DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

Schedules of Controlled Substances; Proposed Placement of 3,4-Methylenedioxy-N-ethylamphetamine, and N-Hydroxy-3,4,methylenedioxy-amphetamine Into Schedule I

AGENCY: Drug Enforcement Administration, Justice.

ACTION: Notice of proposed rulemaking.

SUMMARY: This notice of proposed rulemaking is issued by the Administrator of the Drug Enforcement Administration (DEA) to place 3,4-methylenedioxy-N-ethylamphetamine and N-hydroxy-3,4-methylene-dioxyamphetamine into Schedule I of the Controlled Substances Act (CSA) (21 U.S.C. 801 *et seq.*). This proposed action by the DEA Administrator is based on data gathered and reviewed by DEA. If finalized, this proposed action would impose the regulatory control mechanisms and criminal sanctions of Schedule I on the manufacture, distribution and possession of these two substances.

DATE: Comments must be submitted on or before November 14, 1988.

ADDRESS: Comments and objections should be submitted to the Administrator, Drug Enforcement Administration, 1405 I Street NW., Washington, DC 20537, Attention: DEA Federal Register Representative.

FOR FURTHER INFORMATION CONTACT: Howard McClain, Jr., Chief, Drug Control Section, Drug Enforcement Administration, 1405 I Street NW., Washington, DC 20537, Telephone: (202) 633–1366.

SUPPLEMENTARY INFORMATION: On October 15, 1987, the Administrator of DEA issued a final rule in the **Federal Register** (52 FR 38225) temporarily placing the following substances into Schedule I of the CSA using the emergency scheduling provisions of the CSA (21 U.S.C. 811(b)):

(1) 3,4-methylenedioxy-N-ethylamphetamine.

(2) N-hydroxy-3,4-methylenedioxyamphetamine.

The final rule which became effective on October 15, 1987 was based on a finding by the Administrator that the emergency scheduling of the above-referenced substances was necessary to avoid an imminent hazard to the public safety. Section 201(h)(2) of the CSA (21 U.S.C. 811(h)(2)) requires that the emergency scheduling of a substance expires at the end of one year from the effective date of the order. However, if proceedings to schedule a substance pursuant to 21 U.S.C. 811(a)(1) have been initiated and are pending, the temporary scheduling of a substance may be extended for up to six months. Under this provision, the temporary scheduling of 3,4-methylenedioxy-N-ethylamphetamine and N-hydroxy-3,4-methylenedioxyamphetamine which would expire on October 15, 1988 may be extended to April 15, 1989. This extension is being ordered by the DEA Administrator in a separate action.

DEA has gathered and reviewed the available information regarding the actual abuse and relative potential of abuse for 3,4-methylenedioxy-N-ethylamphetamine and N-byhdroxy-3,4-methylenedioxyamphetamine. DEA, in conjunction with the National Institute of Drug Abuse (NIDA), has provided for the synthesis and biological testing of these two substances. By letter, the Administrator has submitted data which DEA has gathered regarding the two substances to the Assistant Secretary for Health, Department of Health and Human Services. In accordance with 21 U.S.C. 811(b), the DEA Administrator also requested a scientific and medical evaluation of the relevant information and a scheduling recommendation for 3,4-methylenedioxy-N-ethylamphetamine and N-hydroxy-3,4-methylenedioxyamphetamine from the Assistant Secretary for Health.

Both 3,4-methylenedioxy-N-ethylamphetamine (N-ethyl MDA) and N-hydroxy-3,4-methylenedioxyamphetamine (N-hydroxy MDA) are analogs of MDA and MDMA, Schedule I hallucinogens/stimulants, and as such are the type of substances which Congress intended to be considered for scheduling under the CSA. They are recent members of a series of methylenedioxyamphetamines produced in clandestine laboratories for distribution and abuse in the United States. The parent compound in this class, 3,4-methylenedioxyamphetamine (MDA) has been controlled in Schedule I of the CSA since its passage in 1970. More recently 3,4-methylenedioxymethamphetamine (MDMA), because of widespread abuse and studies showing that it is a neurotoxin in rodents, was placed into Schedule I pursuant to 21 U.S.C. 811(a)(1) and effective March 23, 1988.

N-ethyl MDA, also known as MDE or MDEA, is N-ethyl-alpha-methyl-3,4-(methylenedioxy)phenethylamine. It is usually found as the hydrochloride salt in powder, tablet or capsule forms. N-ethyl MDA is sold on the street as "Eve." N-hydroxy MDA, also known as N-OHMDA, is N-hydroxy-alpha-methyl-3,4-(methylenedioxy)phenethylamine. It is also usually found as the hydrochloride salt in powder, tablet or capsule forms. Both N-ethyl MDA and N-hydroxy MDA are structural analogs of MDA and MDMA.

N-ethyl MDA and N-hydroxy MDA behave as central nervous system stimulants in animals. Available scientific data show that these substances produce some pharmacological effects similar to those of MDA and MDMA. All four substances produce centrally mediated analgesic effects in the mouse as measured in several different tests. N-ethyl MDA (20 mg/kg) and N-hydroxy MDA (100 mg/kg) produce an increase in spontaneous locomotor activity in the mouse which is indicative of central nervous system stimulation. During the first three hours after administration, N-ethyl MDA increases spontaneous locomotor activity three times as much as MDA. Data from drug discrimination experiments show that even though N-ethyl MDA and N-hydroxy MDA are not recognized as either amphetamine or DOM by appropriately trained animals, they are recognized as MDMA in rats trained to discriminate MDMA from saline. MDMA is also recognized as N-ethyl MDA by rats trained to discriminate N-ethyl MDA from saline. Baboons trained to self-administer cocaine also self-administer N-ethyl MDA when it is substituted for cocaine. Similar reinforcing properties are observed for MDA, MDMA and other abusable central nervous system stimulants.

In man, N-ethyl MDA at oral doses of 140–200 mgs and N-hydroxy MDA at oral doses of 80–120 mgs produce psychotomimetic effects. The scientific literature indicates that MDA, MDMA, N-ethyl-MDA and N-hydroxy MDA produce a very similar spectrum of psychopharmacological effects in humans. They produce a change in consciousness, an increase in acoustic, visual and tactile sensory perceptions, mood changes and a drive-increasing effect. Effects appear about 30 minutes after ingestion and last for several hours.

N-ethyl MDA and N-hydroxy MDA have been identified by forensic laboratories in drug evidence submissions from many sections of the country. N-ethyl MDA was found infrequently in drug evidence from 1978 to 1982. With the control of MDMA in Schedule I of the CSA, N-ethyl MDA has been identified with increasing frequency by forensic laboratories. At the same time, N-hydroxy MDA began to show up in forensic drug evidence.

Much of the activity with these substances has occurred in the southwestern and midwestern states. MDA analogs have been openly promoted as safe and legal through fliers. N-ethyl MDA has been sold as "Eve" in bars and shops in Texas. DEA has identified several clandestine laboratories which have produced or are capable of producing N-ethyl and N-hydroxy MDA.

The use of MDA and its analogs has been associated with adverse effects on the public health and safety. They are known to cause psychotomimetic effects in man. DAWN (Drug Abuse Warning Network) has reported emergency room mentions of MDA, MDMA and N-ethyl MDA. Two deaths in Texas have been associated with the use of N-ethyl MDA; it was not possible, however, to determine whether N-ethyl MDA directly contributed to the deaths. With the exception of psychotomimetic effects produced in human subjects under controlled experimental conditions, there have been no specific reports of adverse effects, injuries or deaths associated with the use of N-hydroxy MDA. Considering, however, that N-hydroxy MDA has a similar structure and pharmacology to that of MDA and MDMA, it seems likely that adverse effects similar to those produced by MDA and MDMA will also be produced by N-hydroxy MDA. Another concern arising from the use of N-ethyl MDA and N-hydroxy MDA is their possible neuro-toxicity. It has been well documented that MDA and MDMA destroy specific nerve terminals and, in some cases, nerve cells in the brains of laboratory animals. Recently reported studies have provided evidence that N-ethyl MDA also produces neurotoxic effects resembling those of MDA and MDMA. The question of whether N-hydroxy MDA causes neurotoxicity has not been examined.

The above data show that the clandestine production, distribution and use of analogs of MDA, currently in the form of N-ethyl MDA and N-hydroxy MDA, pose a serious hazard to the public safety. DEA is unaware of any commercial manufacturer or supplier of N-ethyl MDA or N-hydroxy or of any recognized therapeutic use of either of these substances.

The DEA Administrator, based on the information gathered and reviewed by his staff and after consideration of the factors in 21 U.S.C. 811(c), believes that sufficient data exists to propose and to support that 3,4-methylenedioxy-N-ethylamphetamine and N-hydroxy-3,4-methylenedioxyamphetamine be placed into Schedule I of the CSA pursuant to 21 U.S.C. 811(a). The specific findings required pursuant to 21 U.S.C. 811 and 812 for a substance to be placed into Schedule I are as follows:

(1) The drug or other substance has a high potential for abuse.

(2) The drug or other substance has no currently accepted medical use in treatment in the United States.

(3) There is a lack of accepted safety for use of the drug or other substance under medical supervision.

Before issuing a final rule in this matter, the DEA Administrator will take into consideration the scientific and medical evaluations and scheduling recommendations of the Secretary of the Department of Health and Human Services in accordance with 21 U.S.C. 811(b). The recommendations of the Secretary regarding scientific and medical matters are binding on the Administrator and if the Secretary recommends that a substance should not be controlled, the DEA Administrator will not control it. The Administrator will also consider relevant comments from other concerned parties.

Interested persons are invited to submit their comments, objections or requests for hearing in writing with regard to this proposal. Requests for a hearing should state with particularity the issues concerning which the person desires to be heard. All correspondence regarding this matter should be submitted to the Administrator, Drug Enforcement Administraton, 1405 I Street, NW., Washington, DC 20537, Attention: DEA Federal Register Representative.

In the event that comments, objections or requests for a hearing raise one or more issues which the Administrator finds warrant a hearing, the Administrator shall order a public hearing by notice in the **Federal Register**, summarizing the issues to be heard and setting the time for hearing.

Pursuant to Title 5, United States Code, section 605(b), the Administrator certifies that the proposed placement of 3,4-methylenedioxy-N-ethylamphetamine and N-hydroxy-3,4-methylenedioxyamphetamine in Schedule I of the CSA will have no impact upon small businesses or other entities whose interests must be considered under the Regulatory Flexibility Act (Pub. L. 96-354). The substances proposed for control in this notice have no legitimate use or manufacturer in the United States. In accordance with the provisions of Title 21, United States Code, section 811(a), this proposal to place 3,4-methylenedioxy-N-ethylamphetamine and N-hydroxy-3,4-methylenedioxyamphetamine into Schedule I is a formal rulemaking "on the record after opportunity for a hearing." Such proceedings are conducted pursuant to the provisions of 5 U.S.C. 556 and 557 and, as such, have been exempted from the consultation requirements of Executive Order 12291 (46 FR 13193).

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 CSA (21 U.S.C. 811(a)), and delegated to the Administrator of DEA by Department of Justice Regulations (28 CFR 0.100), the Administrator hereby proposes that 21 CFR Part 1308 be amended as follows:

PART 1308—[AMENDED]

1. The authority citation for 21 CFR Part 1308 continues to read as follows:

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

2. Section 1308.11 is amended by redesignating paragraphs (d)(8) through (d)(25) to (d)(10) throught (d)(27) and by adding new paragraphs (d)(8) and (d)(9) to read as follows:

§ 1308.11 Schedule I.

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(d) * * *

(8) 3,4-methylenedioxy-N-ethylamphetamine (also known as N-ethyl-alpha-methyl-3,4(methylenedioxy)phenethylamine, N-ethyl MDA, MDE, MDEA . . . 7404

(9) N-hydroxy-3,4-methylenedioxyamphetamine (also known as N-hydroxy-alpha-methyl-3,4(methylenedioxy)phenethylamine, and N-hydroxy MDA . . . 7402

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3. Section 1308.11 is amended by removing paragraphs (g)(3) and (g)(4) and redesignating existing paragraphs (g)(5) and (g)(6) as (g)(3) and (g)(4).

John C. Lawn,

Administrator, Drug Enforcement Administration.

Date: October 12, 1988.

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21 CFR Part 1308

Schedules of Controlled Substances; Proposal To Place 4-methylaminorex into Schedule I

AGENCY: Drug Enforcement Administration, Justice.