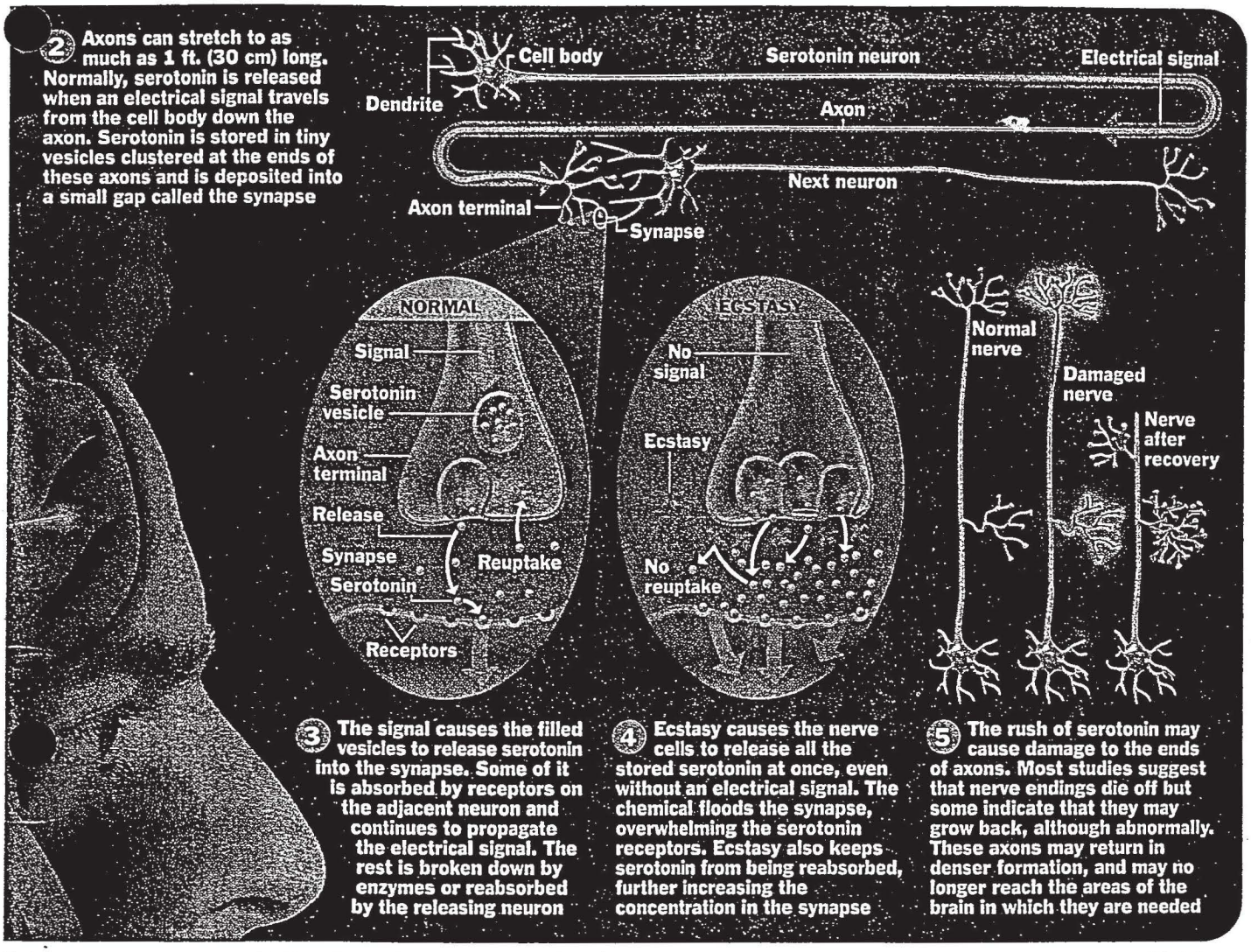
Indeed, much of the ecstasy taking—and the law enforcement under way to end it—has been accompanied by breathlessness. "It appears that the ecstasy problem will eclipse

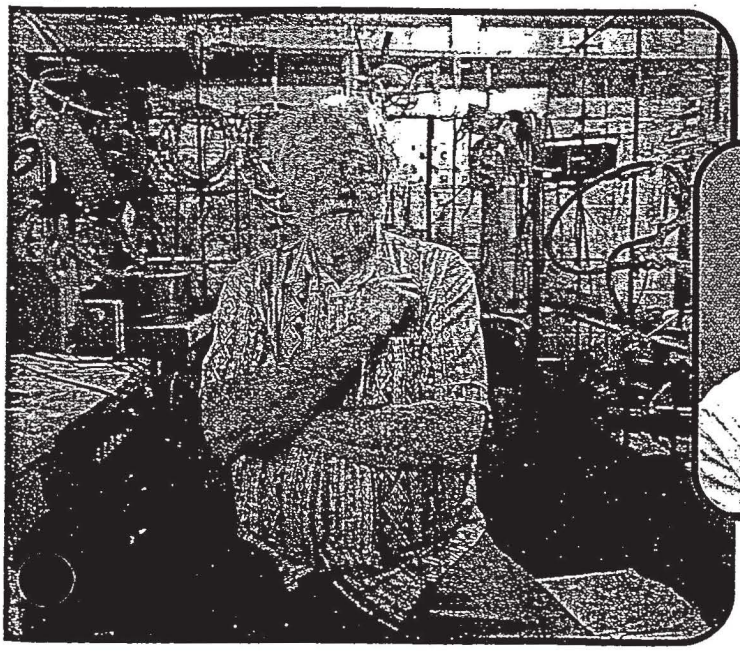


RICAURTE: RON HOLTZ FOR TIME; DOBLIN: MARNIE CRAWFORD SAMUELSON FOR TIME

▲ PRO-MDMA ACTIVIST Doblin, with his kids, believes the drug can help people deal with trauma

◀ NEUROSCIENTIST RICAURTE was the first to record the effects of MDMA on the brain; he says it damages certain cells





▽ BOB WALLACE, a Microsoft millionaire, funds DanceSafe, a prorave group that tests e pills for purity

◁ THE FATHER OF E? No, but Shulgin wrote first about its human use. He still studies drugs at his home lab

△ SUE STEVENS and her late husband used MDMA to help them discuss his cancer. "We weren't escaping from reality," she says

STEVENS: MICHELLE LITVIN FOR TIME; WALLACE AND SHULGIN: MARK RICHARDS—CONTACT FOR TIME

the crack-cocaine problem we experienced in the late 1980s," a cop told the Richmond *Times-Dispatch*. In April, *60 Minutes II* prominently featured an Orlando, Fla., detective dolorously noting that "ecstasy is no different from crack, heroin." On the other side of the spectrum, at *ecstasy.org*, you can find equally bloated praise of the drug. "We sing, we laugh, we share/ and most of all, we care," gushes an awful poem on the site, which also includes testimonials from folks who say ecstasy can treat schizophrenia and help you make "contact with dead relatives."

Ecstasy is popular because it appears to have few negative consequences. But "these are not just benign, fun drugs," says Alan Leshner, director of the National Institute on Drug Abuse. "They carry serious short-term and long-term dangers." Those like Leshner who fight the war on drugs overstate these dangers occasionally—and users usually understate them. But one reason ecstasy is so fascinating, and thus dangerous to antidrug crusaders, is that it appears to be a safer drug than heroin and cocaine, at least in the short run, and appears to have more potentially therapeutic benefits.

Even so, the Federal Government has launched a major p.r. effort to fight ecstasy based on the Internet at *clubdrugs.org*. Last week two Senators, Bob Graham of Florida and Charles Grassley of Iowa, introduced an ecstasy antiproliferation bill, which would stiffen penalties for trafficking in the drug. Under the new law, someone caught selling about 100 hits of ecstasy could be charged as a drug trafficker; current law sets the threshold at about 300,000 pills. "I think this is the time to take a forceful set of initiatives to try to reverse the tide," says Graham.

WHAT'S THE APPEAL OF ECSTASY? As a user put it, it's "a six-hour orgasm." About half an hour after you swallow a hit of e, you begin to feel peaceful, empathetic and energetic—not edgy, just clear. Pot relaxes but sometimes confuses; LSD stupefies; cocaine wires. Ecstasy has none of those immediate downsides. "Jack," 29, an Indiana native who has taken ecstasy about 40 times, said the only time he felt as good as he does on e was when he found out he had won a Rhodes scholarship. He enjoys feeling logorrheic: ecstasy users often talk endlessly, maybe about a silly song that's playing or maybe about a terrible burden on them. E allows the mind to wander, but not into hallucinations. Users retain control. Jack can allow his social defenses to crumble on ecstasy, and he finds he can get close to people from different backgrounds. "People I would never have talked to, because I'm mostly in the Manhattan business world, I talk to on ecstasy. I've made some friends I never would have had."

All this marveling should raise suspicions, however. It's probably not a good idea to try to duplicate the best moment of one's life 40 times, if only because it will cheapen the truly good times. And even as they help open the mind to new experiences, drugs also can distort the reality to which users ineluctably return. Is ecstasy snake oil? And how harmful is it?

This is what we know:

An ecstasy pill most probably won't kill you or cure you. It is also unlike pretty much every other illicit drug. Ecstasy pills are (or at least they are supposed to be) made of a compound called methylenedioxymethamphetamine, or MDMA. It's an old drug: Germany issued the patent for it in 1914 to the German company E. Merck. Contrary to ecstasy lore, and there's tons of it, Merck wasn't trying to develop a diet drug when it synthesized MDMA. Instead, its chemists simply thought it could be a promising intermediary substance that might be used to help develop more advanced therapeutic drugs. There's also no evidence that any living creature took it at the time—not Merck employees and certainly not Nazi soldiers, another common myth. (They wouldn't have made very aggressive killers.)

GLOW STICKS ARE another rave fave; e users' eyes are more sensitive to lights

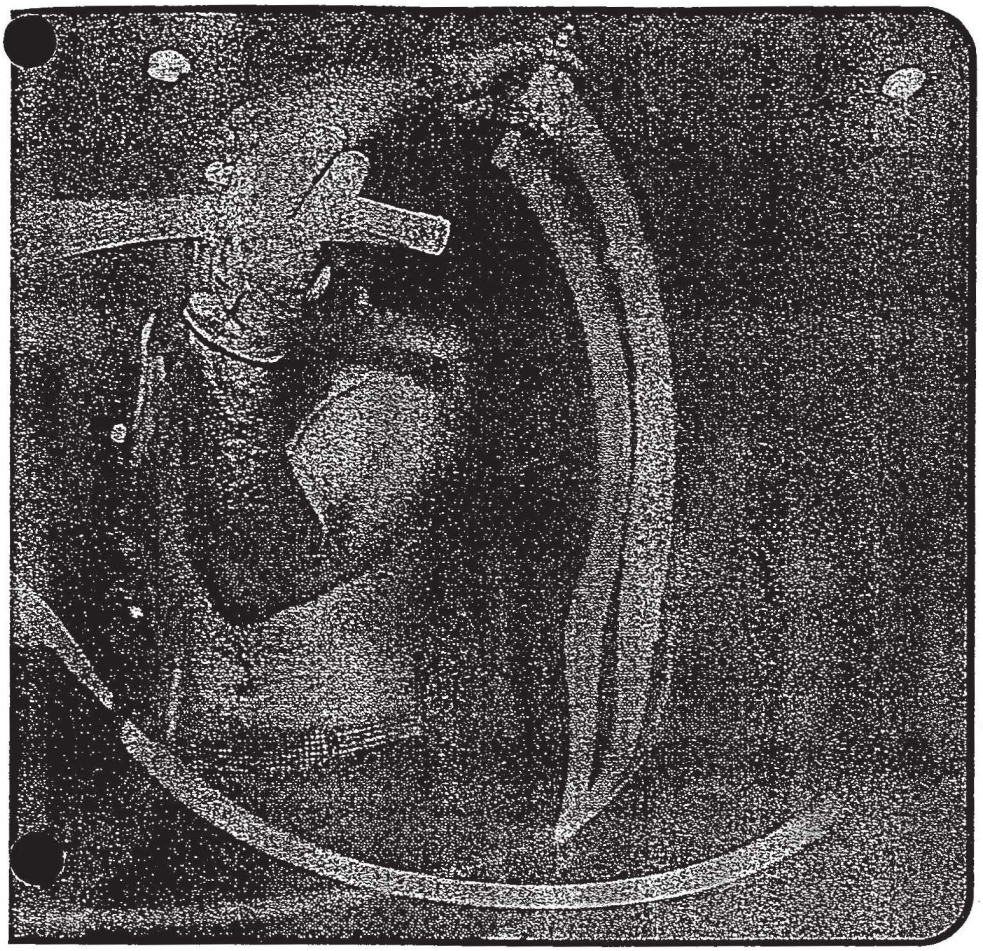
ECSTASY HEIGHTENS the senses. Clubbers like these women in Ithaca, N.Y., find that Vicks VapoRub electrifies the nasal passages

Yet MDMA all but disappeared until 1953. That's when the U.S. Army funded a secret University of Michigan animal study of eight drugs, including MDMA. The cold war was on, and for years its combatants had beeh researching scores of substances as potential weapons. The Michigan study found that none of the compounds under review was particularly toxic—which means there will be no war machines armed with ecstasy-filled bombs. It also means that although MDMA is more toxic than, say, the cactus-based psychedelic mescaline, it would take a big dose of e, something like 14 of today's purest pills ingested at once, to kill you.

It doesn't mean ecstasy is harmless. Broadly speaking, there are two dangers: first, a pill you assume to be MDMA could actually contain something else. Anecdotal evidence suggests that most serious short-term medical problems that arise from "ecstasy" are actually caused by pills adulterated with other, more harmful substances (more on this later). Second, and more controversially, MDMA itself might do harm.

There's a long-standing debate about MDMA's dangers, which will take much more research to resolve. The theory is that MDMA's perils spring from the same neurochemical reaction that causes its pleasures. After MDMA enters the bloodstream, it aims with laser-like precision at the brain cells that release serotonin, a chemical that is the body's primary regulator of mood. MDMA causes these cells to disgorge their contents and flood the brain with serotonin.

But forcibly catapulting serotonin levels could be risky. Of course, millions of Americans manipulate serotonin when they take Prozac. But ecstasy actually shoves serotonin from its storage sites, according to Dr. John Morgan, a professor of pharmacology at the City University of New York (CUNY). Prozac just prevents the serotonin that's already



been naturally secreted from being taken back up into brain cells.

Normally, serotonin levels are exquisitely maintained, which is crucial because the chemical helps manage not only mood but also body temperature. In fact, overheating is MDMA's worst short-term danger. Flushing the system with serotonin, particularly when users take several pills over the course of one night, can short-circuit the body's ability to control its temperature. Dancing in close quarters doesn't help, and because some novice users don't know to drink water, e users' temperatures can climb as high as 110°. At such extremes, the blood starts to coagulate. In the past two decades, dozens of users around the world have died this way.

There are long-term dangers too. By forcing serotonin out, MDMA resculpts the brain cells that release the chemical. The changes to these cells could be permanent. Johns Hopkins neurotoxicologist George Ricaurte has shown that serotonin levels are significantly lower in animals that have been given about the same amount of MDMA as you would find in just one ecstasy pill.

In November, Ricaurte recorded for the first time the effects of ecstasy on the human brain. He gave memory tests to people who said they had last used ecstasy two weeks before, and he compared their results with those of a control group of people who said they had never taken e. The ecstasy users fared worse on the tests. Computer images that give detailed snapshots of brain activity also showed that e users have fewer serotonin receptors in their brains than nonusers, even two weeks after their last exposure. On the strength of these studies as well as a large number of animal studies, Ricaurte has hypothesized that the damage is irreversible.

Ricaurte's work has received much attention, owing largely to the government's well-intentioned efforts to warn kids away from ecstasy. But his work isn't conclusive. The major problem is that his research subjects had used all kinds of drugs, not just ecstasy. (And there was no way to tell that the ecstasy they had taken was pure MDMA.) And critics say even if MDMA does cause the changes to the brain that Ricaurte has documented, those changes may carry no functional consequences. "None of the subjects that Ricaurte studied had any evidence of brain or psychological dysfunction," says CUNY's Morgan. "His findings should not be dismissed, but they may simply mean that we have a whole lot of plasticity—that we can do without serotonin and be O.K. We have a lot of unanswered questions."

Ricaurte told TIME that "the vast majority of people who have experimented with MDMA appear normal, and there's no obvious indication that something is amiss." Ricaurte says we may discover in 10 or 20 years that those appearances are horribly wrong, but others are more sanguine about MDMA's risks, given its benefits. For more than 15 years, Rick Doblin, founder of the Multidisciplinary Association for Psychedelic Studies, has been the world's most enthusiastic proponent of therapeutic MDMA use. He believes that the compound has a special ability to help people make sense of themselves and the world, that taking MDMA can lead people to inner truths. Independently wealthy, he uses his organization to promote his views and to "study ways to take drugs to open the unconscious."

Doblin first tried MDMA in 1982, when it was still legal and when the phrase "open the unconscious" didn't sound quite so gooey. At that time, MDMA had a small following among avant-garde psychotherapists, who gave it to blindfolded patients in quiet offices and then asked them to discuss traumas. Many of the therapists had heard about MDMA from the published work of former Dow chemist Shulgin. According to Shulgin (who is often wrongly credited with discovering MDMA), another therapist to whom he gave the drug in turn named it Adam and introduced it to more than 4,000 people.

Among these patients were a few entrepreneurs, folks who thought MDMA felt too good to be confined to a doctor's office. One who was based in Texas (and who has kept his identity a secret) hired a chemist, opened an MDMA lab and promptly renamed the drug ecstasy, a more marketable term than Adam or "empathy" (his first choice, since it better describes the effects). He began selling it to fashionable bars and clubs in Dallas, where bartenders sold it along with cocktails; patrons charged the $20 pills, plus $1.33 tax, on their American Express cards.

Manufacturers at the time flaunted the legality of the drug, promoting it as lacking the hallucinatory effects of LSD and the addictive properties of coke and heroin. The U.S. Drug Enforcement Administration was caught by surprise by the new drug not long after it had been embarrassed by the spread of crack. The administration quickly used new discretionary powers to outlaw MDMA, pointing to the private labs and club use as evidence of abuse. DEA officials also cited rudimentary studies showing that ecstasy users had vomited and experienced blood-pressure fluctuations.

Most therapeutic use quickly stopped. But Doblin's group has funded important MDMA studies, including Ricaurte's first

work on the drug. Sue Stevens, the woman who took it in 1997 with her husband Shane—he has since died of kidney cancer—learned about the drug from a mutual friend of hers and Doblin's. She believes e helped Shane find the right attitude to fight his illness, and she helps Doblin advocate for limited legal use. Soon his association will help fund the first approved study of MDMA in psychotherapy, involving 30 victims of rape in Spain diagnosed with post-traumatic stress disorder. In this country, the FDA has approved only one study. In 1995 Dr. Charles Grob, a UCLA psychiatrist, used it as a pain reliever for end-stage cancer patients. In the first phase of the study, he concluded the drug is safe if used in controlled situations under careful monitoring. The body is much less likely to overheat in such a setting. Grob believes MDMA's changes to brain cells are accelerated and perhaps triggered entirely by overheating.

SCOTT HOUSTON—CORBIS SYGMA FOR TIME

AFTER E: Young woman coming down at a postrave party

IN 1998, EMERGENCY ROOMS participating in the Drug Abuse Warning Network reported receiving 1,135 mentions of ecstasy during admissions, compared with just 626 in 1997. If ecstasy is so benign, what's happening to these people? The two most common short-term side effects of MDMA—both of which remain rare in the aggregate—are overheating and something even harder to quantify, psychological trauma.

A few users have mentally broken down on ecstasy, unprepared for its powerful psychological effects. A schoolteacher in the Bay Area who had taken ecstasy in the past and loved it says she took it again a year ago and began to recall, in horrible detail, an episode of sexual abuse. She became severely depressed for three months and had to seek psychiatric treatment. She will never take ecstasy again.

Ecstasy's aftermath can also include a depressive hangover, a down day that users sometimes call Terrible Tuesdays. "You know the black mood is chemical, related to the serotonin," says "Adrienne," 26, a fashion-company executive who has used ecstasy almost weekly for the past five years. "But the world still seems bleak." Some users, especially kids trying to avoid the pressures of growing up, begin to use ecstasy too often—every day in rare cases. In one extreme case, "Cara," an 18-year-old Miami woman who attends Narcotics Anonymous, says she lost 50 lbs. after constantly taking ecstasy. She began to steal and deal e to pay for rolls.

Another downside: because users feel empathetic, ecstasy can lower sexual inhibitions. Men generally cannot get erections when high on e, but they are often ferociously randy when its effects begin to fade. Dr. Robert Klitzman, a psychiatrist at Columbia University, has found that men in New York City who use ecstasy are 2.8 times more likely to have unprotected sex.

Still, the majority of people who end up in the e.r. after taking ecstasy are almost certainly not taking MDMA but something masquerading under its name. No one knows for sure what they're taking, since emergency rooms don't always test blood to confirm the drug identified by users. But one group that does test e for purity is DanceSafe, a prorave organization based in Berkeley, Calif., and largely funded by a software millionaire, Bob Wallace (Microsoft's employee No. 9). DanceSafe sets up tables at raves, where users can get information about drugs and also have ecstasy pills tested. (The organization works with police so that ravers who produce pills for testing won't be arrested.) A DanceSafe worker shaves off a sliver of the tablet and drops a solution onto it; if it doesn't turn black quickly, it's not MDMA.

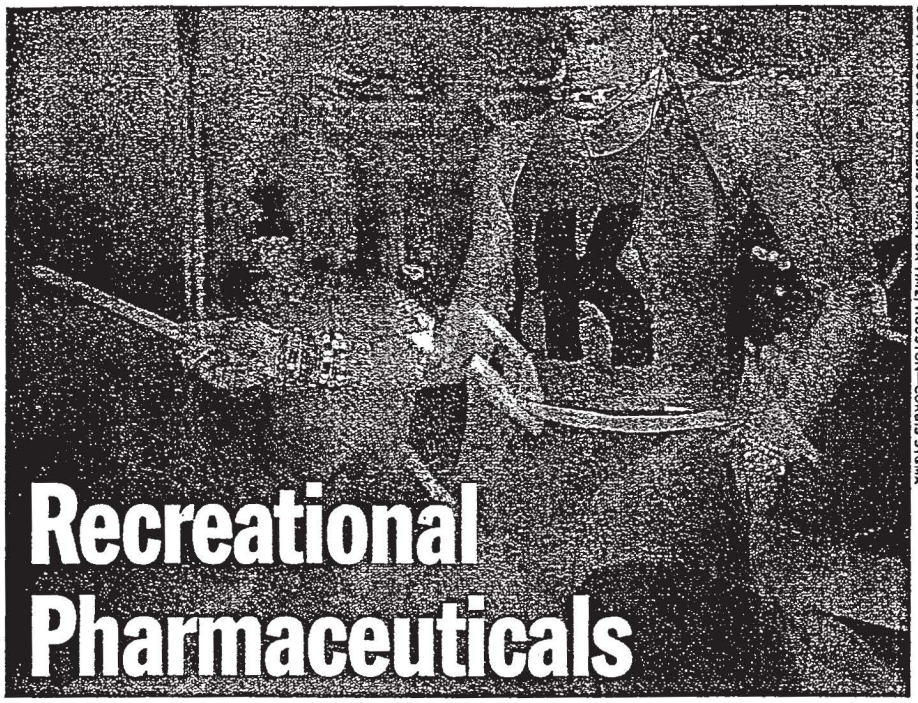
The organization has found that as much as 20% of the so-called ecstasy sold at raves contains something other than MDMA. DanceSafe also tests pills for anonymous users who send in samples from around the nation; it has found that 40% of those pills are fake. Last fall, DanceSafe workers attended a "massive"—more than 5,000 people—rave in Oakland, Calif. Nine people were taken from the rave in ambulances, but DanceSafe confirmed that eight of the nine had taken pills that weren't MDMA.

The most common adulterants in such pills are aspirin, caffeine and other over-the-counters. (Contrary to lore, fake e virtually never contains heroin, which is not cost-effective in oral form.) But the most insidious adulterant—what all eight of the Oakland ravers took—is DXM (dextromethorphan), a cheap cough suppressant that causes hallucinations in the 130-mg dose usually found in fake e (13 times the amount in a dose of Robitussin). Because DXM inhibits sweating, it easily causes heatstroke. Another dangerous adulterant is PMA (paramethoxyamphetamine), an illegal drug that in May killed two Chicago-area teenagers who took it thinking they were dropping e. PMA is a vastly more potent hallucinogenic and hyperthermic drug than MDMA.

Most users don't have access to DanceSafe, which operates in only eight cities. But as demand has grown, the incentive to manufacture fake e has also escalated, especially for one-time raves full of teens who won't see the dealer again. Established dealers, by contrast, operate under the opposite incentive. A Miami dealer who goes by the name "Top Dog" told TIME he obtains MDMA test kits from a connection on the police force. "If [the pills] are no good," he says, customers "won't want to buy from you anymore." It's business sense: Top Dog can earn $300,000 a year on e sales.

AS WRITER JOSHUA WOLF SHENK has pointed out, we tend to have opposing views about drugs: they can kill or cure; the addiction will enslave you, or the new perceptions will free you. Aldous Huxley typified this duality with his two most famous books, *Brave New World*—about a people in thrall to a drug called soma—and *The Doors of Perception*—an autobiographical work in which Huxley begins to see the world in a brilliant new light after taking mescaline.

Ecstasy can occasionally enslave and occasionally offer transcendence. Usually, it does neither. For Adrienne, the Midwestern woman who has been a frequent user for the past five years, ecstasy is a key part of life. "E makes shirtless, disgusting men, a club with broken bathrooms, a deejay that plays crap and vomiting into a trash can the best night of your life," she says with a laugh. "It has done two things in my life," she reflects. "I had always been aloof or insecure or snobby, however you want to put it. And I took it and realized, you know what, we're all here; we're all dancing; we're not so different. I allowed myself to get closer to people. Everything was more positive. But my life also became, quickly, all about the next time I would do it ... You feel at ease with yourself and right with the world, and that's a feeling you want to duplicate—every single week." *—With reporting by Carole Buia/Miami, Greg Fulton/Atlanta, Alice Park/New York, Elaine Shannon and Dick Thompson/Washington*



SCOTT HOUSTON—CORBIS SYGMA FOR TIME; HOUSTON—CORBIS SYGMA

Recreational Pharmaceuticals

Finding new party drugs like K and ecstasy won't be easy

By JOHN CLOUD

IN THE PAST FEW MONTHS, IT'S BECOME nearly impossible to buy Ketaset in New York City's underground drug market. Made by Fort Dodge, an Iowa-based pharmaceutical firm, Ketaset is a brand of ketamine, a compound that blocks certain neuroreceptors, causing hallucinations in high doses and, in lower doses, a fuzzy dissociation—like the warmth of a couple of Jim Beams. Legally, it's used as an anesthetic. Illegally, one snorts ketamine because the fuzziness lasts half an hour and doesn't produce bourbon's four-Advil hangover.

Ketaset's scarcity dates back to August 1999, when the U.S. Drug Enforcement Administration, acting on preliminary evidence that ketamine may lead to dependence, subjected its legal purveyors to strict security rules. But K, as users call it, had already won so many devotees that traffickers were smuggling off-label brands from Mexico. Today Manhattan dealers sell a gram of K for $80, up 100% from 1998.

The recent history of K limns a well-established law of recreational drug use: once users find a substance they like, they will snort or shoot or drop whatever version is available, whatever the cost. Which is why you must look to the market to understand the future of drugs used for anything other than doctor-approved healing. That market can be divided into three groups: the partyers, who just want to have fun (and who sometimes become addicts); the shrinks and shamans, who believe drugs can expand your consciousness; and the scientists, who suspect that illegal drugs—or their chemical cousins—may have marketable legal uses. These groups are distinct but tightly linked: scientific research leads to new drugs, which shamans discover and use in their quests, which often turn out to be as much fun as spiritual. The use of drugs in party settings eventually leads to government crackdowns.

But as a rule, the partyers don't pursue the new drugs; they tend to find a potion and stick with it, sometimes until it kills them. Today's popular party drugs are derived from ancient medicinal herbs: marijuana from hemp, cocaine from coca leaf, prescription painkillers from poppies. It's the shamans who aggressively seek out new substances. Recent additions to the U.S. market include ayahuasco, a plant long used in religious ceremonies in Brazil for its mind-manipulating qualities, and *Salvia divinorum*, a soft-leaved plant native to Mexico that is chewed or smoked for hallucinogenic effects.

New compounds do occasionally come from underground drug labs or, like MDMA (ecstasy), are rediscovered after years of being ignored in scientific literature. In this world, no one is held in greater esteem than Alexander Shulgin.

Shulgin is a biochemist who once studied psychedelics for Dow Chemical. Now 75, Shulgin has synthesized hundreds of compounds in the smelly lab in the woods behind his California home. He and his wife Ann, a therapist, have published two books that are the bibles of underground drug research: *PIHKAL* (Phenethylamines I Have Known and Loved) and *TIHKAL* (Tryptamines I Have Known and Loved). Many of the drugs that have emerged from underground labs can be traced to well-thumbed copies of the Shulgins' books.

It was they who helped popularize MDMA—a signal event in the history of recreational drugs. Ecstasy is easily the biggest advance since LSD. It changed not only the party world but the shaman world, where it was used by psychologists who believed it had therapeutic value. Since MDMA was banned in 1986, scientists have looked for compounds that have the same effects without damaging neurotransmitters, as MDMA can. They haven't had much success.

So today's nonmedical drug research tends to focus on new uses for old substances. That effort is led by Richard Doblin, who runs the Multidisciplinary Association for Psychedelic Studies out of his Belmont, Mass., home. Founded the year MDMA was outlawed, the association uses its $530,000 yearly budget to assist scientists who, with government permission, study the risks and benefits of a wide variety of nonmedical uses for psychedelic drugs and marijuana. Such research is highly political, however, and it can take years for a research protocol to be approved.

A vial of K

The new drugs that appear on the market usually do so after underground chemists read scientific papers and decide to cook something up. Scientists studying how cocaine works in the brain, for example, have developed a version 100 times more powerful. The recipe is available in academic journals, waiting to be exploited.

But the chemicals needed to synthesize such drugs are tracked by authorities, a change from the Shulgins' day. And even if the ingredients were widely available, the scientific expertise is not. According to David Nichols, a student of Shulgin's who is now a professor of chemistry at Purdue, "The underground chemist is typically not going to discover a completely new psychoactive substance. The kinds of things that are easy to make, by and large, have been made." ■

SUMMARY OF PUBLIC COMMENT

Amendment 1: Unauthorized Compensation

Federal Public and Community Defenders
Jon Sands, Assistant Federal Public Defender, District of Arizona

The Federal Public and Community Defenders (FPCD) opposes the addition of a cross-reference provision in §2C1.3 that calls for the use of §2C1.1 if the offense involved a bribe and §2C1.2 if the offense involved an unlawful gratuity. The sentencing court makes this determination based upon information that does not have to qualify as admissible under the Federal Rules of Evidence and using a preponderance standard – thereby relieving the government of the burden of proving beyond a reasonable doubt all of the elements of a bribery or unlawful gratuity offense.

The FPCD is also concerned that the increased use of cross references alters the nature of the guidelines, moving from a mixed charge-offense/real-offense system closer to a pure real-offense system. The FPCD supports the original Commission's rejection of a pure real-offense system after determining that such a system was impractical and "risked return to wide disparity in sentencing practice." See U.S.S.G. Ch. 1, Pt. A(4)(a). The FPCD believes that the proposed amendment is an ad hoc abandonment of that decision.

FPCD does not object to designating §2C1.3 as the offense guideline applicable to the offenses set forth in sections 203-05 and 207-09 or to revising §2C1.3(b)(1) by adding an alternative basis for enhancement.

The New York Council of Defense Lawyers
John R. Wing, President
Brian E. Maas, Chairman, Sentencing Guidelines Committee
767 Fifth Avenue
New York, NY 10153

The New York Council of Defense Lawyers (NYCDL) opposes the proposed amendment due to concern that the proposed addition to the Application Notes of the cross-reference to Guideline §§2C1.1 and 2C1.2 will likely result in defendants convicted of conflict of interest offenses being sentenced inappropriately under the cross-referenced harsher Guidelines. Though some cases sentenced under Guidelines §§2C1.3 and 2C1.4 may involve in some way a bribe or gratuity, it does not necessarily follow that "many of these defendants likely could have been charged under a bribery or gratuity statute...." Rather, it seems likely that these defendants were convicted of a conflict of interest crime either because of a prosecutorial determination that the facts of a case

did not warrant bringing charges under 18 U.S.C. §201 or §202 or from a jury's finding that the evidence did not warrant conviction under the bribery or gratuity statutes.

The proposed amendment may well subject a defendant convicted of a violation of 18 U.S.C. §209 to being sentenced as though his offense involved a bribe or gratuity which was not charged and, therefore, not subjected to a jury finding. This is arguably in violation of the United States Supreme Court's recent decision in New Jersey v. Apprendi, 530 U.S. 466 (2000), since these elements would be found by a judge under a lower standard of proof.

NYCDL recommends that the proposed enhancements to be added to §2C1.3(1)(B) should only apply to willful violations eligible for sentencing under 18 U.S.C. §216(a)(2) and that the amendment should be clarified accordingly. NYDCL is particularly concerned that the proposed two point enhancement for circumstances where the offense involved the promise or receipt of money in consideration for the use of influence will be indiscriminately applied to both willful and non-willful violation.

Amendment 2: Counterfeiting Offenses

Department of the Treasury
Elisabeth A. Bresee, Acting Under Secretary (Enforcement)

The Department of the Treasury supports the decision to raise the base offense level from 9 to 10, but still holds the position that a base offense level of 11 is warranted given the increase in digitally-generated notes. These notes are generally produced and passed in small quantities and the total amount seized often does not register on the fraud loss table in §2F1.1.

Treasury fully supports the intent of the proposed sophisticated means enhancement but has concerns regarding its application. It notes that sophistication cannot be tied to any particular method of production. Accordingly, an enhanced penalty for individuals who go to great lengths to produce a more deceptive note should not be associated with any particular "means." Instead, such an enhanced penalty would be more properly applied to individuals who are able to simulate the unique security features incorporated in our currency.

Treasury recommends applying such an enhancement in cases where a manufacturer has taken additional steps beyond capturing the front and back images of United States currency in an effort to simulate the distinctive counterfeit deterrents defined in 18 U.S.C. § 474A(c)(2). That section defines "distinctive counterfeit deterrent" as including "any ink, watermark, seal, security thread, optically variable device, or other feature or device; (A) in which the United States has an exclusive property interest; or (B) which is not otherwise in commercial use or in the public domain and which the Secretary designates as being necessary in preventing the counterfeiting of obligations or other securities of the United States." 18 U.S.C. § 474A(c)(2).

Treasury supports the Commission's decision to eliminate the "merely photocopy notes" language found in the commentary. Because it is impossible to predict what future technologies may emerge in counterfeiting, Treasury generally objects to referring to particular forms of technology either in §2B5.1 itself or in the commentary.

Treasury strongly believes that the elimination of the adjusted offense level of 15 for manufacturing, even when the two-level enhancement is added, will not provide a sufficient penalty for the expanding group of digitally-based counterfeiters. Because of the difficulties inherent in connecting digitally-based counterfeit to its point of origin, most offenders will be held responsible solely for whatever amount of inventory they have in their possession at the time of the suppression. Because a low inventory translates into a low guideline range, there is incentive for this rapidly expanding group of manufacturers to "print and print often."

Treasury generally agrees that guideline sentences should reflect the degree of economic harm inflicted. In the case of digitally-based counterfeiting, however, economic harm is not always fully measured by the amount seized at the plant suppression. In order to forward the goal of

proportionality in this context, the Treasury asks the Commission to consider either:

1. *Implementing our original proposal of a two-level enhancement for cases involving over $70,000 while retaining the 15 adjusted offense level. As we suggested initially, this would do much to eliminate the windfall created by the cap currently in place; or*

2. *Applying a four-level enhancement for all manufacturing cases rather than the proposed two-level enhancement (or a consistent four-level "sliding scale" enhancement). Manufacturing is a much more serious offense than passing and even a low-dollar manufacturer requires more than an adjusted offense level of 12 to meet the goals of punishment and deterrence.*

Should the Commission reject the above proposals, Treasury suggests retaining the existing structure, at least for this year. Treasury stated that the current lack of proportionality informed its recommendation to add a two-level enhancement for high-volume manufacturers, but the cap currently affects only a very small number of offenders. The elimination of the adjusted offense level of 15 will result in lower sentences for 94% of manufacturers. If the choice is to reduce the penalty for more than 90% of manufacturers or provide a windfall for fewer than 1%, Treasury would prefer the latter.

U.S. Department of Justice, Criminal Division
James K. Robinson, Assistant Attorney General
Laird C. Kirkpatrick, Commissioner Ex-Officio

The DOJ agrees with the increased base offense level and commentary change. However, the DOJ objects to the deletion of the minimum offense level of 15 for manufacturing offenses. Deleting the floor will provide a windfall to many counterfeiters in the form of reduced punishment at a time when technology has made the offense increasingly easier to commit. The DOJ strongly believes that this is the wrong message to send and that the floor of 15 should be retained.

Federal Public and Community Defenders
Jon Sands, Assistant Federal Public Defender, District of Arizona

FPCD opposes increasing the base offense level in §2B5.1 from 9 to 10. FPCD does not oppose the change to subsection (b)(2) or to the language of Application Note 4.

The New York Council of Defense Lawyers
John R. Wing, President
Brian E. Maas, Chairman, Sentencing Guidelines Committee
767 Fifth Avenue
New York, NY 10153

NYCDL opposes the proposed modification of the base offense level in Guideline §2B5.2 for counterfeiting from 9 to 10. In light of the enhancements set out at §2B5.1(b) NYDCL believes that the guidelines as currently structured deal adequately with any enhanced conduct relating to the counterfeiting offenses.

NYDCL supports replacing the minimum level of offense level 15 for manufacturing offenses with a 2 level enhancement. NYDCL recommends rewording Application Note 4 to make clear that the enhancement in subsection B(2) is applicable to defendants who use digital technology to create "photocopy notes" that are passable while still making clear that this enhancement should not be applied to persons who photocopy notes in a way that creates notes so obviously counterfeit as to be unlikely to be accepted.

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The Practitioners' Advisory Group (PAG) does not support the increase in the base offense level from 9 to 10, citing a lack of data demonstrating that the current sanction levels are inadequate or that the proposed increases directly or proportionately address the so-called additional harm cited by Treasury (e.g. "erosion of public confidence in the currency", "large expenditures required to craft and implement anti-counterfeiting safeguards"). Further, there appears to be no reason to increase punishments for all counterfeiters just because technology has afforded a subset of offenders with a better mousetrap. The PAG suggests the Commission consider a 1 level increase as a SOC reserved for digital counterfeiting. Alternatively, the Commission might consider a 2 level increase for such offenses, but limit its imposition to situations where the currency produced (face value) is $5,000 or less. If the dollar amount exceeds $5,000, the fraud table will provide any necessary increment in harm/punishment.

The PAG has no objection to replacing the existing level 15 floor for manufacturing/device possession crimes at §2B5.1(b)(2) with a 2 level increase for such offenders as proposed. However, it appears necessary that the accompanying Application Notes clearly express the Commission's intention that such SOC is meant to address the more sophisticated counterfeiting offense like offset printing.

While the PAG understands the intent of the deletion of the phrase "merely photocopy notes or otherwise," we remain concerned that the use of digital equipment and fancy inkjet printers can still result in the production of obviously phony currency. The PAG suggests that Application Note 4 be amended to read: "Subsection (b)(2) does not apply to persons who, by whatever means, produce items that are so obviously counterfeit..."

Amendment 3: **Tax Privacy**

Federal Public and Community Defenders
Jon Sands, Assistant Federal Public Defender, District of Arizona

FPCD has no objection to the proposed amendment.

The New York Council of Defense Lawyers
John R. Wing, President
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NYDCL does not disagree with the decision to refer the listed violations of Title 26 to Guideline §2H3.1, but suggests that the portion of the amendment which creates a base offense level of 6 should be clarified to indicate that it covers violations of 26 U.S.C. §§7213A and 7216.

NYDCL objects to the addition of a new Application Note 3 advising that the 2 point enhancement for "Abuse of Position of Trust" can be applied to a violation of any of these tax-related offenses. Because this enhancement would be available in almost every case, NYDCL believes that this amendment would function as an automatic enhancement akin to the "more than minimal planning" enhancement as applied in the fraud context. NYDCL opposes this sort of automatic enhancement.

Amendment 4: Circuit Conflict Concerning Stipulations

Families Against Mandatory Minimums
Mary Price, General Counsel
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Families Against Mandatory Minimums (FAMM) supports the proposed amendment to §1B1.2(a). FAMM agrees with the Commission that the majority approach is the better view and is consistent with the Guidelines' language on stipulations and plea agreements. Chapter 6 of the Guidelines favors written stipulations of facts "because of the importance of stipulations and the potential complexity of the factors that can affect the determination of sentences." This interest in accuracy appropriately militates against assuming that statements outside the agreed-upon stipulations establish a higher offense level. Statements made at the plea colloquy are not contained in the plea agreement as contemplated by §1B1.2(a), nor are they necessarily admissions or other statements of fact agreed to by the defendant and the prosecution as discussed in U.S.S.G. §6B. The new amendment to the guideline properly clarifies that these statements are not part of the plea agreement stipulations contemplated by this guideline.

Federal Public and Community Defenders
Jon Sands, Assistant Federal Public Defender, District of Arizona

FPCD supports the proposed amendment. FPCD believes that the addition of the proposed language should ensure that the stipulation method of determining the applicable guideline is used as a "limited" exception to the general rule of §1B1.2.

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NYDCL agrees with the Commission's approach in this proposed amendment which makes clear that statements made by defendants during plea proceedings are not to be considered stipulations for purposes of Guideline §1B1.2 unless the statement was agreed to as part of the plea agreement itself. To clarify that a stipulation needs to have been agreed to as part of the plea agreement before it can increase a defendant's sentence, NYDCL suggests that the

Commission follow the language used in United States v. Nathan, 188 F.3d 190, 201 (3d Cir. 1999). Specifically, the Nathan court stated that the statement would be considered a "stipulation" only if it is part of a defendant's written plea agreement; (ii) is explicitly annexed thereto; or (iii) both the government and the defendant explicitly agree at a factual basis hearing that the facts being put on the record are stipulations that might subject the defendant to the provisions of §1B1.2(a). The use of this wording would reduce the possibility of disputes as to the exact contents of the plea agreement.

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The PAG supports the adoption of the amendment.

Amendment 5: Circuit Conflict Concerning Aggravated Assault

U.S. Department of Justice, Criminal Division
James K. Robinson, Assistant Attorney General
Laird C. Kirkpatrick, Commissioner Ex-Officio

The DOJ agrees with the goal of both options to resolve the circuit conflict in a manner that clarifies that the weapon enhancement in subsection (b)(2) of the guideline applies even though the reason for the application of the aggravated assault guideline is the presence of the weapon. However, both options may inadvertently raise additional issues for litigation. The DOJ would favor a simple statement that the weapon enhancement in subsection (b)(2) applies in a case involving a weapon even where the applicability of the aggravated assault guideline itself is predicated upon the involvement of the weapon.

As between the two options, DOJ believes that Option 1 is more straightforward and consistent with the structure of other guidelines and that, while Option 2 attempts to address several concerns, it may raise similar problems to those in Option 1.

DOJ stated that including an explanation of the Commission's rationale for the applicability of the weapon enhancement is problematic in several respects. First, both options state in proposed Application Note 2 that the base offense level itself incorporates the presence of the dangerous weapon. Also, Note 2 may raise a negative inference that other enhancements in the aggravated assault guideline are not applicable in the absence of a specific statement regarding their treatment in both the base offense level and SOCs. Eliminating the rationale for resolution of the circuit conflict would not cure these problems. However, if the rationale is not deleted, the Note should be clarified to indicate that the presence of a weapon is one of the aggravating factors taken into account in the base offense level.

DOJ also raised concern that the statement at the end of proposed Application Note 2 (that in a case involving a dangerous weapon with intent to cause bodily injury, the court shall apply both the base offense level and the weapon enhancement) the underlined words may lead courts to believe that it is acceptable to avoid application of the weapon enhancement in a case in which the government has not shown an intent to cause bodily injury. Thus, DOJ prefers the simple statement reflected above to the effect that the weapon enhancement in subsection (b)(2) applies in a case involving a weapon where the applicability of the aggravated assault guideline itself is predicated upon the involvement of the weapon.

Federal Public and Community Defenders
Jon Sands, Assistant Federal Public Defender, District of Arizona

FPCD does not support either option concerning §2A2.2. In order to follow the reasoning set

forth by U.S. v Farrow, 198 F.3d 179 (6th Cir. 1999), FPCD recommends that the Commission add the following new Application Note to §2A2.2:

4. *"If the 'dangerous weapon' is not an inherently dangerous object, a single aspect of a defendant's conduct may not be used for two different guideline-calculation purposes. For example, if a defendant's use of a pencil with intent to cause bodily injury makes and assault aggravated, then that use (an aspect of the defendant's conduct) has been taken into consideration in determining that this guideline is the applicable offense guideline and cannot be the basis for applying subsection (b)(2)."*

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NYDCL opposes both of the proposed options presented to the extent that both include language directing that the 4 level enhancement in §2A2.2(b)(2) shall be applied in instances where an ordinary object such as a car or a chair is used in an aggravated assault with the intent to cause bodily injury. It is unclear whether the Commission intends for this enhancement to apply to those situations where an ordinary object becomes a dangerous weapon under §2A2. Further, the proposed amendment options also do not address the double counting concern raised by United States v. Hudson, 972 F.2d 504, 506-07 (2d Cir. 1992) and United States v. Farrow, 198 F.3d 179, 188-93 (6th Cir. 1999). NYCDL stated that the Guidelines already provide a separate enhancement if serious bodily injury is inflicted irrespective of whether a dangerous weapon was used (§2A2.2(b)(3)). Additionally, NYCDL believes that the proposal incorporated in Option 2 is unnecessary because the existing guideline is sufficiently clear as to the availability of a serious bodily harm enhancement.

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The PAG opposes passage of this proposed amendment (either option). They agree with the FPCD position that the Commission should add commentary consistent with the reasoning set forth in United States v. Farrow, 198 F.3d 179 (6th Cir. 1999).

Amendment 6: Circuit Conflict Concerning Fraudulent Misrepresentations

U.S. Department of Justice, Criminal Division
James K. Robinson, Assistant Attorney General
Laird C. Kirkpatrick, Commissioner Ex-Officio

The DOJ agrees with the proposed resolution of this circuit conflict to assure the applicability of the enhancement in question to a defendant working for a charity, for example, who raises funds ostensibly for the charity and then diverts them to personal use. However, the proposed language should be modified to delete the word "solely" from proposed Application Note 5(B) in the phrase "acting 'solely' to obtain a benefit for the organization or agency . . . ." A defendant who represents that he or she was acting to obtain a benefit for the organization or agency, whether or not solely for this purpose, but who diverts the proceeds to personal use is equally culpable.

DOJ is also concerned with a change in Application Note 5 concerning persons presently covered by the enhancement. The proposed amendment language would make the enhancement applicable to a person who misrepresents that he was an "employee or authorized agent" of a charity or other specified organization. This additional change, while likely intended to be non-substantive, is unnecessary and may produce litigation by defendants claiming that a narrowed effect was intended.

DOJ stated that the proscription against application of the Chapter 3 enhancement for abuse of a position of trust or use of a special skill is unnecessary, as proposed in Application Note 5. DOJ recommends deleting the proposed commentary at the end of Application Note 5 regarding the application of §3B1.3. If, however, the Commission is intent upon retaining this commentary, it should be limited to the situation in which the defendant was an employee or agent of a covered organization or agency who represented that he or she was acting for its benefit.

Federal Public and Community Defenders
Jon Sands, Assistant Federal Public Defender, District of Arizona

FPCD agrees with the Commission that the proposed enhancement is appropriate for conduct that seeks to exploit a person's charitable instinct. Further, they believe that the enhancement should not apply simply because the victim of the offense is a charity (or government agency). Charities do not rely exclusively upon gifts and donations; many have entered the marketplace and, like for-profit organizations, sell goods and service. FPCD does not believe the enhancement is appropriate when not-for-profit organizations behave like for-profit organizations. It is unrealistic to assume that a person selling phony lottery tickets and falsely claiming to represent a not-for-profit organization has taken advantage of the purchasers' charitable impulse or trust in government.

FPCD recommends that the Commission strengthen the proposed Application Note 5 by changing the quoted sentence to read: "Embezzlement of funds from a charity ~~alone~~ is not sufficient, by itself, to warrant application of subsection (b)(4)(A)." FPCD also recommends the addition of language indicating that the enhancement applies only to conduct related to soliciting donations to a charity, and not to quid pro quo or gambling transactions.

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NYCDL opposes any amendment of the guideline at this time because, as they noted in 1998, there exists no true conflict among the circuits. Both the 4th and 10th Circuits recognize that the enhancement in §2F1.1(B)(3) is appropriately applied whenever the official of a charitable organization, for the purposes of enriching himself, dupes the public into making contributions that it otherwise would not. The proposed amendment is therefore unnecessary and may invite unintended sentence enhancements wherever an offense involves a charitable organization — a result clearly not intended by the Commission.

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The PAG does not oppose passage of this proposed amendment, but agrees that the Commission should revise Application Note 5 in the manner suggested by the FPCD.