

December 22, 1986

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Dear Rick:

Here is the first draft of the appeal brief. Obviously it is still too long. I can easily think of ways to cut it further, but I thought you had better have the next shot at it (or you can just tell me which parts I should be sure to leave untouched, if you prefer). You will have to correct any language that is in a form inappropriate for the appeal, and revise the "required action" on pages 108-109 of the original brief. I have left out the Table of Contents pending completion. ~~Every~~ will put the footnotes in the appropriate place in the final version.

A point that occurred to me while reading the introductory chapter is that abuse potential is not separately discussed there. Should that be altered?

Another point: is it worth commenting more directly that whatever the Court may think about MDMA, it should want to discourage the extremely careless and arbitrary procedures by which the original decision to schedule MDMA was made? In fact, this casualness is typical of much drug scheduling when there is no opposition with the funds (i.e., usually with a financial interest) to prevent the DEA from doing what it pleases when it pleases.

Thanks again for your help.

Cordially,

James Bakalar

JBB:EFG  
enclosure

## I. INTRODUCTION AND SUMMARY

o "It [MDMA] is an interesting compound, one of potentially great importance to the field that ought to be ...investigated within a research framework."

o "One of the important developments in the field [of psychotherapy] has been the moving together of psychopharmacology and psychotherapy and their combined use to relieve psychiatric problems. A drug which could particularly enhance the psychotherapeutic process is...at the next stage in the whole development...it [MDMA] represents a drug which could potentially have an impact on the psychotherapeutic process itself."

o "This drug [MDMA] since it focuses direction [on the combined effect of a drug and psychotherapy]...is a useful one because it really points the field where it ought to be headed."

o "MDMA is an agent that offers the possibility of moving us into an understanding of some disturbance[s] in interpersonal processes, which is an important aspect of psychiatric disorder, but one which we have really not addressed specifically with our drug treatment. This has to do with some of the anecdotal reports of the effect of MDMA on what I would call attachment behavior, the degree to which two people form some kind of bonding between them...is the aspect of [MDMA] that may have psychotherapeutic importance."

-- DEA witness Dr. John Docherty, former chief of Psychosocial Treatments Research Branch at National Institute of Mental Health. Tr. 7, at 130, 131.

"It should be noted that the Committee held extensive discussions concerning the reported therapeutic usefulness of MDMA. While the Committee found the reports intriguing, it was felt that the studies lack the appropriate methodological design necessary to ascertain the reliability of the observations. There was, however, sufficient interest expressed to recommend that investigations be encouraged to follow-up these preliminary findings. To this end, the Committee urges nations to use the provisions of Article VII of the Convention of

Psychotropic Substances to facilitate research on this interesting substance."

-- Report of the Expert Committee on Drug Dependence of the World Health Organization, dated 18 July 1985 (A.-B 20, Annex II, at p.8).

DEA witnesses and international medical committees of the World Health Organization do not lightly -- or frequently -- issue strong public declarations of the need for medical research into the therapeutic utility of a compound. The need for research on MDMA has been stated even more strongly in this proceeding in the sworn testimony of a dozen other psychiatrists, including the Deputy Editor of the American Journal of Psychiatry (the official journal of the American Psychiatric Association and the leading psychiatric journal in the United States if not the world), two psychiatrists on the faculty of the Harvard Medical School, a Philadelphia psychiatrist expert in drug abuse, a Massachusetts psychiatrist with extensive experience using MDMA in his private practice, four New Mexico psychiatrists including a faculty member at the University of New Mexico School of Medicine, and three California psychiatrists including the state-wide psychiatric consultant to the California Department of Rehabilitation.

It is the legitimate, recognized importance of medical research into MDMA's therapeutic utility that gives this appeal its significance. The record in this case demonstrates that placing a drug in Schedule I under the Controlled Substances Act ("CSA") creates very substantial disincentives and obstacles to research. When the drug in question cannot be patented -- as is the case with MDMA -- those obstacles loom even larger. Even when

a drug legitimately meets the requirements for placement in Schedule I -- high potential for abuse, no accepted medical use, no accepted safety for use under medical supervision -- only important countervailing social policies justify the obstacles to research. If such a drug as MDMA is erroneously placed in Schedule I, society will pay a terrible and unnecessary price. Research that could lead to significant medical advances will be stifled with no countervailing social gain.

That would be the consequence if the Final Rule of the Administrator of the Drug Enforcement Administration were retained. We urge the Court of Appeals not to follow that path. We submit that in interpreting the relevant provisions of the Controlled Substances Act, clear statutory language and the explicit intent of the Congress must prevail over interpretations motivated by ease of administration. We urge this Court to recognize that overwhelming evidence in this case demonstrates that MDMA should be placed not in Schedule I but in Schedule III. In summary, petitioner takes the following positions on the issues discussed in the Final Rule of the Administrator.

[<sup>o</sup> Section on abuse, potential issue base?]

o The Administrator states that the FDA's regulations governing interstate marketing of new drugs determine what "accepted medical use in treatment" is under the Controlled Substances Act (Paragraph 15). Petitioner disputes this. That determination must be made by reference to the professional judgment of the medical community. The proper interpretation was stated by Michael Sonnenreich, the deputy chief counsel of DEA's predecessor agency, in testifying in 1970 before the House

Subcommittee which drafted the Controlled Substances Act. He stated that, "This basic determination...is not made by any part of the federal government. It is made by the medical community. The precise test, for reasons more fully set out below, is whether the use of a drug in treatment is accepted by reputable physicians within the medical community.

o The Administrator states that "Accepted safety for use under medical supervision" has in effect the same meaning as "accepted medical use in treatment": that the drug has been approved by the FDA for interstate marketing (Paragraph 17). The statute should not be read so as to make part of its language superfluous. Accepted safety is to be judged by expert medical opinion based on a review of currently known scientific information. "Accepted safety" must be contrasted with "accepted use". The latter requires a medical judgment about both safety and effectiveness. ~~The former focuses exclusively on safety.~~ A drug which has no accepted use because its effectiveness has not yet been accepted may still have "accepted safety".

~~To section 108(b)(1) of the Act, the Administrator invoked as a reason for placing MDMA in Schedule I the determination of the Secretary of Health and Human Services on whether MDMA had an accepted medical use or accepted safety under medical supervision. <sup>(and potential for abuse?)</sup> But this determination is binding on the Attorney General only if (i) it is in accordance with the law; (ii) it is not arbitrary and capricious; (iii) all relevant scientific and medical evidence introduced during the hearing before the Administrative Law Judge was before the HHS Secretary at the time his determination was made. In the present~~

case none of these conditions has been satisfied. First, the Secretary's original determination was based on an erroneous legal standard. Second, the determination was arbitrary and capricious because the Secretary (1) failed to consider relevant factors, and failed to exercise legally mandated discretion because of the erroneous standard applied; (2) acted on the basis of an incomplete record because DEA staff failed to provide HHS with important, relevant information from its files and because critically important judgments of the National Institute on Drug Abuse were not communicated to the Secretary; and (3) failed to follow HHS' own established procedures of consulting with its expert advisory committee and with the medical community. Third, both agency counsel and Drs. Grinspoon, Greer et al., have introduced vast amounts of evidence on medical and scientific issues into the record of this proceeding that were not before the HHS Secretary at the time of the Secretary's original determination. Given these circumstances, the HHS determination on MDMA cannot be legally binding.

o The Agency has not sustained its burden of proving that MDMA has no accepted medical use in treatment or its burden of proving that MDMA has no accepted safety for use under medical supervision. The existing record on medical practice in the States of New Mexico and California, in the absence of any rebuttal testimony by the Agency staff, necessitates a finding that -- at least in those states -- limited use of MDMA in a psychotherapeutic practice for carefully selected patients for carefully selected conditions, subject to the review of a peer

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review committee, would constitute currently accepted medical use in treatment and accepted safety for use under medical supervision.

o The record demonstrates that MDMA should be placed in Schedule III because it has a potential for abuse less than a high potential and an accepted medical use in treatment in the United States. But even if the Administrator were to determine that MDMA did not have an accepted use in treatment in the United States, it would still be appropriate to place MDMA in Schedule III. A substance with less than a high potential for abuse and no accepted medical use should be placed in Schedule III, IV, or V, depending upon its relative potential for abuse. In a preliminary ruling, the Administrative Law Judge recognized this as one of two alternative interpretations open to the Administrator. The other alternative was not to schedule MDMA at all.

The basis for the above conclusions is set out in more detail below.

## II. ADVERSE EFFECTS ON RESEARCH OF PLACEMENT IN SCHEDULE I

The Administrator in his Final Rule made no reference to the evidence presented in the case showing that the placement of a drug in Schedule I strongly discourages medical research on that drug. Therefore, he has not weighed all relevant factors in making his decision.

First, placing a drug in Schedule I creates bureaucratic delays in getting approval from the government to proceed with

research as well as added administrative burdens in carrying it out. A research project on a Schedule I drug must be affirmatively approved by the FDA before it can commence. 21 C.F.R. 1301.42(a)-(c); Tr. 8, at 82.

In addition, a researcher who wants to do research on a drug in Schedule I must secure a special registration from the DEA and must submit a research protocol that meets specifications set by the DEA. 21 C.F.R. SS 1301.22(a)(8), 1301.33, 1301.42. Testimony in this case established that two researchers who had applied to the DEA two to three months prior to the hearings for registrations to do Schedule I research on MDMA had still not received approval from the DEA at the time of hearings. Tr. 8, at 94. Moreover, the official in charge of processing their applications testified that such an application could pend at the DEA indefinitely or, in the words of the official, "ad infinitum." Tr. 8, at 94.

Further, researchers on Schedule I drugs are subject to additional reporting and security procedures, beyond those imposed on research Schedule II through V drugs. As the clinical research director for Hoffmann-LaRoche testified, these increased requirements are often "so burdensome that some clinicians prefer to deal with different drugs rather than evaluate Schedule I" drugs. Tr. 8, at 104. If these burdens have such an effect on well-financed drug company researchers, imagine the impact on academic researchers in the case of MDMA, which cannot be patented.

Second, the placement of a drug in Schedule I also has



strongly adverse effects outside the government. The criteria for placing a drug in Schedule I are so negative that they raise grave concern on the part of both researchers and volunteers about even being associated with such a drug.

In 1970, when the Administration originally proposed the legislation that became the Controlled Substances Act it recognized that Schedule I would carry a highly adverse reputation. The Administration felt that this reputation would be so strong that it proposed the DEA should not have the authority to move a drug out of Schedule I to any schedule other than Schedule II. (Hearings on Drug Abuse Control Amendments. Before the Subcomm. on Public Health and Welfare of the House Comm. on Interstate and Foreign Commerce, 91st Cong., 2nd Sess. 707 (1970) (hereafter "House Hearings").

The clinical research director of Hoffmann-LaRoche testified that, in her opinion, disclosure on patient consent forms of the criteria for Schedule I drugs and of the identity of other Schedule I substances such as heroin and LSD would strongly discourage both investigators and volunteers from participating in clinical studies. Tr. 8, at 102. She said that Hoffmann-LaRoche would not conduct research on a drug that was placed in Schedule I unless it was truly an extraordinary break-through life-saving drug. Tr. 8, at 110. She did not believe her attitude was in any way unique among the pharmaceutical companies. Tr. 8, at 122.

Similarly, academic researchers interested in researching Schedule I substances find it very difficult to obtain approvals for research from institutional review boards. Lipton,

Tr. 7, at 151, 163-64. One researcher expressed his frustrations as follows: "Based on [my experience] I would say that an investigator might look forward to a delay of a year or longer in getting his work with a Schedule I drug under way." GG-49.

Finally, the record graphically reflects the historical effects of placement in Schedule I under the CSA. Dr. Grinspoon, an international authority in this area and a well-respected psychiatrist on the faculty of the Harvard Medical School, testified that he was familiar with the literature in the field of Schedule I drugs. He pointed out that in the 1940s, 1950s and 1960s, extensive research was taking place on many Schedule I drugs in the area of psychiatric research. GG-16; Tr. 6, at 65. He testified that the present time there is virtually no research. Tr. 6, at 104-5.

Confirming Dr. Grinspoon's testimony, the Food and Drug Administration reported that it had received and approved in the last five years precisely one application to carry out research on Schedule I drugs in the area of psychotherapy. GG-57.

If MDMA does not meet the requirements for placement ~~in~~ Schedule I, it would be socially counterproductive -- indeed tragic -- to discourage research into what a number of leading academic and clinical psychiatrists testified might be a drug that represents an entire new class of valuable psychotherapeutic agents. Let us now consider whether MDMA can fairly be said to meet the requirements for placement in Schedule I.

III. UNDER CSA'S SCHEDULING CRITERIA, MDMA SHOULD BE PLACED IN SCHEDULE III, NOT IN SCHEDULE I.

A. Potential for Abuse

In order to place a substance in <sup>any</sup> Schedule under the CSA, a finding must be made that it has a "potential for abuse." Then the its relative potential for abuse must be determined. Substances with a "high" potential for abuse are to be placed in either Schedule I or II. Those with less than a "high" potential for abuse are to be placed in Schedules III, IV, or V. The statute itself provides no further direct guidance as to what is meant by "potential for abuse." However, the provisions of 21 U.S.C. S 811(c), and the legislative history of the Controlled Substances Act do provide important additional guidance.

1. Eight Factors To Be Considered

The Administrator has based his decision in the Final Rule, placing MDMA in Schedule I, largely on theoretical similarities between other drugs and MDMA based on chemical structure or assumed pharmacological effects. But the provisions of 21 U.S.C. S 811(c) mandate that the DEA take into account eight factors in making "any finding" in determining the Schedule in which to place a drug. These eight factors are as follows:

- (1) Its actual or relative potential for abuse.
- (2) Scientific evidence of its pharmacological effect, if known.
- (3) The state of current scientific knowledge regarding the

substance.

- (4) Its history and current pattern of abuse.
- (5) The scope, duration, and significance of abuse.
- (6) What, if any, risk there is to the public health.
- (7) Its psychic or physiological dependence liability.
- (8) Whether the substance is an immediate precursor of a controlled substance.

21 u.S.C. S 811(c) (emphasis added).

Thus the DEA is not free to make a determination concerning a drug's relative potential for abuse without considering all these factors. In particular, the DEA may not make its determination based largely on theoretical similarities between drugs. Rather the DEA is mandated to take into account the actual experience "on the streets." As we shall see, the legislative history confirms this interpretation. See infra pp.

~~30-39~~ — \* — .

## 2. Legislative History on "Potential for Abuse"

The Controlled Substances Act originated with a bill submitted by the Administration and passed with a few amendments by the Senate on January 28, 1970. This was S 3246, the Controlled Dangerous Substances Act of 1969. 116 Cong. Rec. S1671 (1970).

The House Subcommittee on Public Health and Welfare of the House Committee on Interstate and Foreign Commerce then held eleven days of hearings in February and March, 1970 and drafted a

"clean" bill amending the Administration and Senate versions. It was introduced as titles I and II of HR18583. 116 Cong. Rec. H332987 (September 23, 1970). This version was ultimately enacted into the Controlled Substances Act of 1970.

Therefore the testimony before the House Subcommittee on Public Health and Welfare, the report of the House Committee on Interstate and Foreign Commerce on H.R. 18583, and the floor debates of the House and Senate are the critical references in determining the intent of Congress.

a. House Committee Report

With respect to the definition of the term "potential for abuse," the House report refers to regulations promulgated under the sections of the Federal Food, Drug, and Cosmetic Act which were predecessor statutes to the Controlled Substances Act.

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These regulations, as quoted by the House Report, provided as follows: The Director may determine that a substance has potential for abuse because of its depressant or stimulant effect on the central nervous system or its hallucinogenic effect if:

- (1) There is evidence that individuals taking the drug or drugs containing such a substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or of the community; or
- (2) There is significant diversion of the drug or drugs containing such a substance from legitimate drug channels; or
- (3) Individuals taking the drug or drugs containing such a substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs in the course of his professional practice; or
- (4) The drug or drugs containing such a substance are new drugs so related in their action to a drug or drugs already listed as having a potential for abuse to make it likely that the drug will have the same potentiality for abuse as such drugs, thus making it reasonable to assume that there may be significant use contrary to or without medical advice, or that it has a substantial capability of creating hazards to the health of the user or to the safety of the community.

Report on Comprehensive Drug Abuse Prevention Control Act of 1970 of House Comm. on Interstate and Foreign Commerce, H.R. Rep. No. 91-1444, 91st Cong., 2d Sess. (Part I), at 34 (1970) (hereafter "House Report").

The House report then goes on:

(1) The Committee made clear that it "did not intend that potential for abuse be determined on the basis of isolated or occasional non-therapeutic purposes.' The Committee felt that there must exist 'a substantial potential for the occurrence of significant diversions from legitimate channels, significant use by individuals contrary to professional advice, or substantial capability of creating hazards to the health of the user or the safety of the community'...." House Report, at 35 (emphasis added).

(2) The Committee went further in explaining what it meant by "a substantial potential" for significant diversion or significant use. The Committee declared that:

the term "substantial" means more than a mere scintilla of isolated abuse, but less than a preponderance. Therefore, documentation that, say, several hundred thousand dosage units of a drug have been diverted would be 'substantial' evidence of abuse.

House Report, at 35.

The above excerpts provide guidance on the minimum potential for abuse before a substance is included even in the lowest schedule of the Act, i.e., Schedule V.

Thus, in order for a drug to be controlled even at the Schedule V level, the Committee intended that there be evidence that at least "several hundred thousand dosage units" of a drug had been diverted, or that there be other evidence establishing "a substantial potential" for either "significant diversion," "significant use by individuals," or "substantial capability of creating hazards to the health of the user or the safety of the

community."

b. Evolution of Five Schedules

Further light is shed on congressional intent by following the evolution of the five Schedules which now appear in 21 U.S.C. S 812(b). The bill originally submitted by the Administration and the bill originally passed by the Senate in January, 1970 contained only four schedules. The four schedules in the Senate bill, S. 3246, are set out in the margin. (3) The House Committee rewrite creates five schedules for the first time, 116 Cong. Rec. H33607 (September 24, 1970).

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(3)

Schedule I -- (1) a high potential for abuse; (2) no accepted medical use in the United States; (3) a lack of accepted safety for use under medical supervision.

Schedule II -- (1) a high potential for abuse; (2) currently accepted medical use in the United States or currently accepted medical use with severe restrictions; (3) abuse may lead to severe psychic or physical dependence.

Schedule III -- (1) a potential for abuse less than the substances listed in Schedules I and II; (2) well documented and approved medical use in the United States; (3) abuse may lead to moderate or low physical dependence or high psychological dependence.

Schedule IV -- (1) a low potential for abuse relative to the substances listed in Schedule III; (2) currently accepted medical use in the United States; (3) limited physical dependence and/or psychological dependence liability relative to the substances listed in Schedule III.

116 Cong. Rec. S1673-74 (January 28, 1970).

Schedule III in the Senate bill was divided by the House Committee into two schedules -- namely, Schedule III and Schedule



## IV.

The original Administration bill and the Senate bill placed in their Schedule III all of the following drugs: all amphetamines; methamphetamine; barbiturates; combination compounds containing enough narcotics to make them highly addictive; minor tranquilizers; and mild sleeping preparations.

Dr. Henry Brill of the AMA Committee on Alcoholism and Drug Dependence testified before the House Subcommittee as follows:

In Schedule III of both S. 3246 [the Senate bill] and H.R. 17343 [the Administration bill], however, there is a confusing admixture of drugs of very different degrees of hazard: for example, methamphetamine and chloral hydrate.

House Hearings, at 231-32.

A major pharmaceutical house specifically suggested the course that the House Subcommittee ultimately adopted in the following words:

Our suggestion is that a new schedule be established and inserted between the present Schedules III and IV of the Drug Abuse Legislation H.R. 13743. This new schedule would be designed to insure that drugs of low abuse potential, such as the minor tranquilizers and long-acting barbiturates, are not classified together with amphetamines and short-acting barbiturates which raise far more severe drug-abuse problems.

House Hearings, at 776.

The House Subcommittee also received substantial evidence of the nature and extent of the drug abuse problems posed by amphetamines, methamphetamines, and barbiturates. Congressman Pepper, as Chairman of the House Select Committee on Crime,

testified at great length.

Dr. Stanley Yolles, then Director of the National Institute of Mental Health, testified that:

more than 8 billion amphetamine tablets are manufactured yearly, and ... a significant percentage are diverted to illicit channels...Swallowing stimulants in increasing amounts is becoming more widespread...

House Hearings, at 177.

In addition, Dr. Yolles testified that

"...barbiturates are the No. 1 method of committing suicide by chemical means. Some 10 billion sedative dosage units will be produced this year, enough to provide each man, woman and child with 50. At least half of this supply gets into the illicit market."

House Hearings, at 177-179.

The House bill's new Schedule III contained amphetamines, short-acting barbiturates, methamphetamine and multiple ingredient compounds that included sufficient levels of narcotics to be highly addicting. The House bill's new Schedule IV contained the minor tranquilizers, longer-acting barbiturates, and milder sleep preparations. The original Schedule IV of the Senate and Administration bills became Schedule V in the House bill. This system was incorporated into the Controlled Substances Act.

This legislative history helps us to understand that Schedule III was intended to include drugs with enormous "potential for abuse" which had been demonstrated by actual widespread abuse. Representative Pepper attempted to move amphetamines out of Schedule III and into II. See 116 Cong. Rec. H33603-H33609. But his purpose was "to subject the dangerous

drugs to a quota system of control." 116 Cong. Rec. H33609. He did not argue that amphetamines did not meet the criteria for Schedule III. It is also highly instructive that no one expressed any view that the highly abused barbiturates placed in Schedule III by the House bill were improperly classified.

It is even more important to look at the words of the Subcommittee members who drafted the House bill. Congressman Paul Rogers, the second-ranking Democrat on the Subcommittee, responded to Rep Pepper's proposed amendment as follows:

The reason it [methamphetamine] is in Schedule III and was put there by the Committee is that the medical and scientific people, as well as the law enforcement people, said that is where it should be.

116 Cong. Rec. H33612-13 (Sept. 24, 1970).

Representative Carter, the ranking Republican member of the Subcommittee spoke similarly.

116 Cong. Rec. 33613 (September 24, 1970).

The House then defeated Rep. Pepper's amendment. 116 Cong. Rec. H33618 (4).

(4)

Petitioner recognizes that the DEA through administrative action has moved amphetamines and some barbiturates from Schedule III to Schedule II. The DEA's decision to exercise its authority in this respect in no way can effect the intent of Congress as to the nature of the abuse potential appropriate for drugs in Schedule III.

c. Conclusions to be Drawn

Schedule V was designed for drugs which had "substantial potential" for a "significant diversion," a "significant use" outside of medical supervision or "a substantial capacity" to harm the health of users or the community. Schedule IV would involve

drugs as to which there was an even higher potential for abuse. The House Committee and the Congress took notice of the widespread abuse of minor tranquilizers such as Valium and Librium that were placed in Schedule IV. See 116 Cong. Rec. S1683-89 (Jan. 28, 1970); 116 Cong. Rec. S.35516-23 (Oct. 7, 1970).

Schedule III was intended to include drugs of very substantial potential for abuse including amphetamines and barbiturates. Schedules I and II were reserved for drugs of "high potential for abuse" -- which needed to be placed under production quotas. See also Conference Report, H.R. Rep. 91-1603, at 9.

Petitioner submits that it is this continuum which the DEA must apply to determine the Schedule into which MDMA should be placed.

### 3. Proof of Relative Abuse Potential Required Based on Evidence of Actual Experience

The need to prove relative potential for abuse was appreciated from the outset, as Mr. Sonnenreich specifically testified. (House Hearings, at 141).

Moreover, for drugs that are "on the street," the Agency must base its judgment on relative levels of actual abuse. Again this subject is illuminated by testimony of Mr. Sonnenreich:

Mr. Sonnenreich. I would disagree with that, Congressman. No. 1 [the determination about a high potential for abuse] is clearly the street abuse problem or the abuse problem as found by agents of the Bureau of Narcotics and Dangerous Drugs...  
House Hearings, at 165.

Mr. Sonnenreich. But there are two criteria: One is potential and one is actual, the high potential for abuse. If it is a new drug and we want to classify it,

the first question is does it have any potential for abuse and that is theoretical, that is a scientific determination. Then we have the second part of the determination, is there any actual abuse? If it is a known drug, we have to go out and find out whether or not there is actual abuse and that is a law enforcement determination.

Now if it is a theoretical drug that is not out on the streets, the answer is purely hypothetical and medical. If it is a known drug that is on the street, of course we have to collect the other information and point our diversion...

Mr. Sonnenreich. There is always, in every one of these schedules, a pharmacological input, but then when we get into this, we are then talking about getting the information and then we have to get all three factors--actual abuse, the using without a medical prescription and the pharmacological information. The it must be analyzed to see whether or not, in fact, we have a legally sufficient case to proceed.

House Hearings, at 718-19 (emphasis added).

It is clear from this testimony that where there is "a known drug that is out on the street," the determination of "potential for abuse" must be made on a basis that includes comparative information and evidence about what is actually occurring and <sup>comparison</sup> with the abuse of other drugs. This was the intent of the drafters -- both in the Administration and on the Committee.

#### 4. Case Law

As far as counsel for Dr. Grinspoon can determine, there have been no decided cases interpreting the requirements involving the relative potential for abuse criteria of the Controlled Substances Act. Two cases under the 1965 amendments to the Federal Food, Drug and Cosmetic Act, the CSA's predecessor statute, discussed the method of determining that a drug had a

"potential for abuse", which would allow it to be subject to some control. See Carter-Wallace, Inc. v. Gardner, 417 F.2nd 1086 (4th Cir. 1969), cert. denied, 398 U.S. 938 (1970); Hoffmann-LaRoche, Inc. v. Kleindienst, 478 F.2nd 1 (3d Cir. 1973).

Both the Third Circuit and the Fourth Circuit agreed that the Agency was required to examine future or potential abuse. But courts in both cases felt called upon to rely on extensive evidence of the actual abuse of the drugs involved. The Carter-Wallace case involved the drug meprobamate, which had been on the market for 10 years at the time of the control action. The court there recited evidence showing that meprobamate produced tolerance, physical dependence and withdrawal symptoms; that it had been used in a number of cases for suicide and attempted suicide; that its use in attempted suicides was surpassed only by barbiturates; that the record disclosed significant diversion of the drug from legitimate trade, and so on. 417 F.2d at 1090-91. (In light of this strong evidence of widespread abuse, it is interesting to note that meprobamate was placed in Schedule IV under the CSA.)

Similarly, in the Hoffman-LaRoche case, the record demonstrated extensive actual abuse of Librium and Valium; for example, the record demonstrated a very substantial diversion of Librium from proper channels; showed that users of Librium and Valium had developed tolerance and withdrawal symptoms; that individuals had developed psychic dependence on both Librium and Valium, and so on. 478 F.2d at 8-11. (It is also instructive to note that Librium and Valium were placed in Schedule IV of the CSA

even with the substantial evidence of abuse.)

5. Evidence on Potential for Abuse and Proposed Findings of Fact

We now turn to consider the evidence with respect to relative abuse potential of MDMA.

The Agency has the burden of proof in seeking to place MDMA into Schedule I. 21 C.F.R. S 1316.56. Therefore, the initial issue is whether the Administrator of the Drug Enforcement Administration has met its burden of proving that MDMA has a high potential for abuse. Petitioner submits that it has not.

The DEA seized its first sample of MDMA in 1972. A.-B2, Attachment 1. Scientists have been writing about the drug in the open literature since the 1970s. GG-18; GG-1. The record, therefore, reflects nearly 14 years of experience with MDMA.

Petitioner is not in any way seeking to deny the evidence that MDMA is used outside therapeutic settings. Nor is he seeking to deny that any drug not used under medical supervision is potentially dangerous. It is for that reason that Petitioner has advocated from the very beginning of this proceeding that MDMA should be scheduled. Nevertheless the Agency has not sustained its burden of proving that MDMA has a "high" potential for abuse justifying its classification in Schedule I.

During the Administrative Law hearing, Agency counsel addressed the evidence in the record bearing on abuse by humans in its proposed Findings of Fact numbered 43 to 72. Notable by its absence is any comparison of the evidence on abuse of MDMA with to abuse of other drugs. The reason is that, by every

measure in the current record, MDMA abuse can only be found to be low or moderate in comparison to the abuse of other substances scheduled under the Controlled Substances Act.

(a) Fourteen-year Record Concerning

MDMA

The record contains <sup>several types</sup> ~~a number~~ of evidence.

(1) Medical Examiner Reports

Contained in the Drug Abuse

Warning Network Data

The National Institute on Drug Abuse (NIDA) publishes annually a compilation of drug abuse information collected through its Drug Abuse Warning Network (DAWN). This system collects reports from selected (currently more than 700) hospital emergency rooms in the United States. The reports record all visits to those emergency rooms for medical problems associated with drug abuse. <sup>s</sup> (5)

From 1972 through September 15, 1983, there had been a grand total of eight mentions of MDMA in the DAWN system. A.-B2, at 7, Attachment 5. During the period 1972 through 1983, the DAWN system was reporting approximately 175,000 drug mentions each year. GG-7. Tr.5, at 76-77. MDMA does not compare with the frequency with which Schedule II drugs appear on the list. Nor, in fact, does it compare with the mentions of Schedule III drugs or Schedule IV drugs. Indeed, the Department of HHS called the eight mentions of MDMA "not significant." Exhibit A.-B4, at 2.

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~~(B)~~  
 5 National Institute on Drug Abuse, Data from the Drug Abuse Warning Network (DAWN), Annual Data 1983, at 1.

(2) DAWN Medical Examiner Mentions

The DAWN system also compiles from selected medical examiners in the United States data reflecting drugs mentioned in connection with drug abuse deaths. From 1972 through September 15, 1983, MDMA was mentioned in connection with one drug abuse death. A-B2, Attachment 5, at 22. The identification is seriously suspect. A-B18; Tr. 3, at 50-52; GG-30. But, more importantly, the DAWN data system reports approximately 3,000 drug abuse deaths each year. Tr. 5, at 74.

(3) Community Epidemiological Data of the National Institute on Drug Abuse

The National Institute on Drug Abuse also compiles drug abuse information from its designated representatives in 20 metropolitan areas. From June, 1981 through December, 1984, these Community Epidemiological Work Group meetings were held every six months. During those meetings more than 120 different drugs were discussed; MDMA was never mentioned. Stipulations by parties, Tr. 6 at 10-13.

(4) Laboratory Seizures

The record reflects that during the period 1972 through 1983, DEA seized four clandestine drug laboratories which had the capacity to manufacture MDMA. A.-B2, at Attachment 4. During

this 12-year period, DEA seized approximately 2,400 laboratories. Tr. 63-64.

Other DEA figures indicate that during the 7-year period 1977 through 1983, DEA seized 31 laboratories that in total had the capacity to produce 14,000 kilograms of MDA. Tr. 5, at 66. During the same period of time, DEA seized two laboratories with a capacity to manufacture 2.7 kilograms of MDMA. Tr. 5, at 67.

(5) Exhibits of Drug Evidence

Submitted to DEA Laboratories

During the period 1972 through 1983, DEA laboratories received a total of 44 evidentiary exhibits of substances identified as MDMA. A.-B2, at Attachment 1. During the same period of time, DEA laboratories were receiving between 30,000 and 40,000 drug exhibits each year. Tr. 5, at 60.

(6) Data from Drug Treatment

Facilities

DEA called one witness from a drug treatment facility: Daryl Inaba of the Haight-Ashbury Free Medical Clinic in San Francisco, California. Mr. Inaba testified that out of approximately 400 clients each month, the Free Clinic had between three and four patients who reported drug abuse problems with the family of drugs including MDA, MDMA, MMDA, etc. Tr. 2, at 77-78. Thus, Mr. Inaba estimated tht clients using MDMA would be less than one percent of the total client load and could be less than one-quarter of one percent. Id. Furthermore, Mr. Inaba testified that the Free Clinic had tested three samples of drugs that their clients had believed were MDMA and discovered that only one of the

three was in fact MDMA. Tr. 2, at 87. If this was the drug abuse clinic the agency chose to testify, it is fair to conclude that other clinics reported even less experience with MDMA.

Dr. Lance Wright, a witness called by Drs. Grinspoon, Greer, et al., is a Philadelphia psychiatrist with affiliations at Hahnemann University, at the University of Pennsylvania, and as a Staff psychiatrist in drug abuse treatment at the Philadelphia V.A. Hospital. Dr. Wright testified that there had been no reported incidents of MDMA abuse in the treatment system in the Philadelphia area, and that he had spoken with colleagues in New York and Boston and had found no evidence of problems there. Wright Direct, at 1-2.

(7) DEA Written Survey in 1979

In mid-1979, Frank Sapienza of the DEA staff wrote to 17 law enforcement agencies in the United States seeking information on synthesis and trafficking in MDMA. Tr. 5, at 42. The responses were:

- o Nine of the agencies did not respond at all;
- o Five responded that they had not encountered any MDMA;
- o Three wrote to the DEA that they had received some samples of MDMA.

Tr. 5, at 42.

(8) MICROGRAM Request of 1982

The Drug Enforcement Administration issues a publication

entitled "MICROGRAM" for law enforcement personnel. It is sent to about 1,400 law enforcement agencies and forensic laboratories -- 1,200 in the United States and 200 abroad. Tr. 7, at 171. In 1982, the DEA included in two or three issues of MICROGRAM a request for information on any trafficking or synthesis of MDMA that the agencies had encountered. Tr. 5, at 46-47.

The DEA received precisely three responses to its inquiry. Tr. 5 at 48-49.

(9) MICROGRAM Request of 1985

In March 1985, DEA published another notice in MICROGRAM. The Drug Enforcement Administration received no responses whatsoever to this inquiry. GG-41, at 2.

(10) ( PharmChem Laboratories  
Sample Analyses

The DEA also submitted evidence indicating that a private testing laboratory -- Pharm Chem -- had received samples of MDMA to be analyzed during the period 1976-1984. The highest number of samples ever received during a year was 18, and during most years there were less than five samples of MDMA a year. In any case, the Agency's reliance on a private laboratory only underlies the weakness of their case.

(11) Testimony by Expert Witnesses

All witnesses on both sides agreed that individuals did not use MDMA intensively and that there was no tendency toward dependence upon MDMA. All the psychiatric witnesses testified tht

increasing the dosage and frequency of use produced more unpleasant than pleasant effects. Greer Direct, at 9-11; Zinberg Direct, at 1; Ingrasci Direct, at 5; Wolfson Direct, at 10-11; Strassman Direct, at 11-12; Downing Direct, at 8; Wright Direct, at 2. In addition, Richard Seymour on the staff of the Haight-Ashbury Free Clinic testified that their clinic did not see recurrent, long-term, or habitual use of MDMA. Seymour Direct, at 3. Prof. Ronald Siegel, a witness for the Agency, also testified that his informal interviews did not detect habitual use. Siegel Direct, at 2-3. (6)

(b) No Proof of High Potential for Abuse

Thus, every piece of officially compiled data reflects a low absolute level of MDMA usage with no trend toward any increase over the 12 year period. All evidence indicates that MDMA use is many times less prevalent than use of MDA. Every witness who addressed the issue, including DEA witnesses, agreed that MDMA was not used in high amounts or with high frequency. Moreover, this low level of use existed despite the fact that MDMA was not a controlled substance, and therefore there was no criminal deterrent. In sum, the evidence compels a finding that MDMA does not have a high potential for abuse and should not be placed in Schedule I.

6. (Evidence on Chemical Structure,  
Pharmacology, and Animal Data)

Agency counsel at the hearing devoted their first 42

Findings of Fact on the issue of potential for abuse to a discussion of the findings of the Secretary of HHS on (1) the chemical structure relationships between MDMA and other drugs; (2) the pharmacological effects of MDMA and other drugs; (3) animal drug discrimination studies; (4) animal self-administration studies; and (5) recent studies of the biochemical effects of certain drugs in rat brains.

The Administrator in his Final Rule derives most of his evidence on abuse potential from these findings (Paragraphs 19-64). Petitioner has already argued that the significance of any such evidence must give way, in the case of a drug that is "on the street", to evidence on the actual extent of human abuse. Petitioner submits further these findings are often of questionable value in themselves.

As Dr. Morris Lipton, the head of one of the nation's leading biomedical research centers, emphasized in his direct testimony, chemical similarity may or may not be a good guide to the actual effects of a compound in the human body. Lipton Direct, at 1-2. (8) Furthermore, the animal studies cited by Agency counsel in this case simply do not prove anything with respect to abuse potential. On the issue of these ambiguous chemical and pharmacological findings, petitioner refers the Court to the Proposed Findings of Fact and Conclusions of Law of Drs. ~~Greer and Grinspoon et al.~~<sup>Greer and Grinspoon et al.</sup>, January 15, 1986, pp. 47-58.

In any case, these HHS findings provide no basis whatsoever for coming to a conclusion about MDMA's relative abuse potential. As the Administrative Law Judge, Francis L. Young, in

treatment in the United States." Petitioner submits that this phrase means what it says -- namely, that a determination must be made as to whether the medical community accepts the use of a particular drug in medical treatment. The statutory language does not mean something wholly different from its plain meaning, as the Administrator has concluded -- namely, whether or not a manufacturer has been licensed by the FDA to engage in the interstate shipment and sale of the drug. There are many non-medical reasons why a manufacturer might not have obtained such approval -- lack of financial return is the most frequent in actual practice.

Petitioner submits that his position is the only one consistent with the statutory language, the legislative history, accepted interpretations of the Food, Drug, and Cosmetic Act, and the existing responsibility of the states to regulate medical practice.

1. The Statutory Language of the Controlled Substances Act

The Supreme Court of the United States has declared that "the meaning of the statute must, in the first instance, be sought in the language in which the act is framed, and if that is plain, .... the sole function of the Courts is to enforce it according to its terms." Caminetti v. United States, 242 U.S. 470, 61 L. Ed. 442, 37 S. Ct. 917 (1917).

"One who questions the application of the plain meaning rule to a provision of an act must show either that some other section of the act expands or restricts its meaning, that the provision itself is repugnant to the general purview of the act, or that the act

considered in pari materia with other acts, or with the legislative history of the subject act, imports a different meaning."

Sutherland Stat Const S 46.01, at 74 (4th ed.) (footnotes omitted).

In this case all these factors do not alter but reinforce the plain meaning. By departing from it, the Administrator has ignored legislative history, ignored other provisions of the CSA, contradicted long-standing interpretations of the Federal Food, Drug, and Cosmetic Act, ignored the rights of individual states to approve the intrastate marketing of drugs, and ignored the responsibilities of states to regulate medical practice.

In determining "accepted medical use in treatment" the relevant evidence is medical opinion with respect to whether the use of a particular substance in medical treatment is accepted in the medical community. Such evidence is familiar in the law of medical malpractice and the law of medical licensing and discipline within the various states, as will be set out further below.

The statute nowhere refers to the question whether a substance has an NDA or has been otherwise approved by the Food and Drug Administration for interstate shipment and sale. The Congress knows how to write such a provision as numerous cross-reference in the CSA to the Food, Drug, and Cosmetic Act demonstrate. See 21 U.S.C. S 802 (12); 21 U.S.C. S 811 9g)(1): 307 (c) (2) (A) S 307 (e) of the Controlled Substances Act, 21



U.S.C. SS 827 (c)(2)(A), 827 (f),, SS 305(a), 305(b) of the Controlled Substances Act, 21 U.S.C. SS 825 (a), 825 (b); SS 309 (a), 309 (b), of the Contralled Substances Act, 21 U.S.C. SS 829 (a), 829 (d).

## 2. Legislative History

Testimony by three Administration witnesses during consideration of the Comprehensive Drug Abuse, Prevention and Control Act of 1970 (Pub. L. 91-513) demonstrates that "accepted medical use" was to be determined by the medical community on the basis of medical evidence -- not exclusively by looking at whether FDA had approved an NDA. These witnesses were: Michael R. Sonnenreich, Deputy Chief Counsel of the Bureau of Narcotics and Dangerous Drugs, the DEA's predecessor agency; John Ingersoll, Director of BNDD; Dr. Rogert Egeberg, Assistant Secretary of HEW. Relevant portions of their testimony were as follows:

Mr. Rogers: Under Schedule I drugs. Would HEW or the Department of Justice be able to determine on a drug a lack of accepted safety for use under medical supervision?

Dr. Egeberg: I would think that HEW would expect to have a good deal to say on that.

Mr. Rogers: All right. HEW would have the competence there. I think this would be admitted. What about no accepted medical use in the United States.

Dr. Egeberg: Well, I would think that HEW would be the primary source, through its various agencies and its contacts, for information on that subject.

House Hearings, at 194 (emphasis added).

Mr. Ingersoll: I must also point out that this review [prior registration of researchers by the Department of Justice] is only required

for Schedule I substances which the medical profession has already determined to have no legitimate medical use in the United States.

House Hearings, at 678 (emphasis added).

Mr. Rogers: So the only category of [Schedule] I is simply for research?

Mr. Sonnenreich: Yes, sir, and that is because they have no medical use as determined by the medical community.

House Hearings, at page 696 (emphasis added).

Mr. Sonnenreich: Mainly, our feeling is that the trigger on your Schedule I drugs which are really different from your II, III and IV drugs. It is this basic determination that is not made by any part of the federal government. It is made by the medical community as to whether or not the drug has medical use or doesn't.

Mr. Rogers: If it has medical use, Food and Drug probably would have authorized it, wouldn't they?

Mr. Sonnenreich: I assume so, sir.

House Hearings, at 718 (emphasis added).

### 3. The D.C. Circuit Ruling

The D.C. Circuit in *NORML v. DEA*, 559 F. 2d 745, 750 (D.C. Cir. 1977), rejected the idea that an NDA determined whether a substance had an "accepted medical use":

...respondent [DEA] further argues that placement in Schedule I is mandated because there is "no approved New Drug Application" for marihuana. This reference is to the procedure by which persons who wish to ship substances in interstate commerce apply to the Secretary of HEW for approval of a New Drug Application (NDA) under the Federal Food, Drug, and Cosmetic Act]. Respondent argues that this procedure establishes whether a substance has "an accepted safety for use," [and concludes that "[r]escheduling of marihuana would be impossible under the [Controlled Substances] Act without a reappraisal from the Secretary of Health,

Education, and Welfare."

The interrelationship between the two Acts is far from clear....Respondent provides no reason to suppose Congress intended that the NDA institutional check necessarily precede the CSA check. Even if NORML were to obtain approval of an NDA for marijuana, it would then have to apply to DEA to reschedule the drug. We think it not inappropriate for NORML to apply first rescheduling under the CSA. (citations omitted). The D.C. Circuit's decision is consistent with the

longstanding recognition that the Food and Drug Administration does not determine what is and what is not accepted medical use of drugs.

4. The Food and Drug Administration Does Not Regulate Medical Practice Or Determine Accepted Medical Use
  - a. Food, Drug and Cosmetic Act

The FDCA Act was enacted in 1938 after legislative efforts spanning several years. (6). The first bill to pass either house of Congress that was substantially similar to the present Act included within its definition of "drug" the qualification that it did not apply "for the regulation of the legalized practice of the healing art." (7) While the definition of "drug" as ultimately enacted did not include this proviso (see U.S.C. 721 (g)), the legislative history nonetheless made it very clear that Congress did not intend the Act to apply to the state-regulated practice of medicine.

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(6)  
See generally Dunn, Federal Food, Drug and Cosmetic Act (1938).

(7)  
74th Cong., 1st Sess. 201 (b), 79 Cong. Rec. 8351 (1935).

Moreover, Congress has in several other respects

specifically provided for deference to state law under the Food, Drug, and Cosmetic Act. The drug provisions of the Act do not apply, for example, to drugs wholly in intrastate commerce. 21 U.S.C. ss 321 (b), 331. The Act also relies on state law to determine who is entitled to practice medicine within a state and who, under the prescription drug provisions of the Act, may be authorized to administer prescription drugs. 21 U.S.C. S 353 (b). Further, the Act generally defers to state law in areas that do not directly conflict with it. (9)

(9)

Act (Pub. See, e.g., Section 202 of the 1962 Amendments to the FDC L. 87-781, 76 Stat. 780)

b. Repeated FDA Interpretations Emphasize that the FDA Does Not Regulate Medical Practice

The Food and Drug Administration has repeatedly interpreted the provisions of the Food, Drug, and Cosmetic Act to forbid the FDA from regulating the practice of medicine. In particular, the FDA has frequently allowed as legal the widespread practice of physicians using marketed drugs for uses which the FDA has not approved: that is, for uses outside the confines of their labelling.

In 1975, the Food and Drug Administration wrote as follows:

Advances in medical knowledge and practice inevitably precede the labeling revision by the manufacturer and formal labeling approval by the Food and Drug Administration. Good medical practice and patient interest thus require that physicians be free to use drugs according to their best knowledge and judgment. Certainly where a physician uses a drug for a use not in the approved labeling, he has the responsibility to be well informed about the drug and to base such use on a

firm scientific rationale or on sound medical evidence, and to maintain adequate medical records of the drug's use and effects, but such usage in the practice of medicine is not in violation of the Federal Food, Drug and Cosmetic Act.

40 Fed. Reg. 15393-94 (1975) (emphasis added).

In June, 1983, the FDA repeated its view that it does not have the authority to regulate the practice of medicine:

Once a drug product has been approved for marketing, a physician may, in treating patients, prescribe the drug for uses not included in the drug's approved labeling. The primary legal constraints in that situation are State laws on medical practice and products liability law. The IND Rewrite proposal would codify the Agency's longstanding position that the regulations do not apply to the "practice of medicine," though the proposal does not purport to define with specificity such practice in terms of the Act.

48 Fed. Reg. 2673 (June 9, 1983).

Finally, the Food and Drug Administration reemphasized this position in a filing with the United States Court of Appeals for the District of Columbia Circuit in 1983.

Chaney v. Heckler, 718 F. 2d 1174, 1179 (D.C. Cir. 1983),  
rev'd \_\_\_ U.S. \_\_\_, 84 L. Ed. 2d 714 (1984). (footnotes omitted).

C. The Case Law Has Consistently  
Determined that the FDA Does  
Not Regulate Medical Practice

As the court in United States v. Evers, 453 F. Supp. 1141 (M.D. Ala. 1978), aff'd 643 F. 2d 1043 (5th Cir. 1981) observed:

When the physicians go beyond the directions given in the package insert it does not mean they are acting illegally or unethically, and

Congress does not intend to empower the FDA to interfere with medical practice by limiting the ability of physicians to prescribe according to their best judgment.

453 F. Supp. at 1149-50.

The observations of one state court in invalidating an effort under State law to prosecute a doctor for prescribing an unapproved drug are extremely pertinent:

To require prior state approval before advising - prescribing -- administering -- a new treatment modality for an informed consent patient is to suppress innovation by the person best qualified to make medical progress. The treating doctor, the clinician, is at the cutting edge of medical knowledge.

To require the doctor to use only orthodox 'state sanctioned' methods of treatment under threat of criminal penalty for variance is to invite a repetition in California of the Soviet experience with Lysenkoism.

People v. Privitera, 141 Cal. Rptr. 764, 774 (Cal. App. 1977).  
d. Use of Drugs Not Approved by the FDA

Similarly, it is clear that the Food and Drug Act does not determine the medical propriety of using drugs that have not been approved at all by the Food and Drug Administration for interstate shipment and sale. In the Administrative Law hearing, Drs. Grinspoon, Greer, et al., submitted as their exhibits 15 and 38, opinions of the Legislative Counsel of the state of California and the California State Attorney General, indicating that doctors within the state of California are legally free to exercise their medical judgment to prescribe and administer drugs that have not been approved either by the FDA or by the State for commercial

shipment and sale. These opinions specifically concluded, as follows, in the words of the Legislative Counsel of California:

The [California] Sherman Food, Drug, and Cosmetic Law does not prevent a physician from prescribing, or a pharmacist acting pursuant to the order of a physician from dispensing, a drug not approved in a federal or state new drug application....

The Food and Drug Administration of the United States Department of Health and Human Services has also informed us that, in its opinion, it does not have the authority under the Federal Food, Drug, and Cosmetic Act to prevent a physician, or a pharmacist acting pursuant to the order of a physician, from prescribing a drug not approved in a federal new drug application.

Letter dated May 26, 1981, from Bion M. Gregory, Legislative Counsel, to Honorable John R. Garamendi, at 1,3 (emphasis added). The Agency introduced no testimony or documentary evidence to rebut these two documents.

(i) Drugs Marketed Intra-State

The Food and Drug Act does not regulate drugs which are manufactured and distributed wholly within one state. 21 U.S.C. SS 321 (b), 331. The states have acted to regulate the manufacture, shipment and sale of drugs wholly within a single state. See, e.g., Calif. Health and Safety Code SS 26670(b)-26676; N.Y. Educ. Law, Art. 137, S6817(b)-(c) (McKinney 1985. Drugs which are legally manufactured within a particular state, and administered by physicians within that state obviously can constitute accepted medical use in treatment in the United States.

(ii) Orphan Drugs and Treatment INDS

There is a group of so-called orphan drugs which have

been recognized by the Congress as ~~being~~ drugs which have medical utility and accepted medical use in treatment, but where financial rewards are not sufficiently great to motivate a pharmaceutical company to pursue the FDA approval process. Historically, ~~in these situations~~, these drugs have been made routinely available to physicians as so-called "compassionate INDs" or "treatment INDs". In recommending that the House of Representatives approve the Orphan Drug Act which was enacted into law in 1983, the House Commerce Committee made the following observations:

In this status, the sponsoring company will make the drug available, with FDA's approval, to individuals who are not a part of the research plan for the drug but who need the drug for treatment of the disease or disorder for which the drug is being tested. The sponsor can do this with FDA approval, under current FDA procedures, either at its own request or, on the sponsor's discretion, at the request of an individual physician who wants the drug for a patient.

The compassionate IND mechanism is particularly important for orphan drugs. Often there aren't alternative therapies to the drug being tested; and the testing period is lengthy. In some cases, clinical trials are not actively being conducted.

It is the Committee's understanding that the request for compassionate IND status for most orphan drugs have been from individual physicians. The materials required to be submitted by those physicians are often voluminous and usually held by the sponsoring company. The Committee believes this is not only inefficient, but also fails to attain the broadest possible distribution of orphan drugs to afflicted individuals.

To make this system more efficient, the Committee's bill would require FDA to encourage the sponsor of a designated drug to assume responsibility for adding to the tests individuals who need the drug for treatment. Under this procedure, often called "open protocols," a physician would make a request for the drug directly to the sponsor and the sponsor would have FDA's prior approval to add new individuals at the sponsor's discretion. The sponsor and the physician would, as under current procedures, have to collect all clinical data requested by FDA.



Report of the House Committee on Energy and Commerce on the Orphan Drug Act, 97th Cong. 2nd. Sess., H.R. Rep. No. 97-840, at 11-12 (1982) (emphasis added).

Shortly after the Congress passed the Orphan Drug Act in early 1983, the Food and Drug Administration published a proposed rule in the Federal Register which explicitly recognized the fact that drugs which are in the "investigational" phase are used for "treatment" in many, many circumstances. The regulations which FDA proposed in June, 1983, would expand existing practice in accordance with the statutory directives in the Orphan Drug Act.

No one can deny that orphan drugs and drugs with "treatment" INDs have an "accepted medical use in treatment in the United States." But these drugs do not have an NDA approved by the FDA. Plainly, the interpretation of the CSA urged by agency counsel is inconsistent not only with the plain meaning of the statutory language, not only with the CSA's legislative history, not only with the longstanding interpretation of the FDCA that the FDA does not regulate medical practice, not only with the recognition under the FDCA that states can approve drugs for intrastate marketing, but with the recognition that many drugs become accepted as treatment by the medical community long before an NDA is finally approved.

Furthermore, if a doctor obtains a veterinary drug, or a chemical from a chemical supply house, or an herb from nature and administers it to his or her patient, the Federal Food, Drug and Cosmetic Act does not govern either the propriety or the

"accepted" or "nonaccepted" nature of that medical practice. If a physician were to sell or to market outside of his own practice a drug which was not approved by the FDA, then and only then would the physician come under the jurisdiction of either the relevant State or the Federal Food and Drug Act. Otherwise, it is exclusively the laws of the State in which the physician is practicing and the law of medical malpractice that determine whether the physician is engaging in "accepted medical practice" or, in the case of a drug, whether a drug has an "accepted medical use in treatment."

5. Accepted medical use must be determined on the basis of evidence from the relevant medical community.

"Accepted medical use" means accepted by the medical community. In medical malpractice cases, the courts have recognized that different physicians may have different but equally "acceptable" views. The courts have judged that a method of treatment is acceptable when it is supported by reputable, respectable, medical experts. See, e.g., Baldor v. Rogers, 81 So.2d 658 (Fla. 1955); Young v. United States, 574 F. Supp. 571 (D. Del. 1983); Furey v. Thomas Jefferson University Hosp., 472 A.2d 1083 (Pa. Super. 1984).

One of the leading treatises in the field of medical malpractice has stated the test as follows:

...it appears well settled that if a physician pursues a course followed by a 'respectable minority' of the profession or an established school of thought, he is within the boundaries of permissible conduct. Again, mere differences of methods do not imply deviation from the standard of care if it appears that

each method can reasonably be regarded as acceptable.

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...But whether the minority's practice is truly 'respectable' or 'reputable' is of course a proper subject for expert evidence. The 'respectable minority' doctrine does not mean that any quack, charlatan or crackpot can set himself up as a 'school' and so apply his individual ideas without liability." Prosser, Law of Torts, S 166 (3d ed.).

D. Louisell & H. Williams, Medical Malpractice, S 8.04, at 8.57, 8.56n (1985 ed.). This test is well established in the law, and it is the appropriate test under the CSA.

6. Evidence in the Record With Respect to the Accepted Medical Use of MDMA and Proposed Findings of Fact

a. New Mexico

Dr. George Greer, a psychiatrist in private practice in New Mexico, testified that he used MDMA therapeutically in his private practice. He provided for the record a detailed study that he wrote in 1983 on his clinical observations of the effects of MDMA. GG-14. He testified that it was his professional view that MDMA had therapeutic value for three specific categories of patients; couple counseling; treatment of psychological sequelae of traumatic life events such as rape or child abuse; and patients suffering from chronic pain. Tr. 3, at 43-44.

Three New Mexico psychiatrists -- one on the faculty of the University of New Mexico School of Medicine; one the Medical Director of the Sandoval County Human Services Clinic; and one a board certified psychiatrist working in community mental health and private practice in New Mexico -- all testified that Dr.

Greer's use of MDMA constituted medically accepted use in treatment.

Dr. Rick J. Strassman

Dr. Strassman is a Board-certified psychiatrist on the faculty of the University of New Mexico School of Medicine. He testified:

As a member of [Dr. Greer's] peer review board in New Mexico, I have reviewed his inclusionary and exclusionary criteria for entrance into the protocol, informed consent forms, protocol for administration of MDMA...., the setting in which sessions occur, his results of followup, etc. In my opinion, he has included appropriate safeguards and has not experienced significant adverse reactions to this form of treatment, and that all individuals have experienced significant benefit. Therefore, within the standards of practice set forth by the physicians' community, MDMA has a currently accepted medical use in the hands of a qualified clinician (e.g., Dr. Greer).

Strassman Rebuttal Testimony, at 1-2.

Dr. Rodney A. Houghton:

Based on his experience as a former chief resident in the Department of Psychiatry at the University of New Mexico; as a psychiatrist who had conducted psychiatric clinics in four rural New Mexico counties; as a psychiatrist who had served as an expert on psychiatric care concerning the State Mental Health Programs; as a psychiatrist who had been medical consultant to the Social Security Administration reviewing psychiatric disability cases for the Disability Determination Unit of New Mexico; as a member of the committee reporting to the state agency responsible for funding and maintaining standards for community mental health

programs; and as a clinical assistant professor of the University of New Mexico Department of Psychiatry, as well as a general member of the American Psychiatric Association and the New Mexico Psychiatric Association, Dr. Houghton testified as follows:

In my expert opinion, as one who is familiar with the accepted standards of psychiatric practice in New Mexico, indeed, having established many of those standards for five rural communities and community programs throughout the state, I believe Dr. Greer's use of MDMA is an accepted and safe medical practice. I base this opinion not only on my own experience and what I believe to be acceptable, but also on my conversations with teachers and colleagues about his work.

Houghton Rebuttal Testimony, at 3-5.

Dr. Will L. MacHendrie

Dr. MacHendrie submitted sworn direct testimony as follows:

I am a board certified psychiatrist and for the past five years I have been working in community mental health and private practice in New Mexico.

For the past two and one-half years, I have been on the Peer Review Committee for Dr. George Greer's use of MDMA. In that capacity, I have extensively reviewed his methodology and his results regarding therapeutic use of MDMA. I feel that there is definitely a medically accepted use of this drug in treatment, and that there is acceptable safety for use under medical supervision.

MacHendrie Rebuttal Testimony, at 1.

b. California

Three psychiatrists from the State of California testified about the use of MDMA for therapeutic purposes in a psychiatric practice. Dr. Philip Wolfson, a psychiatrist in private practice in San Francisco, California, and Dr. Joseph Downing, a psychiatrist in private practice in San Francisco,

California, both testified that they had used MDMA therapeutically in their practices in California. Wolfson Direct, at 2-14; Downing Direct, at 407. Both further testified that for appropriate patients with appropriate indications use of MDMA was considered good medical practice and accepted medical practice within their community of physicians. Tr. 2, 146-47.

In addition, Dr. Robert D. Lynch, a psychiatrist in private practice in California who also serves as the statewide psychiatric consultant to the California Department of Rehabilitation, testified that in his professional opinion, use of MDMA by a psychiatrist in his or her practice for particular therapeutic purposes constituted good medical practice. Tr. 2, at 116-17.

c. Other Psychiatric Witnesses

In addition to the four New Mexico psychiatrists and the three California psychiatrists, Drs. Greer, Grinspoon, et al., submitted the testimony of four other psychiatrists -- Dr. Norman Zinberg, a psychiatrist on the faculty of the Harvard Medical School; Dr. Morris Lipton, a psychiatrist who is the Deputy Editor of the American Journal of Psychiatry, the official journal of the American Psychiatric Association; Dr. Lance Wright, a psychiatrist in private practice and on the faculty of the Hahnemann Medical School in Philadelphia who specializes in drug abuse treatment; and Dr. Richard Ingrassi, a psychiatrist who had utilized MDMA in his private practice in Massachusetts. All testified that, in their professional opinion, the administration of MDMA by a psychiatrist in the course of his or her medical practice to

appropriately screened patients for appropriate indications constituted accepted medical use of MDMA. Tr. 7, at 154-57, 167-68; Tr. 5, at 176-77; Tr. 5, at 150-51; Tr. 7, at 57-58

Both Dr. Docherty and Dr. Kleinman, the two psychiatrists called by agency counsel, testified that they personally would not use MDMA in their practices. But neither expressed any view about whether MDMA use by other psychiatrists would be accepted in specific circumstances by reputable psychiatrists. Dr. Docherty did specifically testify that "there is an area where this drug might make sense to be used." Tr. 7, at 140. Dr. Kleinman acknowledged the important role that anecdotal evidence plays in physicians' clinical judgments. Tr. 5, at 179-82. Dr. Kleinman further testified on cross-examination that physicians employ many medical procedures that have not been proven to be safe and effective through double-blind clinical trials, Tr. 5, at 182-89. Dr. Kleinman also testified that the decision to employ a particular medical procedure or treatment, including use of a drug, without the benefit of a controlled clinical trial would in many circumstances constitute acceptable medical practice. Tr. 5, at 184-85, 187-88.

#### 7. Conclusion

The Final Rule of the Administrator made no reference whatsoever to the testimony on accepted medical use. On the basis of the evidence in this record, we submit that the Agency has not met its burden of proving that the careful use of MDMA for appropriately screened patients for appropriate conditions does not constitute accepted medical practice.

C. Accepted Safety Under Medical Supervision

1. Proper Interpretation

The third criterion set out by the Controlled Substances Act for placing a substance in Schedule I is that the substance have no accepted safety for use under medical supervision.

The Administrator's position is that the entire third criterion for Schedule I is superfluous. That is, the Agency argues that this criterion (accepted safety) has precisely the same meaning as the second criterion (accepted medical use): *FDA approved for interstate marketing.* Under elementary rules of statutory construction, this approach must be rejected.

What, then, is the proper interpretation of the third criterion for including a substance in Schedule I?

Plainly, there can be circumstances where reputable physicians are withholding judgment as to whether a drug is effective, and yet believe that it could be safely used under medical supervision. This is not a hypothetical situation. It exists during much of the early clinical testing of many drugs.

Petitioner submits that when reputable physicians conclude that a drug is ready for clinical testing, they have made a judgment that a drug has accepted safety for use under medical supervision. In some cases reputable physicians might judge that a drug could be safely used under medical supervision even though the drug was still undergoing pre-clinical animal testing in the United States under FDA rules. It might be a drug that was in widespread use in another country, for example. Or a drug might have been used intrastate within one state for a substantial



period of time, or it might be made from naturally occurring substances which are known to be safe.

2. Evidence in Accepted Safety of MDMA  
and Proposed Findings of Fact

MDMA is generally administered only once or at most twice -- at the beginning of a course of psychotherapy -- to the patient, and it is administered in the presence of the psychiatrist. There are very few other drugs that are administered with the physician actually present, and there are few other oral medications that are administered only once or at most twice in relatively low doses.

The injection LD-50 (lethal dose) in animals has been established, GG-18; and the oral LD-50 has been estimated. GG-40. The oral doses administered therapeutically are less than one percent of the LD-50 in animals, indicating a very high margin of safety. Clinical trials with humans were reported in 1978 in a monograph, published by the National Institute on Drug Abuse. GG-1, at 12. Dr. Greer has reported on his clinical experiences administering MDMA to patients. GG-14. Dr. Ingrassi has reported on his clinical observations in administering the drug to nearly 100 individuals over 5 years. Ingrassi Direct, at 1-5. Dr. Downing has reported on an informal study of the physiological effects of MDMA on some 20 human volunteers. GG-8.

The overwhelming weight of medical opinion evidence received in this proceeding concurred that sufficient information on MDMA existed to support a judgment by reputable physicians that MDMA was safe to use under medical supervision. (13)

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(13)

It is important to note parenthetically that judgments about the "safety" of a drug are risk/benefit judgments. Every drug on the market as an approved FDA drug has side effects and potential dangers. It is well know, for example, in the field of psychiatry that chronic administration of the major tranquilizers can produce severe and disabling side effects. Yet, on a risk/benefit judgment, the FDA has approved these drugs as "safe," and psychiatrists prescribe these drugs.

D. Restrictions That Would Apply to MDMA Schedule III

The dual effects of the Food, Drug and Cosmetic Act and the Controlled Substances Act would impose severe restrictions on MDMA's availability if it were placed in Schedule III. No one could manufacture MDMA legally without approval from the Drug Enforcement Administration, and no one could obtain it from another source without obtaining an IND from the Food and Drug Administration. A physician could not legally manufacture MDMA even for use in his or her own practice before seeking approval from the DEA by registering to conduct research on it as a Schedule III substance. 21 C.F.R. S 1301.22(b)(5).

The DEA has no obligation to approve the manufacture of MDMA under such circumstances. To obtain MDMA from another source, the physician would have to obtain an IND in order to allow the drug to be shipped to him. In short, placing MDMA in Schedule III would not permit anyone to utilize MDMA in any setting without formal and explicit government approval. It would only remove obstacles to research created by the effects of Schedule I.

IV. Legal Effect of the Recommendations of the  
Department of Health and Human Services

In the Final Rule the Administrator treated as determinative the conclusion of the Assistant Secretary of the Department of Health and Human Services made on June 6, 1984, to the effect that MDMA has no currently accepted medical use in treatment, no accepted safety for use under medical supervision, and a high potential for abuse. (Paragraphs 8 and 91 of the Final Rule). But this determination is binding only if three conditions are satisfied: (i) the original determination by the Secretary of HHS was in accordance with law; (ii) the determination was not arbitrary and capricious; and (iii) all significant scientific and medical evidence relevant to the HHS Secretary's determination introduced in this proceeding was before the HHS Secretary at the time the HHS Secretary's determination was made. In the present case none of these conditions had been satisfied.

A. The June 6, 1984 HHS Transmittal

The record of the HHS consideration of MDMA is as follows:

Accepted Medical Use and Safety

Dr. Edward Tocus, the staff member of the Department of Health and Human Services who reviewed the DEA Control Recommendation proposing that MDMA be placed in Schedule I, testified at the Administrative Law hearing that at the time he reviewed this recommendation and prepared the HHS documents, he believed that the statutory phrase "accepted medical use in treatment in the United States" required that a drug be approved by the Food and Drug Administration for interstate shipment and sale. Tr. 9, at 66-67. Further, he testified that his

understanding of the law was that if HHS concluded that a drug should be scheduled but had not been approved for interstate shipment and sale, "the only alternatives were Schedule I or no schedule at all." Tr. 9, at 67.

Further, Dr. Tocus testified that in formulating its recommendations on MDMA, the Department of HHS did not consult any organization of medical professionals. Tr. 7, at 118. Dr. Tocus further testified that the Department of HHS did not refer the issue to the FDA's Drug Abuse Advisory Committee. Tr. 98 at 117. Yet Dr. Tocus also testified that he had been told that there was some therapeutic interest in MDMA. Id. In addition, Dr. George Greer had communicated his interest in MDMA both to the Assistant Secretary for Health and to the FDA. Tr. 3 at 14; letter of George Greer to DEA Administrator, August 22, 1984.

#### Potential for Abuse

Dr. Tocus requested comments on the DEA proposal to schedule MDMA and Schedule I from the National Institute on Drug Abuse -- as he was required to do by HHS departmental procedures. Tr. 9, at 45-46. The National Institute on Drug Abuse responded in memorandum form. GG-55. The NIDA memorandum notes that "the direct evidence that MDMA has any abuse potential in animals is not substantiated, based on the data DEA provided." That memorandum concludes that "NIDA does not have any objection to placing MDMA under Schedule I of the CSA." but NIDA reaches no conclusion that MDMA has a "high" potential for abuse. GG-55.

The NIDA memorandum was not forwarded to the Commissioner of the FDA and was not forwarded to the Assistant

Secretary for Health. Tr. 9, at 46. None of the underlying documents prepared at the Department of HHS ever reached the conclusion that MDMA had a "high" potential for abuse.

The Commissioner of Food and Drugs forwarded the package to the Assistant Secretary of Health with the conclusion that "MDMA has significant potential for abuse." No mention was made of any higher level of abuse potential. GG-54.

HHS Action is Not Valid

Petitioner respectfully submits that HHS's review and analysis did not constitute legally valid agency action.

First, HHS applied the wrong law with respect to the interpretation of "accepted medical use in treatment." [This legal error by HHS alone requires that this matter be referred back to HHS for a reexamination of the evidence and for a new determination. (14)]

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(14)

See NLRB v. Pipefitters Union, 429 U.S. 507, 522 n.9 (1977). See also Prill v. NLRB, 755 F. 2d 941, 947-48 (D.C. Cir. 1985), appeal pending (agency decision cannot be sustained when based on an erroneous view of the law); United States Customs Service v. FLRA, 739 F.2d 829 (2d Cir. 1984) (agency order cannot stand if the underlying standard upon which it relied is not in accordance with law). Baber v. Schweiker, 539 F. Supp. 993, 995-96 (D.D.C. 1982) (deference to agency expertise does not apply to erroneous conclusions of law, which require reversal of agency's decision).

Second, the FDA failed to consider "all relevant factors" by failing to consult with relevant medical organizations. (15)

(15)

An agency is under a clear obligation to examine the relevant data prior to issuing an agency rule or decision. Failure to consider an important aspect of the problem will render an agency action arbitrary and capricious. Motor Vehicle Manufs. Ass'n v. State Farm Mutal Automobile Insur. Co., 463 U.S. 29, 42-43 (1983). See also Electricity Consumers Resource Council v. FERC, 747 F.2d 1511, 1518 (D.C. Cir. 1984) (order vacated where agency failing to consider relevant factors and to articulate a reasonable basis for its decision); Asarco, Inc. v. U.S. EPA, 616 F.2d 1153 (9th Cir. 1980) (court went outside agency record to evaluate properly whether agency acted arbitrarily and capriciously by failed to consider all relevant factors and found agency inquiry inadequate and remanded the matter to the agency); RSR Corp. v. EPA, 528 F. Supp. 1251 (N.D. Tex. 1984) (agency's failure to consider important aspects of problem rendered its decision arbitrary and capricious).

This failure demonstrates the arbitrary and capricious nature of the agency's decision, particularly in light of the fact that Dr. Tocus was on notice that there might be some therapeutic interest in MDMA. Third, the responsible official, the Assistant Secretary for Health, wholly failed to exercise the discretion that he was obligated to exercise under the Act. This failure developed because HHS staff <sup>wrongly</sup> ~~improperly~~ believed that HHS did not have discretion to consider placement of MDMA in any schedule other than Schedule I if there was not an outstanding approved NDA for the drug. (16)

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Finally, Petitioner respectfully submits that the conclusion contained in the June 6, 1984 transmittal on high potential for abuse is arbitrary and capricious because it does not explain how the Assistant Secretary for Health reached a conclusion which differed from that of the Commissioner of Food and Drugs, and which had no support in the underlying analyses

prepared at HHS. (17)

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(16)

See, e.g., Bethlehem Steel Corp. v. EPA, 638 F. 2d 994, 1004 (7th Cir. 1980) (agency decision's failure to demonstrate and reflect the exercise by the administrator of "reasoned discretion" required remand to the agency).

(17)

An agency must articulate a satisfactory explanation for its actions, including a rational connection between the facts found and the choices made. Motor Vehicle Manufs. Ass'n v. State Farm Mutal Automobile Insur. Co, 463 U.S. 29, 43 (1983). Agency action is arbitrary and capricious if the agency offers an explanation that runs counter to the evidence before the agency. Id.

Furthermore, the Department of Health and Human Services did not follow its own procedures, which require solicitation of evaluation and recommendations from the Drug Abuse Advisory Committee.

Drug Enforcement Administration, Drug Enforcement, Spring, 1975, at 34.

The Charter of the Committee, signed by the Secretary of HHS, reads as follows:

The Committee advises the Commissioner of Food and Drugs regarding the scientific and medical evaluation of all information gathered by the Department of Health and Human Services and the Department of Justice with regard to safety, efficacy, and abuse potential of drugs or other substances and recommends actions to be taken by the Department of Health and Human Services with regard to marketing, investigation, and control of such drugs or other substances. GG-62.

This reflects the obligation of the Commissioner to seek the advice of the Advisory Committee on all drug abuse matters.

It is elementary administrative Law that an agency is obligated to follow its own procedures. (18)

(18)

See, e.g., Morton v. Ruiz, 415 U.S. 199, 235 (1974) (it

is incumbent upon agencies to follow their own procedures); Oglala Sioux Tribe v. Andrus, 603 F.2d 707 (8th Cir. 1979) (agency's failure to follow its own procedure requires remand to agency). Petitioner respectfully submits that failure to do so represents arbitrary and capricious agency conduct.

In short, the June 6, 1984 transmittal is so inadequate that it cannot be considered to be the "scientific and medical evaluation and recommendations" required by Section 811 of the CSA. As in NORML v. DEA, 559 F.2d 735 (D.C. Cir. 1977), the DEA cannot validly act on the basis of an invalid HHS referral. 559 F.2d, at 747-50.

B. New, Significant Evidence in Record

Even if the June, 1984 transmittal were not obviously arbitrary and capricious, that transmittal could not, in the present circumstances, be held to be binding on any issue.

During the Administrative Law hearing, very substantial amounts of evidence relevant to the three statutory criteria (medical use, medical safety, potential for abuse), were received into evidence. The Administrator of DEA must make his decision on scheduling MDMA on the basis of the entire record in this proceeding. To do otherwise would violate the requirements that apply to agency decision-making under the Administrative Procedure Act. (19)

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(19) See 5 U.S.C. S 706(2).

The Administrator cannot ignore vast amounts of evidence on scientific and medical issues directly relevant to his decision on the ground that the June 6, 1984 transmittal is binding. This



position would make his action plainly arbitrary and capricious and not based on substantial evidence.

C. Required Action

(I have not tried to rewrite pages 108 and the first half of 109 of the brief dealing with ~~the~~ required action, because I do not know how the new legal situation has changed the definition of the required action. JB)

V. THE LEGAL EFFECT OF THE INTERNATIONAL  
SCHEDULING OF MDMA

As reflected by the record in this proceeding, the Expert Committee on Drug Dependence of the World Health Organization has recommended that MDMA be scheduled in Schedule I internationally. A.-B20. MDMA may be so scheduled at some time in the coming months (*has been?*)

For a drug that has not been approved for interstate shipment and sale by the Food and Drug Administration, such as MDMA, placement in Schedule III would allow the DEA to fully satisfy the obligations of the United States under Schedule I of the Convention of Psychotropic Substances of 1971. The combined effect of the Food, Drug and Cosmetic Act and the Controlled Substances Act satisfies the requirements of Article 7 of the Convention of Psychotropic Substances. The government through the DEA and the FDA would have total control over who can manufacture MDMA and in what amounts, who can possess it and in what ways, who

can distribute <sup>it</sup> ~~and~~, to whom, and for what purposes it ~~can be~~  
~~distributed~~. Under these circumstances there is no doubt that the  
DEA and FDA can ~~exercise and~~ fulfill the obligations of the  
Convention of Psychotropic Substances by placing MDMA in Schedule  
III.

#### VI. CONCLUSION

For the reasons set out above, Petitioner respectfully  
submits that MDMA should be placed in Schedule III under the  
Controlled Substances Act.