PURDUE UNIVERSITY SCHOOL OF PHARMACY AND PHARMACAL SCIENCES

August 17, 1984

Administrator
Drug Enforcement Administration
1405 I Street, N.W.
Washington, D.C. 20537

Attn: DEA Federal Register Representative

Dear Sir:

It has come to my attention that the DEA intends to place the substance 3,4-methylenedioxymethamphetamine (MDMA) into Schedule I of the Controlled Substances Act (CSA). I have also read the report entitled "Schedule I Control Recommendation Under the CSA for 3,4-Methylenedioxymethamphetamine (MDMA)" prepared by the Drug Control Section, Office of Diversion Control, dated January 1984. While it is clear that MDMA is being produced and distributed on the illicit market, it is not so clear to me that MDMA represents an obvious health hazard. According to the above report, MDMA has only been reported in 8 DAWN emergency room and 1 medical examiner mentions, since 1972.

Furthermore, it is not at all clear that the toxicity associated with MDMA will in any way necessarily resemble that produced by MDA. Although the basic portions of the two molecules are identical, the addition of the N-methyl to MDA to yield MDMA has some very distinct effects on the pharmacology. The most curious finding is that it is the dextro isomer of MDMA which is more active, whereas with MDA it is the levo isomer. In my opinion this may reflect a fundamental difference in the way the two compounds work and, by extension, in the type of toxicity that might be expected. It is my opinion that the literature cited in the above-named report is inadequate to firmly conclude a similarity between the known toxicity of MDA and the expected toxicity of MDMA. While it is argued in the report that there is an analogy between amphetamine/methamphetamine and MDA/MDMA, the more active isomer of both amphetamine and methylamphetamine is the dextro isomer, whereas the more active isomers of the MDA/MDMA compounds are levo and dextro, respectively, reflecting a fundamental difference in the pharmacology of amphetamine versus methylenedioxyamphetamine. This difference is a point of some interest to us and merits additional and detailed investigation.

Of considerable interest also is the apparently very encouraging use of MDMA as an adjunct to psychotherapy. The relatively mild effects and short duration of action of MDMA make it an ideal candidate for evaluation in this capacity, and I have noted this in review articles. Although my knowledge of clinical use of

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MDMA is only hearsay, I am aware that such use was not sanctioned through the filing of an appropriate Investigational New Drug application through FDA. Nevertheless, you are aware that FDA does not in fact have a protocol to deal with this type of drug. Drug-assisted psychotherapy represents a novel medical approach which has received scant attention in the recent literature. Therefore, neither FDA nor professional medical societies have procedures to deal with such compounds. It is of great concern to me that in the interest of preventing unauthorized access to this material, that DEA may also prevent legitimate investigation. It is a very naive position indeed to expect that registration as a schedule I substance will not stifle further clinical studies.

Furthermore, it is completely unrealistic to expect that a pharmaceutical company will develop MDMA as a drug. It is not patentable, and questions of cost/benefit could not be adequately addressed for a psychoactive compound that is not designed to treat major psychiatric illness such as schizophrenia.

While I well understand the political need to restrict access to a substance currently being used in a nonapproved way, and the concerns by the law enforcement agencies, I am very disturbed by the possibility that the proposed regulation may prevent the further development of a material that could prove to be a major advance in the therapy of a variety of nonmajor emotional disturbances or psychiatric disorders.

It would seem to me to be more appropriate to postpone scheduling of this material until such time that FDA could define a protocol for the evaluation of such substances and that clinicians could be provided the opportunity to offer evidence either for or against the utility of MDMA-assisted psychotherapy. It seems to me that, although MDMA may in fact be a popular recreational drug, the low incidence of DAWN mentions would suggest a minimal danger to the public while such a consideration was underway.

Thank you for the opportunity to express my opinions.

Sincerely,

David E. Nichols

David E. Nichols, Ph.D.
Professor of Medicinal Chemistry

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