

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. 84-48]

Schedules of Controlled Substances; Scheduling of 3,4-Methylenedioxymethamphetamine (MDMA) Into Schedule I of the Controlled Substances Act; Remand

AGENCY: Drug Enforcement Administration.

ACTION: Final rule.

SUMMARY: This is a final rule placing the drug 3,4-methylenedioxymethamphetamine (MDMA) into Schedule I of the Controlled Substances Act (CSA) following a remand from the United States Court of Appeals for the First Circuit. This rule will classify MDMA as a Schedule I hallucinogenic controlled substance and is the culmination of a formal rulemaking on the record conducted before an Administrative Law Judge of the Drug Enforcement Administration (DEA). The original final rule placing MDMA in Schedule I was published on October 14, 1986, with an effective date of November 13, 1986. (51 FR 36552). On review by the United States Court of Appeals for the First Circuit the rule was vacated and remanded to the Administrator for further findings. Following a review of the record in this matter, the Administrator concludes that MDMA should be classified as a Schedule I

controlled substance. This rule will impose the criminal and regulatory controls of Schedule I on the manufacture, distribution and possession of MDMA.

EFFECTIVE DATE: The effective date of this order is March 23, 1988.

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SUPPLEMENTARY INFORMATION: On October 14, 1986, the Administrator of DEA, following rulemaking on the record which included a hearing before an Administrative Law Judge, issued a final rule placing MDMA into Schedule I under the Controlled Substances Act. (52 FR 36552) The effective date of this rule was November 13, 1986. In this final rule, the Administrator made findings required by the statute, 21 U.S.C. 812(a), and concluded that MDMA met the criteria for placement of substances into Schedule I. The Administrator found that MDMA: (1) Had no currently accepted medical use in treatment in the United States; (2) lacked accepted safety for use under medical supervision; and (3) had a high potential for abuse.

On September 19, 1987, the United States Court of Appeals for the First Circuit issued its opinion on the Petition for Review of the Order of the Drug Enforcement Administration. See, *Grinspoon v. Drug Enforcement Administration*, 828 F.2d 881. The mandate was issued on December 22, 1987. The Court found that the Administrator applied an incorrect standard in determining the meaning of the phrases "currently accepted medical use in treatment in the United States" and "lack of accepted safety for use under medical supervision." Specifically the Court stated that—

The Administrator erroneously applied an interpretation of the "accepted medical use in treatment in the United States" and "accepted safety for use . . . under medical supervision" criteria of section 812(b)(1) that directly conflicts with congressional intent. We therefore vacate the Administrator's determination that MDMA should be placed in Schedule I of the CSA and remand the rule for further consideration by the DEA. On remand, the Administrator will not be permitted to treat the absence of FDA interstate marketing approval as conclusive evidence that MDMA has no currently accepted medical use and lacks accepted safety for use under medical supervision. 828 F.2d 881, 891.

The Court did not provide any further parameters for the Administrator in reconsidering his decision, stating that it would not infringe on the

Administrator's statutory authority to develop such a standard.

The Administrator concludes that further hearings are not necessary in this matter since the record below is extraordinarily complete and since all the parties had the opportunity to provide evidence and brief all the relevant issues, which included:

What constitutes "currently accepted medical use in treatment in the United States" within the purview of 21 U.S.C. 812(b)?

What constitutes "accepted safety for use . . . under medical supervision" within the purview of 21 U.S.C. 812(b)?

Does MDMA have a "currently accepted medical use in treatment in the United States" within the purview of 21 U.S.C. 812(b)?

Is there a lack of "accepted safety for use [of MDMA] under medical supervision" within the purview of 21 U.S.C. 812(b)?

The Administrator further concludes that since all parties have had ample opportunity to be heard on these issues, there is no necessity to publish his conclusions as a proposed rule, but rather as a final rule.

Findings

The Administrator adopts the following findings regarding "accepted medical use in treatment in the United States" and "accepted safety for use under medical supervision" which were published as part of the original final rule found at 51 FR 36552 (October 14, 1986); 1, 2, 3, 4, 5, 6, 7, 8, 11, 12, 13, 14, 15, 16, 44, 45, 46, 47. These findings are incorporated into this final rule as though they were set out fully herein. The Administrator further finds, based upon the record in the proceedings conducted before the Administrative Law Judge:

A. The published scientific and medical literature and the information from the files of the Food and Drug Administration do not establish or support claims of therapeutic use of MDMA, as an adjunct to psychotherapy, in treatment in the United States.

B. There are insufficient and inadequate studies and reports characterizing MDMA from a chemical, toxicological and pharmacological perspective to justify use of MDMA in humans.

C. There were no published accounts of MDMA's pharmacology or toxicology until 1973, when an animal study conducted by the U.S. Army Chemical Corps was released. It showed that the acute lethal doses of MDMA and MDA were similar.

D. Three reports published by Alexander Shulgin and others beginning in 1976 mention the effects of MDMA in humans. These studies describe MDMA's psychopharmacological profile in relation to other psychoactive drugs such as marijuana, psilocybin and MDA. Minimal descriptions of test procedures were included, and the studies included no data to indicate a potential therapeutic utility of MDMA as an adjunct to psychotherapy in humans.

E. The therapeutic use of MDMA is not mentioned in any medical, psychiatric or psychotherapy textbooks, pharmacopeia or clinical pharmacology textbooks.

F. An unpublished study entitled "MDMA: A New Psychotropic and its Effects in Humans" was prepared by Dr. George Greer. Dr. Greer is a psychiatrist in New Mexico with a private practice and little or no background as a researcher. His report describes the administering of MDMA to 29 individuals for a variety of reasons ranging from curiosity and fun to a desire to change consciousness and behavior patterns. Only nine of the individuals had diagnosable psychiatric disorders. Dr. Greer reported that all the individuals experienced "positive" effects and relatively few side effects.

The conclusions were based upon the subjective observations of Dr. Greer and a nurse, as well as conclusions of the subjects. Dr. Greer described the study as anecdotal and not a study designed to determine the efficacy of MDMA. Experts in psychiatry, psychotherapy and pharmacology concluded that Dr. Greer's study did not provide a reasonable basis for regarding MDMA as efficacious for enhancing therapeutic benefits of psychotherapy, and lacked scientific merit. They agreed that the study was not scientifically sound and produced only anecdotal results. The study contained no controls; it was not a blind or double blind study and thus significant bias was introduced; there were no criteria to measure improvement or change; there was no defined therapeutic procedure; and the investigator lacked standing as a scientist and researcher.

G. An unpublished study entitled, "MDMA Pilot Study—Physiological, Psychological and Sociological Study," by Dr. Joseph J. Downing examined the effects of MDMA in 21 healthy individuals with no diagnosable psychiatric disorders. Dr. Downing is not a researcher and has little or no experience in designing and conducting toxicological or clinical studies. All the subjects had previously used MDMA and a variety of other psychoactive drugs. The individuals brought their own alleged MDMA to the study and determined the dose to be taken. The subjects concluded that they had "benefitted" from the use of MDMA. Dr. Downing concluded that "there is insufficient evidence to judge accurately either harm or benefit." Scientific experts who reviewed Dr. Downing's work concluded that his study suffers from the same problems as Dr. Greer's and that it has little or no scientific merit. An FDA pharmacologist, experienced in evaluating the safety and efficacy of drugs, concluded that the study presents no data or evidence to support a claim that MDMA is effective as a therapeutic agent.

H. Four psychiatrists presented evidence that they had used MDMA in their practices. Several other psychiatrists testified that use of MDMA by these individuals was consistent with accepted medical practice in their community. Each physician also described MDMA only in terms of therapeutic potential. All agreed that no scientific studies were done on which to conclude that MDMA has therapeutic utility. Most of these physicians had used MDMA themselves. The number of physicians who have used MDMA in their practices is very small in relation to the physician population.

I. The World Health Organization (WHO) Expert Committee on Drug Dependence reviewed MDMA for possible scheduling under the 1971 Convention on Psychotropic Substances in April 1985. The Expert Committee included internationally recognized experts in the field of psychiatry, clinical pharmacology and other medical professions. The Committee found that MDMA had no defined therapeutic use. The Committee further noted that the anecdotal data regarding MDMA's clinical utility were intriguing but that the studies lacked appropriate methodological design to ascertain the reliability of the observations and results. The Expert Committee recommended that MDMA be placed into Schedule I of the Convention because there was insufficient evidence to indicate that the substance has therapeutic usefulness. The United States is a party to the 1971 Convention on Psychotropic Substances.

J. Published scientific literature does not support the safety of MDMA for use in humans. It strongly suggests that MDMA may not be safe for human use.

K. Unpublished studies by Drs. Greer and Downing indicate that all individuals who took MDMA under their supervision experienced unpleasant side effects ranging from nausea and vomiting to ataxia, anxiety attacks, hallucinations and short-term memory

loss. Dr. Greer's and Dr. Downing's studies suffer from severe methodological and other problems which lead experts to conclude that they contain no scientific evidence to assess the safety of MDMA. Dr. Downing concluded that there is insufficient evidence to accurately judge MDMA's safety.

L. The substance administered by Dr. Greer in his study, as well as that administered by the other psychiatrists, was made by them under the supervision of a medicinal chemist and was not manufactured or tested under controlled conditions.

M. The substances ingested by the subjects in Dr. Downing's study were provided by the subjects themselves, and were of unknown origin, composition and purity.

## Discussion

In order for a drug or other substance to be placed into Schedule I, a finding is required that the substance has "no currently accepted medical use in treatment in the United States." The other four Schedules require a finding that the drug or other substance has a "currently accepted medical use in treatment in the United States." The United States Court of Appeals for the First Circuit has indicated that "currently accepted medical use in treatment in the United States," does not mean that a drug or other substance is lawfully marketed in the United States pursuant to the Federal Food, Drug and Cosmetic Act of 1938. While the Court clearly stated that whether a substance is lawfully marketed in the United States may be a factor to be considered in making a determination of accepted medical use, it may not be the sole factor upon which the Administrator relies in making that determination.

The characteristics of a drug or other substance with an accepted medical use in treatment include scientifically determined and accepted knowledge of its chemistry; the toxicology and pharmacology of the substance in animals; establishment of its effectiveness in humans through scientifically designed clinical trials; general availability of the substance and information regarding the substance and its use; recognition of its clinical use in generally accepted pharmacopeia, medical references, journals or textbooks; specific indications for the treatment of recognized disorders; recognition of the use of the substance by organizations or associations of physicians; and recognition and use of the substance by a substantial segment

of the medical practitioners in the United States. The drug MDMA has not been approved for marketing in the United States by the Food and Drug Administration. The chemistry, toxicology and pharmacology of MDMA have not been sufficiently studied in animals to provide a scientific basis for experimentation or clinical use in humans. The published literature contains no references to the clinical use of MDMA nor animal studies to indicate such a clinical use. Recognized texts, reference books and pharmacopeia contain no references to the therapeutic use of MDMA. The two unpublished studies supporting the therapeutic use of MDMA which were presented during the hearings, do not contain any data which can be assessed by scientific review to draw a conclusion that MDMA has a therapeutic use. Indeed, the psychiatrists who conducted the studies admit that the information which they obtained was anecdotal, and that the studies were not scientifically controlled.

Evidence in the record indicates that at least four psychiatrists have administered MDMA in their practice to approximately 200 subjects. These physicians were not conducting scientific studies with MDMA, they were administering the drug as if it was an approved product which had been scientifically tested. The evidence they presented was merely anecdotal accounts of observations of patients.

While many witnesses in this proceeding, including those presented by the agency, indicated that MDMA may have a potential therapeutic use, such a potential use is not sufficient to establish accepted medical use. A panel of international experts reached the same conclusion, namely that there was insufficient evidence to indicate that the substance had therapeutic usefulness.

The evidence in the record in this proceeding does not support a finding that MDMA has a "currently accepted medical use in treatment in the United States." MDMA's lack of marketing approval by the Food and Drug Administration, coupled with the absence of reliable scientific data to establish the therapeutic usefulness and absence of widespread acceptance and recognition in the medical community, clearly demonstrates that it has "no currently accepted medical use in treatment in the United States."

The second of the three factors required for placement of a substance in Schedule I is that there is "lack of accepted safety for use of the drug or other substance under medical supervision." The United States Court of Appeals for the First Circuit indicated

that "lack of accepted safety for use of the drug or other substance under medical supervision," is not conclusively demonstrated by lack of FDA approval for marketing of a drug or other substance in the United States. The fact that a drug or other substance is not lawfully marketed in the United States may be a factor to be considered in determining whether a substance lacks accepted safety for use under medical supervision, but it is not conclusive.

Before a drug may be tested in humans, the Food and Drug Administration, the agency charged by Congress with determining the safety and efficacy of drugs, requires that it be safe as demonstrated by animal testing. The first requirement in determining the safety of a substance is that the chemistry of the substance must be known and reproducible. The next step is to conduct animal toxicity studies to show that the substance will not produce irreversible harm to organs at proposed human doses. Limited clinical trials may then be initiated but they must be carefully controlled so that adverse effects can be monitored and studies terminated if necessary. Very little of this information has been generated for MDMA. Safety in humans is evaluated as a risk/benefit ratio for a specific use. Any side effects found in human testing are required to be made known to the physician in labeling or package inserts which accompany the drug. MDMA is not available under these conditions.

The claims of safety by the psychiatrists who have administered MDMA are based on gross observations of the few subjects treated as well as self-evaluation by the subjects. These anecdotal observations, while useful in the overall evaluation of a substance, cannot substitute for controlled studies in animals and humans. There have been studies in animals to show that MDMA produces long term serotonergic nerve terminal degeneration. Such effects would not necessarily be observed immediately in individuals who had taken the drug. The long term safety of MDMA has not been established through reproductive or carcinogenic studies. Since MDMA has not been shown to be effective for treating a specific condition, it is impossible to make a risk/benefit analysis of the drug. Two psychiatrists who testified on behalf of the agency in the proceedings indicated that they would not administer MDMA to humans until and unless further studies had been conducted to establish its safety and lack of neurotoxicity.

Although a few psychiatrists claim that there has been relatively little

reported major harm to individuals who have used MDMA, this does not establish that MDMA is safe for use under medical supervision. Scientists and prudent physicians have concluded that administration of MDMA to humans must not occur until further animal studies are conducted to adequately assess its potential toxicity in humans. Based upon the lack of MDMA's established safety by animal and human testing, the lack of an FDA finding that MDMA is safe and may be safely administered to humans, its neurotoxicity in animals, and scientific and medical opinions that further testing is necessary prior to human use, the Administrator concludes that MDMA lacks accepted safety for use under medical supervision.

MDMA has no accepted medical use in treatment in the United States and lacks accepted safety for use under medical supervision. The Administrator previously found that MDMA had a high potential for abuse, a finding that was upheld on review by the United States Court of Appeals for the First Circuit. The Administrator therefore concludes that MDMA should be placed into Schedule I of the Controlled Substances Act.

#### List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Narcotics, Prescription drugs.

Under the authority vested in the Attorney General by section 201(a) of the Controlled Substances Act (21 U.S.C. 811(a)) and delegated to the Administrator of the Drug Enforcement Administration by regulations of the Department of Justice, 28 CFR 0.100(b), the Administrator hereby orders that Part 1308, Title 21, Code of Federal Regulations, be amended as follows:

#### PART 1308—SCHEDULES OF CONTROLLED SUBSTANCES

1. The authority citation for Part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b).

2. Section 1308.11 is amended by redesignating the existing paragraphs (d)(7) through (d)(24) as (d)(8) through (d)(25) and adding a new paragraph (d)(7) as follows:

#### § 1308.11 Schedule I.

(d) \* \* \*

(7) 3,4-  
methylenedioxyamphetamine  
(MDMA)..... 7405

Dated: February 13, 1983.

John C. Lawn,

Administrator.

[FR Doc. 83-0901 Filed 2-19-83; 8:45 am]

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