DEWEY, BALLANTINE, BUSHBY, PALMER & WOOD
1775 PENNSYLVANIA AVENUE, N. W.
WASHINGTON, D. C. 20006

TELEPHONE: (202) 862-1000
TELECOPIER: (202) 862-1095
TELEX: 897070

140 BROADWAY, NEW YORK, N.Y. 10005
101 PARK AVENUE, NEW YORK, N. Y. 10178
TELEPHONE: (212) 820-1100
TELEX: 961289 (IF BUSY 12-6825)
TELECOPIER: (212) 820-1403

45, AVENUE GEORGE V
75008 PARIS, FRANCE
TELEPHONE: 720. 85. 21
TELEX: 842 620297

CABLE: DEWBALAW

JOSEPH A. CALIFANO, JR.
PHILIP W. BUCHEN
O. NILE BELL
FENTON J. BURKE*
ALAN WM. WOLFF
FELIX B. LAUGHLIN
CHARLES A. SEVERS, III
JOHN M. SAMUELS*
RICHARD COTTON
LAWRENCE F. O'BRIEN, III
W. CLARK McFADDEN II
GERALD M. ROSBERG
HAMILTON P. FOX, III
JOHN J. SALMON
R. MICHAEL GADBAW
MICHAEL H. STEIN
MYLES V. LYNK
RESIDENT PARTNERS

*MEMBER N. Y. BAR: NOT ADMITTED D. C.

January 17, 1986

MEMORANDUM FOR INTERESTED PARTIES

Re: Brief on MDMA Scheduling

I enclose a copy of the brief that we filed on behalf of Dr. Lester Grinspoon, Dr. George Greer, Professor James Bakalar, and Professor Tom Roberts in the DEA Proceeding which is considering the appropriate scheduling of MDMA under the Controlled Substances Act.

As most of you know, this brief represents the culmination of a major effort by many people, which included the submission of the written direct testimony of 16 witnesses (12 of whom are psychiatrists), the submission of 62 documentary exhibits, participation in 8 cross-examination sessions which generated more than 1,000 pages of transcripts, and submission of numerous other written materials in the course of the DEA proceeding. Many of you played important parts in this effort, and I therefore thought you would be interested to see the enclosed brief.

If you have any comments or thoughts on the brief (if you have the endurance to read it), I would be interested in hearing from you. There is likely to be an oral argument before the Administrative Law Judge in late February, and any comments would assist me in preparing for it.

I would expect that the Administrative Law Judge will issue a decision no earlier than late March or April, and it might be considerably later than that.

Regards to you all.

Richard Cotton

Enclosure

UNITED STATES DEPARTMENT OF JUSTICE

Drug Enforcement Administration

In The Matter of	)	
	)	Docket No. 84-48
MDMA SCHEDULING	)	
	)	

BRIEF, INCLUDING PROPOSED FINDINGS OF FACT AND CONCLUSIONS OF LAW, ON BEHALF OF DRS. GREER AND GRINSPOON, PROFESSORS BAKALAR AND ROBERTS

Richard Cotton
Dewey, Ballantine, Bushby,
Palmer & Wood
1775 Pennsylvania Avenue, N.W.
Washington, D.C. 20006
(202) 862-1004

Attorney for Drs. Greer and Grinspoon, Professors Bakalar and Roberts

January 15, 1986

TABLE OF CONTENTS

UNITED STATES DEPARTMENT OF JUSTICE

Drug Enforcement Administration

In The Matter of	)	
	)	Docket No. 84-88
MDMA SCHEDULING	)	

BRIEF ON BEHALF OF DRS. GREER AND GRINSPOON, PROFESSORS BAKALAR AND ROBERTS

I. INTRODUCTION AND SUMMARY

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

- "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 that whole development. . . . it [MDMA] represents a drug which could potentially have an impact on the psychotherapeutic process itself."

- "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."

- "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 behav-

> ior, the degree to which two people form some kind of a 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.[1]

> "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 on 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

---

[1] In citing the transcripts in this proceeding and the documentary exhibits, this Brief will use the same citation form established by Agency counsel in their Brief.

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 in 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 the present proceeding 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 -- such as is the case with MDMA -- those obstacles loom even larger. If 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 -- important countervailing social policies may justify the obstacles and disincentives to research that are created.

But, if a drug such as MDMA does not meet the requirements established by the Controlled Substances Act for placement in Schedule I and is erroneously placed in Schedule I, then society will pay a terrible and unnecessary price. Research that could lead to significant medical advances in the field of psychotherapy will be stymied and stifled wholly unnecessarily -- for no countervailing social gain.

Regrettably, that would be the consequence if the position urged by Agency counsel were adopted in this case. We urge the Administrative Law Judge and the Administrator not to follow that path. We submit that the relevant provisions of the Controlled Substances Act should not be interpreted in a strained fashion: clear statutory language and the explicit intent of the Congress must prevail over interpretations motivated by ease of administration. We urge the Administrative Law Judge and the Administrator to recognize that the overwhelming evidence in this case demonstrates that while MDMA should be controlled under the Controlled Substances Act, it should not be placed in Schedule I. We submit that the record in this case clearly establishes that MDMA should be placed in Schedule III of the Controlled Substances Act.

In summary, Drs. Greer, Grinspoon, et al., take the following positions on the issues outlined by the Administrative Law Judge in a Memorandum to the Parties dated March 29, 1985.

- The determination of "currently accepted medical use in treatment in the United States" must be made by reference to the professional judgment of the medical community. The proper interpretation of this phrase was stated by Michael Sonnenreich, then 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 as to whether or not the drug has medical use or it doesn't." 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.

- The statutory phrase "accepted safety for use under medical supervision" is a determination to be made on the basis of expert opinion from the medical community based on a review of currently known scientific information about a drug. The proper interpretation of this criterion is best understood by contrasting the statutory phrase "accepted safety" with the previous criterion of "accepted use." The criterion of "accepted use in medical treatment" requires a medical judgment about <u>both</u> safety <u>and</u> effectiveness. The criterion of "accepted safety for use under medical supervision" focuses exclusively on safety. A drug which has no accepted use because its effectiveness has not yet been accepted may still have "accepted safety."

• The determination by the Secretary of Health and Human Services (HHS) whether a substance has an accepted medical use or accepted safety under medical supervision is binding on the Attorney General 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 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. Greer, Grinspoon, 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.

- Based on the evidence in the record, the Agency has not sustained its burden of proving that MDMA has no accepted medical use in treatment in the United States. Nor has the Agency sustained 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 on the part of 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 review committee, would constitute currently accepted medical use in treatment in the United States, and would constitute accepted safety for use under medical supervision.

- The record demonstrates that MDMA should be scheduled in Schedule III under the Controlled Substances Act. The evidence in the record demonstrates that MDMA does have a potential for abuse, but the record further demonstrates that MDMA's potential for abuse is <u>less than</u> a high potential. Further, the current record establishes that MDMA has an accepted medical use in treatment in the United States. Even if the Administrative Law Judge 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. Drs. Greer, Grinspoon, et al., have urged that the proper interpretation of the Controlled Substances Act is that a substance with less than a high potential for abuse and no accepted medical use in the United States 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 interpretation as one of two alternative interpretations recommended to the Administrator.

The basis for our conclusions as to each of the above issues is set out in more detail below.

II. ADVERSE EFFECTS ON RESEARCH OF PLACEMENT IN SCHEDULE I

The record in this case leaves no doubt whatsoever that the placement of a drug in Schedule I in fact strongly discourages medical research on that drug.

First, placing a drug in Schedule I creates bureaucratic delays in getting approval from the government to proceed with such 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. For research with drugs in other Schedules, the researcher must submit an IND application to the FDA but may proceed with the research in the event that the FDA does not disapprove his application within 30 days. Tr. 8, at 65-66.

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. §§ 1301.22(a)(8), 1301.33, 1301.42. Testimony in this case establishes that two researchers who had applied to the DEA two to three months prior to the hearings in this case for registrations to do Schedule I research on MDMA had still not received approval from the DEA at the time of the hearings. Tr. 8, at 94. Moreover, the official in charge of processing their applications testified that there was no time limit that requires the DEA to act on an application within any period of time. The official 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 on Schedule II through V drugs. As the clinical research director for Hoffmann-LaRoche testified, even though these matters are "only a question of good work, time and money," at some point these increased requirements become "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, it is clear from the record in this case that, wholly apart from the additional requirements imposed by the Government for carrying out research on Schedule I drugs, the placement of a drug in Schedule I has strongly adverse effects outside the government. The criteria for placing a drug in Schedule I are so negative (i.e., high potential for abuse, no accepted medical use and no accepted safety even under medical supervision) that they raise grave concern on the part of both researchers and volunteers in clinical experiments about even being associated with such a drug. In addition, there is a guilt-by-association effect on a drug that is placed in a Schedule that includes heroin and LSD.

In this connection, it is interesting to note that 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 that the DEA should not have the authority to move a drug out of Schedule I to any schedule other than Schedule II:

> Mr. Rogers. So why should we put a prohibition in the law saying you can't remove I to III and IV?
>
> Mr. Sonnenreich. Because these specific drugs in Schedule I have certain emotionalism around them. We felt that if Congress saw fit to remove those, that would be one thing, but it should not be in the hands of any administrative official to do it automatically.

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., 2d Sess. 707 (1970) (hereafter "House Hearings").

The combined effect on research of the added bureaucratic requirements, the negative perception of the criteria associated with Schedule I, and the effect of being grouped with heroin and LSD is devastating. 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 would strongly discourage both investigators and volunteers from participating in clinical studies. Tr. 8, at 102. It was her strongly held view that, in light of these difficulties, 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. The Hoffmann-LaRoche clinical research director further testified that 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 much more difficult to obtain approvals for research from institutional review boards given the extremely negative perception of Schedule I substances. Lipton, Tr. 7, at 151, 163-64. For example, one researcher experienced in doing research with Schedule I drugs recently expressed his frustrations with the obstacles placed in the way of doing research on such

drugs: "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 actual, empirically confirmed results of these effects. 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. His testimony and writing reflect the fact that in the 1940s, 1950s and 1960s, extensive research was taking place on many Schedule I drugs in the area of psychiatry research. GG-16; Tr. 6, at 65. He testified that his review of the literature at the present time indicates that virtually no research is currently being carried out. 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.

Finally, there is direct testimony in the record of two different research projects on MDMA that were adversely affected by the emergency placement of MDMA into Schedule I. Dr. Robert Lynch, statewide psychiatrist consultant to the California Department of Rehabilitation, testified that he was interested in carrying out a research project on MDMA involving clients of the California Depart-

ment of Rehabilitation. Dr. Lynch testified that he had begun steps to carry out such a research project, including obtaining approval from the director of the department and writing for further information to the Food and Drug Administration. Tr. 2, at 100. But, Dr. Lynch testified that the placement of MDMA in Schedule I had caused him to rethink whether he could carry the research project out and that its future was in doubt. Tr. 2, at 100, 103-4.

Dr. Grinspoon testified that a group of researchers at Harvard Medical School had been planning a research project on MDMA. He testified that the emergency placement of MDMA in Schedule I had cast a "pall" over the project and that he was now uncertain whether that project would proceed. Tr. 6, at 90-91.

In sum, if MDMA is to be placed permanently in Schedule I, that decision must be made with a full understanding of its consequences. Those consequences will simply and undeniably be that research into MDMA's therapeutic potential will be discouraged, stifled, and made infinitely more difficult than if it were in a lower schedule. If MDMA -- evaluated objectively and fairly -- does not meet the requirements for placement on 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 a Schedule under the CSA, a finding must be made that the substance has a "potential for abuse." Then the substance's 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. § 811(c), and the legislative history of the Controlled Substances Act do provide important additional guidance.

1. Eight Factors To Be Considered

The provisions of 21 U.S.C. § 811(c) mandate that the DEA take into account eight specified 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. § 811(c) (emphasis added).

Thus, the DEA must take into account all of the above factors in making a determination with respect to potential for abuse and relative potential for abuse. The most important lesson that 21 U.S.C. § 811(c) teaches with respect to the current proceeding is that the DEA is not free to make a determination concerning a drug's relative potential for abuse without considering the history and current pattern of abuse of that drug relative to experience with other controlled drugs; the scope, duration, and significance of abuse of a particular drug relative to that of other drugs; the risk to the public health posed by abuse of a particular drug relative to that of other drugs; and a drug's psychic or physiological dependence liability relative to that of other Scheduled drugs.

In short, we submit that the provisions of 21 U.S.C. § 811(c) mean that the DEA may not make a determination of relative potential for abuse based exclusively on theoretical similarities between drugs based on chemical

structure or pharmacological effects. Rather, the DEA is mandated by the statute to take into account the actual experience "on the streets" with the drug when making a determination of its relative potential for abuse. As we shall see, the Act's legislative history confirms this interpretation. See infra pp. 30 to 33.

2. Legislative History on"Potential for Abuse"

The legislative history of the CSA provides very important guidance in defining the term "potential for abuse." In order to discuss the legislative history of the Controlled Substances Act, it is necessary to describe briefly the evolution of the Act. The Administration originally submitted a bill that was introduced in both the House and the Senate. The Senate passed S. 3246, The Controlled Dangerous Substances Act of 1969, on January 28, 1970. 116 Cong. Rec. S1671 (1970). The Senate-passed bill was essentially the Administration bill.

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. Subsequently, the House Subcommittee drafted a clean bill amending in many important particulars both the Administration and Senate versions and introduced the Subcommittee's "clean" bill as Titles I and II of H.R. 18583. 116 Cong. Rec. H332987 (September 23, 1970). It was the Subcommittee's version of the bill that 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 in enacting various provisions of the CSA.

a. House Committee Report

With respect to the definition of the term "potential for abuse," the House report provides some guidance on defining that term. Specifically, the House report refers to the definition that existed in regulations promulgated under the sections of the Federal Food, Drug, and Cosmetic Act which were the predecessor statutes to the Controlled Substances Act.[2]

---

[2] 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 are 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 are 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

(Footnote continued)

Most significantly, however, the House report then goes on to make the following critically important observations:

> (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). The Committee also noted, of course, that it did not intend the agency "to wait until a number of lives have been destroyed or substantial problems have already arisen before designating a drug as subject to controls of the bill." Id.

(Footnote 2 continued from previous page)

> (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 diversions from legitimate channels, 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 1), at 34 (1970) (hereafter "House Report").

(2) The Committee went further in explaining what it meant by declaring that "a substantial potential" had to exist 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 despite the fact that tens of millions of dosage units of that drug are legitimately used in the same time period.

House Report, at 35.

(3) The Committee also observed that "misuse of a drug in suicides and attempted suicides, as well as injuries resulting from unsupervised use, are regarded as indicative of a drug's potential for abuse."

House Report, at 35.

The single most important fact to be noted about these observations by the House Committee is that they apply to the question of whether <u>any</u> potential for abuse has been established sufficient to warrant control under the Controlled Substances Act. In other words, the above excerpts from the House Committee Report are seeking to provide guidance on the <u>minimum</u> potential for abuse that must be identified before a substance is included even in the <u>lowest</u> schedule of the Act, <u>i.e.</u>, Schedule V. In the excerpts quoted above, the Committee Report was attempting to define the level of abuse that would warrant any control whatsoever of a drug. If a drug did not attain the level of potential

of abuse described in the House Report, the drug would then go uncontrolled.

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." Only on the basis of this evidence would any control at all -- i.e., Schedule V -- be warranted.

It follows that, in order to move a substance into Schedule IV, the government would have to show a more substantial level of abuse than described by the Committee as the minimum necessary for any control at all. In order to move a substance to Schedule III, the Agency would have to show further evidence of an even higher potential for abuse. And finally, in order to move a substance into either Schedule I or II -- as having a "high" potential for abuse -- the government would have to make a showing three orders of magnitude above the level of abuse potential described in the House Committee's report.

b. Evolution of Five Schedules

Further light is shed on congressional intent with respect to the relative levels of "potential for abuse" required to place drugs into the different Schedules by

following the evolution of the five Schedules which now appear in 21 U.S.C. § 812(b). The bill originally submitted by the Administration and the bill that was 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, however, creates five schedules for the first time, 116 Cong. Rec. H33607 (September 24, 1970).

Schedules I and II in the Senate bill are essentially the same as Schedules I and II established by the

---

[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).

House bill. However, Schedule III in the Senate bill was divided by the House Committee into two schedules -- namely, Schedule III and Schedule IV. It is the division of Schedule III as it existed in the original Administration version and in the Senate bill into two separate schedules in the House bill that sheds light on the nature of the potential for abuse necessary to place substances in various schedules.

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 sufficiently high levels of narcotics that the compounds could be highly addictive; minor tranquilizers; and mild sleeping preparations.

When the Senate bill went over to the House, the House Subcommittee on Public Health and Welfare heard bitter criticism of the breadth of the Schedule III created by the Senate bill and the Administration bill. For example, Dr. Henry Brill of the AMA Committee on Alcoholism and Drug Dependence testified 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. . . . We believe that the drugs now grouped under Schedule III should be divided into at least two distinct classifications with the more hazardous and less useful substances clearly separated from the less hazardous and more useful ones, so as to permit control techniques appropriate to each.

House Hearings, at 231-32.

Professor Neil Chayet, a lawyer then serving on an advisory committee to the National Institute of Mental Health and representing a group of scientists, physicians and legal experts, testified:

> It is difficult to fathom how drugs such as chloral hydrate, chlordiazepoxide (Librium) and diazepam (Valium) can be classed in the same Schedule with methamphetamines, one of the most abused and deadly of substances.

House Hearings, at 313.

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

> The purpose of this supplemental statement is to review the evidence introduced before this committee. We believe that this evidence, particularly the cogent testimony of medical and scientific witnesses, clearly establishes the need to revise the four schedules in the Proposed Administration Bill.
>
> 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.

In addition to these criticisms of the breadth of the Schedule III classification in the Senate Bill and in the Administration Bill, 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 before the House Subcommittee on Public Health and Welfare describing the widespread extent of abuse, illegal sales and adverse health effects of amphetamines and methamphetamine. House Hearings, at 579-594.

Indeed, Representative Pepper even introduced into the record the hearings that his Select Committee had held on "Crime in America -- Why 8 Billion Amphetamines?" House Hearings, at 595.

In other testimony, 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 about the widespread extent of abuse of barbiturates. He testified that

> "... barbiturates are the No. 1 method of committing suicide by chemical means. Suicidal or accidental deaths due to barbiturates exceed 3,000 a year in the United States. Many more are rescued from overdosages in hospitals. 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. . . . The trend seems to be that increased numbers of people are abusing barbiturates, with a tendency to move to larger amounts of more harmful agents."

(House Hearings, at 177-179.

Having received this evidence -- (1) facts and figures about the extraordinary and widespread extent of abuse and concomitant dangers of amphetamines, barbiturates, and methamphetamines, and (2) expert opinion that Schedule III in the Administration and Senate bills was too broad, the House Subcommittee acted. The Subcommittee split the Schedule III in the Administration and Senate bills into two separate schedules. 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 sleeping preparations. The original Schedule IV of the Senate and Administration bills became Schedule V in the House bill. The Schedules contained in the House's bill were then enacted into the Controlled Substances Act.

What this legislative history helps us to understand is that Schedule III was intended to include drugs with enormous "potential for abuse" which had been demonstrated by actual widespread abuse. Indeed, amphetamines were so notoriously and widely abused that a major effort on the floor of the House was made by Representative Pepper to move amphetamines out of Schedule III and into II. See 116 Cong. Rec. H33603 - H33609. Two primary elements are instructive about the floor debate. First, the reason that Congressman Pepper and most of his supporters advanced for

moving amphetamines from Schedule III to II was because they wanted, in the words of Rep. Pepper, "to subject the dangerous drugs to a quota system of control." 116 Cong. Rec. H33609.

Congressman Pepper did not argue that amphetamines did not meet the criteria for being placed in Schedule III. Rather, he argued that, in view of the massive diversion of amphetamines from legal manufacturers into illicit channels, it was important that Congress mandate they be subject to the quota provisions which applied to Schedule II drugs and did not apply to Schedule III drugs. Thus even those who supported moving amphetamines from Schedule III to Schedule II appeared to accept the fact that the highly abused amphetamines could, under the criteria set out for Schedule III, properly be classified as Schedule III drugs. It is also highly instructive to note 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 was the second-ranking Democrat on the Subcommittee that drafted the bill. (Subcommittee Chairman Jarman specifically noted on the House floor that Rep. Rogers "contributed in such a major manner to the development of this legislation and its presentation to the House." 116 Cong. Rec. H33303 (September 24, 1970)). Rep. Rogers responded to Rep. Pepper's proposed amendment as follows:

> Mr. Rogers of Florida. That is exactly what the bill provides. If the able gentleman would permit me to explain this, we have directed that the Attorney General control these drugs [amphetamines and methamphetamine]. This is a controlled drug. It is not in Schedule II. It is in Schedule III. The reason it 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 that is where it should be. That is the testimony and this committee spent almost 50 sessions going into it. We have medical and scientific decisions as to where it should be. There is no department of the Government that is rougher on the abuser and that is more for law and order than the Department of Justice. Do you know what they said? They say it should not be done in this legislative way -- just dump everything in a schedule, even though the scientists and the department have determined amphetamines should be in Schedule III.

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

In further response to Congressman Pepper's amendment, Representative Carter, the ranking Republican member on the House Subcommittee that drafted the bill, spoke in opposition to moving amphetamines from Schedule III to II as follows:

> Mr. Carter. Mr. Chairman, I want to say to the distinguished gentleman in the well that no one is more interested in controlling drugs than we. If the gentleman would look at Schedule III, he will find that 'amphetamine, its salts, optical isomers, and salts of its optical isomers' and 'methylphenidate,' and all the drugs which the gentleman has mentioned are there.
>
> Under the bill which we have drawn, from the time this drug is manufactured and is sold and is transported and goes to the drug store, it must be completely

> controlled and accounted for. There is very little chance of diversion under this bill. We are taking care of the legislation which the gentleman wants, right here in the bill.

116 Cong. Rec. H33613 (Sept. 24, 1970).

The House then defeated Rep. Pepper's amendment, voting to leave amphetamines in Schedule III. 116 Cong. Rec. H33618.[4]

In sum, the legislative history plainly indicates that the "potential for abuse" that must be demonstrated in order to place a drug into Schedule III was very, very substantial. The House Subcommittee made a deliberate decision to place amphetamines and barbiturates in Schedule III based on extensive documentation of enormous abuse. Schedule III was differentiated from Schedule IV which was to contain drugs of significant but lesser potential for abuse, such as the minor tranquilizers. But Schedule III was also differentiated from Schedule I and Schedule II which, under the House Committee's bill, required the further showing of a "high" potential for abuse.

---

[4] Drs. Grinspoon, Greer, et al., recognize 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 affect the intent of the Congress as to the nature of the abuse potential appropriate for drugs in Schedule III. It is clear that the Congress intended the DEA to exercise the authority given to it to move drugs from one schedule to another when facts and circumstances so warranted. But the fact that the DEA has exercised that authority does not rewrite history and change the nature of the abuse potential that Congress contemplated when it created Schedule III.

c. Conclusions to be Drawn

Thus, from the legislative history, we do in fact gain an understanding of the continuum of "potential for abuse" reflected in the Schedules established under the Controlled Substances Act. Schedule V was to be 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. Such a drug should have either a demonstrated track record or the clear potential to involve the diversion or consumption of "several hundred thousand dosage units." Then Schedule IV would involve drugs as to which there was a higher potential for abuse such as the minor tranquilizers. The House Committee and the Congress recognized that there was widespread abuse of minor tranquilizers such as Valium and Librium at the time it created Schedule IV for the minor tranquilizers. See 116 Cong. Rec. S1683-89 (Jan. 28, 1970); 116 Cong. Rec. S.35516-23 (Oct. 7, 1970).

Then, 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.

Drs. Greer, Grinspoon, et al., submit that it is this continuum which the Administrative Law Judge and 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

It is obvious, of course, from the mere existence of varying degrees of abuse potential required by each of the various Schedules that the findings to be made by the Agency must be based on evidence of relative potential for abuse. This need to prove relative potential for abuse was appreciated from the outset. Mr. Sonnenreich specifically testified as follows:

> Mr. Sonnenreich . . . and then there is the second decision that has to be made . . . as to not only that it should be controlled but which Schedule it should be controlled in. This involves decisions such as whether or not it has currently accepted medical use in the United States, whether or not in terms of relativity its relative potential for abuse is for Schedule II, for Schedule III, or Schedule IV.

House Hearings, at 141 (emphasis added).

Moreover, for drugs that are "on the street," the Agency must prove the relative potential for abuse of individual drugs based on relative levels of actual abuse. Again this subject is illuminated by testimony of Mr. Sonnenreich before the House Subcommittee:

> 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. Rogers. Now I would like for you to tell us

on your schedules [how] you determine what drugs fall within which schedule . . . Start with schedule I on page 12. It is actual or relative potential for abuse.

* * *

Mr. Sonnenreich. High potential for abuse would be considered pretty much as a law enforcement provision. We would have to go out and see what is happening. . . .

Mr. Rogers. What about the characteristics of the drugs? Would that be a consideration?

Mr. Sonnenreich. Almost all of the drugs you have in the narcotic category of schedule I are known already in terms of their addictive quality and things of this nature, but what we are talking about here is their high potential of abuse.

Mr. Rogers. No, this is already determined because we are classifying these drugs as such. This is for new substances that you may classify.

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 out diversion.

Mr. Rogers. On Schedule II on page 18, 1, a high potential for abuse. We have discussed that.

Mr. Sonnenreich. No, sir, it is different here. Now you are talking about something else. You are talking about a drug that is probably commercially available, a drug that has medical use that is on the street and in this case the criteria and the triggers become far more a law enforcement decision and the legal decision as to whether or not it can go in there because you are dealing with a commercial product to begin with.

> You have to demonstrate diversion, you have to show that it is being prescribed by doctors and being used outside the prescription modality, which is a law enforcement function.
>
> Mr. Rogers. First of all, you have to determine whether the characteristics of the drug have any effect for abuse.
>
> 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. Then 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).

We submit that two propositions are evident from this legislative history. First, in order to properly classify a substance in one of the five schedules in the Controlled Substances Act according to its relative potential for abuse, there must be evidence of a substance's relative potential for abuse.

Second, it is clear from the exchange between Mr. Sonnenreich and Rep. Rogers 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 with the drug compared to the abuse of other drugs.

In short, consistent with common sense, as reflected by the above quoted legislative history, it is clear that the intent of the drafters -- both in the Administration and on the Committee -- was that determinations about

relative abuse potential were to be made on the basis of comparative evidence about the nature of the actual abuse taking place on the street.

4. Case Law

As far as counsel for Drs. Greer, Grinspoon, et al., 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 discussed the nature of the determination under the CSA's predecessor statute for a finding that a drug had "a potential for abuse," in order for the drug to be controlled at all under the 1965 amendments to the Federal Food, Drug and Cosmetic Act. See Carter-Wallace, Inc. v. Gardner, 417 F.2d 1086 (4th Cir. 1969), cert. denied, 398 U.S. 938 (1970); Hoffmann-LaRoche, Inc. v. Kleindienst, 478 F.2d 1 (3d Cir. 1973).

Both of these cases analyzed, to some extent, the meaning of the phrase "a potential for abuse." Both the Third Circuit and the Fourth Circuit agreed the phrase required the agency to examine future or potential abuse. But, the striking aspect of both opinions is the extent to which the 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; that 11% of the criminal convictions for illegal sales of prescription drugs during the decade 1956-66 had involved meprobamate; that a significant number of alcoholics use the drug. The Fourth Circuit recited all of this evidence in coming to the conclusion that meprobamate had "a potential for abuse." 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 there demonstrated extensive actual abuse of Librium and Valium. 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; that individuals had attempted unsuccessfully to discontinue taking Librium and Valium when a dependency had developed and had gone to excessive lengths to maintain the supply of the two drugs; and that Librium-Valium withdrawal persisted over a longer period of time than barbiturate withdrawal. In short, the court looked extensively to evidence of actual experience with both Librium and Valium before reaching a determination concern-

ing "a potential for abuse." 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 in the record with respect to the nature of the abuse potential of MDMA. What is critical here is the relative potential for abuse of MDMA, for only a determination about the relative potential for abuse can determine the Schedule into which MDMA should be placed.

Agency counsel has the burden of proof in seeking to place MDMA into Schedule I. 21 C.F.R. § 1316.56. Therefore, the initial issue is whether Agency counsel has met its burden of proving that MDMA has a high potential for abuse. Drs. Greer, Grinspoon, et al., agree that MDMA has a potential for abuse, but we submit that the evidence demonstrates that MDMA does not have a high potential for abuse.

The DEA seized its first sample of MDMA in 1972. A.-B2, Attachment 1. The scientific literature introduced into this proceeding indicates that scientists have been writing about MDMA in the open literature since the 1970s. GG-18; GG-1. The record, therefore, reflects nearly 14 years of actual experience with MDMA in determining its potential for abuse.

Agency counsel devotes their first 42 Findings of Fact on the issue of potential for abuse to a discussion of (1) the chemical structural 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. As we will discuss below, this evidence does not provide any support for finding that MDMA has a high potential abuse. But putting that to one side for the moment, the significance of this evidence with respect to a drug's potential for abuse by humans must, of necessity, give way in the case of a drug that is "on the street" to evidence with respect to the actual extent of human abuse.

Agency counsel addresses the evidence in the record bearing on abuse by humans in its proposed Findings of Fact numbered 43 through 72. Notable -- by its absence -- is any comparison of the evidence on abuse of MDMA relative 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 drugs scheduled under the Controlled Substances Act.

We are not in any way seeking to downplay any of the evidence in the record about the use of MDMA outside therapeutic settings. Nor do we seek to downplay in any way the fact that any drug not used pursuant to medical supervision is potentially dangerous. The evidence plainly demon-

strates that use outside therapeutic settings is taking place. It is for that reason that Drs. Greer, Grinspoon, et al., have advocated from the very beginning of this proceeding that MDMA should be scheduled.

But, by the same token, we strongly believe that Agency counsel have not sustained their burden of proving that MDMA has a "high" potential for abuse justifying its classification in Schedule I.

Because the evidence of the extent of actual abuse of MDMA over the past 14 years is by far the most important evidence bearing on the finding of the relative abuse potential of MDMA, we turn first to that evidence. Subsequently, we will consider the evidence in the record on chemistry, pharmacology and animal data.

(a) Fourteen-year Record Concerning MDMA

The record contains twelve separate categories of evidence bearing on the extent of use of MDMA over the past 14 years. We will discuss each one in turn.

(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 data collection system collects reports from selected (currently more than 700) hospital emergency rooms in the United States. The reports collected record all visits to those emergency rooms for medical problems associated with

drug abuse. According to NIDA, the major objectives of the DAWN system include the following:

- To monitor drug abuse patterns and trends and to detect new abuse entities and new combinations;
- To assess health hazards associated with drug abuse.[5]

The record reflects that 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. Thus, the eight mentions of MDMA occurred during a period during which DAWN reported roughly 5 million mentions of other drugs. Exhibit 7 of Drs. Greer, Grinspoon, et al., reproduces the summary page of the annual DAWN reports. Plainly, MDMA does not even remotely compare with such Schedule I drugs as heroin, marijuana, and LSD. During the time period that MDMA was mentioned 8 times, MDA was mentioned 344 times -- more than 40 times as frequently. A.-B4, at 2. 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.

---

[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 data system of the National Institute on Drug Abuse 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 evidence in the record reflects the fact that the identification of the drug involved in that overdose death is seriously suspect. A-B18; Tr. 3, at 50-52; GG-30. But, more importantly, the DAWN data system reports on approximately 3,000 drug abuse deaths each year. Tr. 5, at 74. Therefore, during the 1972 through 1983 period, the DAWN system reported on approximately 30,000 to 35,000 drug abuse deaths. MDMA was mentioned only once -- and there is substantial question as to whether it was accurately identified in that instance.

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

The National Institute on Drug Abuse also compiles drug abuse information on a regular and methodical basis from its designated representative in 20 metropolitan areas throughout the United States. From June, 1981 through December, 1984, the National Institute on Drug Abuse convened these Community Epidemiological Work Group meetings every six months. NIDA specifically states that the work group proceedings are intended to (1) provide accurate and timely assessment of drug abuse patterns and trends and (2) iden-

tify emerging drugs of abuse. During each of these twice yearly meetings there was substantial discussion by each representative from each of the 20 metropolitan areas of the drug abuse patterns in those metropolitan regions. In the course of those discussions, more than 120 different individual drugs were discussed and the nature and extent of the drug abuse associated with each of those drugs was identified.

During that period of time MDMA was never mentioned by any NIDA representative from any metropolitan area. Stipulation by parties, Tr. 6, at 10-13.

(4) Laboratory Seizures

The evidence in 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 of time, DEA was seizing approximately 200 clandestine laboratories each year, meaning that DEA seized approximately 2,400 laboratories. Tr. 63-64. Only four had a capacity to produce MDMA.

Further, 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. These exhibits were received by the DEA laboratories at a steady rate of between 3 and 5 exhibits each year throughout the 12-year period. Ibid. During the same period of time, DEA laboratories were receiving between 30,000 and 40,000 drug exhibits each year. Tr. 5, at 60. The DEA made no effort to ascertain how MDMA seizures compared to MDA seizures or to the seizures of any other drugs. Id.

(6) Data From Drug Treatment Facilities

DEA called one witness from a drug treatment facility. That witness was Daryl Inaba from the Haight-Ashbury Free Medical Clinic in San Francisco, California. Mr. Inaba testified that out of a total case load 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 that 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.

Thus the actual percentage of their clients in reality using MDMA might be even less. If this was the drug abuse clinic the agency chose to have 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 the 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 response that the DEA received to those 17 letters were:

- Nine of the agencies did not respond at all;
- Five responded that they had not encountered any MDMA;
- 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 publishes a publication entitled "MICROGRAM". This publication is intended exclusively for law enforcement personnel. It is sent to approximately 1,400 law enforcement agencies -- 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 from law enforcement agencies 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. This edition of MICROGRAM similarly went to some 1,400 law enforcement agencies and forensic laboratories. The Drug Enforcement Administration received no responses whatsoever to this inquiry. GG-41, at 2.

(10) MDMA Use in Texas

The DEA put on the testimony of only one special agent of the Drug Enforcement Administration. This single agent was from Dallas, Texas. The agent testified that, prior to June or July 1984, the DEA had no information with respect to MDMA use in the Dallas area. Tr. 3, at 117. Moreover, Agent Chester testified that information had come to his attention concerning other non-controlled drugs prior to June 1984. Tr. 3, at 118. Subsequently, the agent's

direct testimony indicates that MDMA was used and detected by the DEA in certain night clubs and that it was, at least by reputation, available on campuses in the Dallas area. The DEA put in no first hand testimony whatsoever from any other area of the country, and had no other special agents testify.

(11) PharmChem Laboratories Sample Analyses

The DEA also submitted evidence indicating that a private testing laboratory -- PharmChem -- 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. These are very low numbers. Moreover, given the extensive nature of the government's efforts to obtain information on the abuse of drugs through NIDA, agency counsel's reliance on PharmChem only underlines the weakness of their case. The agency is turning to any source it can just to prove there is some abuse of MDMA.

(12) Testimony by Expert Witnesses

One subject produced total unanimity among every expert witness that addressed the issue. Both agency witnesses and witnesses for Drs. Grinspoon, Greer, et al., agreed that individuals did not use MDMA intensively and that there was no tendency toward dependence upon MDMA whatsoever. All the psychiatric witnesses testified that increasing the dosage and frequency of use produced more un-

pleasant 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

All the evidence is consistent.

- First, every piece of officially compiled data reflects a low absolute level of MDMA usage.

---

[6] Prof. Siegel also provided an estimate of the number of dosage units of MDMA he believed were being distributed in the United States. Prof. Siegel claimed to have made his estimates based on interviews with illicit manufacturers and distributors, and he recounted a number of alleged contacts with law violators. Tr. 8, at 36-40. Prof. Siegel testified that many of the things he was told were "weird." Tr. 8, at 38-39. In terms of his own "research" on MDMA use, Prof. Siegel testified that he had no protocol for his research. Tr. 8, at 48. He testified that for purposes of his research he had a list of the procedures he utilized and the order in which the procedures are administered. Tr. 8, at 48. He was asked to produce this list for the record, id., but he merely provided a typed letter written after his testimony which is not even remotely a scientific document. GG - 58. We submit that Prof. Siegel's estimates do not have a credible foundation. Even taking Prof. Siegel's estimate at face value, his estimate would suggest that the annual production of MDMA in the United States is approximately 360,000 dosage units per year. The House Report on the Controlled Substances Act suggested that evidence of diversion of several hundred thousand dosage units would constitute sufficient evidence of "potential for abuse" to justify controlling a drug, but not of a "high" potential for abuse.

- Second, every piece of officially compiled data reflects a steady level of low usage -- with no trend toward any increase over the 12 year period.

- Third, all evidence in the record comparing actual MDMA usage to MDA usage reflects MDMA's usage being many times less prevalent than MDMA.

- Fourth, every witness including DEA witnesses who addressed the issue held the view that MDMA was not used in high amounts or with high frequency. All of the psychiatrists who had interviewed people who had used MDMA or who had administered MDMA felt that the nature of MDMA's effects meant that people did not seek to use higher doses or to use it frequently.

In sum, the evidence demonstrates that MDMA has been used outside the medical setting. That finding justifies control. But the relatively moderate to low extent of its use compels a finding that it does not have a high potential for abuse.

During the cross-examination sessions, Agency witnesses occasionally sought to explain why individual pieces of data showing a low level of MDMA usage should not be taken at face value. Drs. Greer, Grinspoon, et al., respectfully submit that the consistently low numbers reflected across the entire spectrum of evidence in the record -- including every official compilation of data measuring drug use and abuse in the U.S. -- cannot be explained away.

Moreover, it is important to recognize that MDMA during this period was not a controlled substance. If individuals wanted to produce it or buy it, there was no risk of arrest or criminal deterrent to doing so. Despite this, the incidence of use of MDMA remained relatively low.

Under these circumstances, Drs. Greer, Grinspoon, et al., respectfully submit that the evidence cannot support a finding that MDMA has a "high" potential for abuse. On the basis of its potential for abuse, the evidence requires that MDMA should be found to have less than a high potential for abuse and should be placed in Schedule III.

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

One overriding point should be made regarding the data discussed in Agency Counsel's Proposed Findings of Fact 1 through 39 with respect to potential for abuse: None of the data recited in those findings provides any basis whatsoever to come to a conclusion about MDMA's relative potential for abuse. We will comment briefly on each category of evidence.

Chemistry

The Agency's Proposed Findings of Fact 1-7 and 9-11 establish that MDMA is a member of a family of chemicals, many of which are psychoactive in one way or another. But the mere existence of that chemical similarity provides no reliable guide to a drug's potential for abuse.

The table reproduced on the next page of this brief is from a document surveying the phenethylamines (see Agency Proposed Finding of Fact number 1). This summary was prepared by the U.S. Department of Health and Human Services. HHS's summary lists 28 phenethylamines. (The list reproduced in the Table sets out 30 numbered compounds because two of the compounds are listed twice, under different names.) At the time the document was prepared in December 1983, 17 of these phenethylamines were not scheduled under the CSA at all; eight were scheduled in Schedule I; two were scheduled in Schedule II; and one was scheduled in Schedule IV.

Subsequently, the Expert Committee on Drug Dependence of the World Health Organization reviewed the abuse potential of all 28 phenethylamines. The Committee recommended that nine of the 17 that are not currently scheduled in the U.S. should be scheduled and controlled internationally. (A.-B20) But the WHO committee did not recommend that the remaining eight phenethylamines be scheduled internationally.[7] As reflected in Agency Exhibit B-20, the World Health Organization has recommended that seven of the phenethylamines that it reviewed should go into Schedule I

---

[7] The eight phenethylamines that are not now scheduled domestically and that have not been recommended for control internationally by the WHO are: clobenzorex (stimulant); fenbutrazate (stimulant); furfenorex (stimulant); morazone (stimulant); para-oxyamphetamine (stimulant); 4-bromo-2,5-dimethoxyphenethylamine (hallucinogen); N,N-dimethylamphetamine (stimulant); and N-ethyl-3,4-methylenedioxyamphetamine (hallucinogen).

SUMMARY OF THE PHENETHYLAMINES

		Medical Use in USA	CSA Schedule	Year Enacted	Stimulant	Hallucinogen	Preclinical Abuse Liability	Clinical Abuse Liability
1.	CATHINE	NO	NO		+			+
2.	CATHINONE	NO	NO		+		+	+
3.	CLOBENZOREX	NO	NO		+			
4.	DIMETHOXYAMPHETAMINE	NO	I H	1973	+	+		
5.	DIMETHOXYBROMOAMPHETAMINE	NO	I H	1973		+		+
6.	ETHYLAMPHETAMINE	NO	I S	1982	+		+	
7.	FENBUTRAZATE	NO	NO		+			
8.	FENCAMFAMINE	NO	NO		+		+	+
9.	FENETYLLINE	NO	I S	1981	+		+	
10.	FENPROPOREX	NO	NO		+			
11.	FURFENOREX	NO	NO		+			
12.	LEVAMFETAMINE	NO	II S		+		+	
13.	LEVOMETHAMPHETAMINE	NO	II S	1971	+		+	
14.	MEFENOREX	NO	NO		+			
15.	METHOXYAMPHETAMINE* (See 19).							
16.	METHOXYMETHYLENEDIOXYAMPHETAMINE# (See 29)							
17.	METHYLENEDIOXYAMPHETAMINE	NO	I H			+	+	+
18.	MORAZONE	NO	NO		+			
19.	PARA-METHOXYAMPHETAMINE*	NO	I H	1973	+	+	-	
20.	PARA-OXYAMPHETAMINE	NO	NO		+			
21.	PEMOLINE	YES	IV S	1975	+		-?	
22.	PROPYLHEXEDRINE	YES[1]	NO		+			+
23.	PYROVALERONE	NO	NO		+			
24.	TRIMETHOXYAMPHETAMINE	NO	I H			+		
25.	4-BROMO-2,5-DIMETHOXYPHENETHYLAMINE	NO	NO			+		
26.	2,5-DIMETHOXY-4-ETHYLAMPHETAMINE	NO	NO			+	-	
27.	N,N-DIMETHYLAMPHETAMINE	NO	NO		+			
28.	N-ETHYL-3,4-METHYLENEDIOXYAMPHETAMINE	NO	NO			+		
29.	5-METHOXY-3,4-METHYLENEDIOXYAMPHETAMINE#	NO	I H			+		
30.	3,4-METHYLENEDIOXYMETHAMPHETAMINE	NO	NO			+		
	DIETHYLPROPION	YES	IV S	1973	+		+	+
	MESCALINE	NO	I H			+	-	
	PHENMETRAZINE	YES	II S	1971	+		+	+

1: Over-the-counter preparations
+: Positive report
-: Negative report
H: Hallucinogen
*: 15 & 19 are identical compounds
S: Stimulant
CSA: The Controlled Substances Act (CSA) of the USA

I: Schedule I of CSA
II: Schedule II of CSA
IV: Schedule IV of CSA
#: 16 & 29 are identical compounds
1972: Year the law is enacted

Department of Health and Human Services, "PHENETHYLAMINES", December, 1983

under the Convention on Psychotopic Substances, four should go into Schedule II, and six should go into Schedule IV. Plainly, the simple fact that a chemical is a phenethylamine tells little about where it should be scheduled.

Consider also the research done by Dr. Hardman, an Agency witness, set out in Dr. Hardman's paper which appears as Exhibit GG-18. Dr. Hardman experimented with eight compounds which he identified by Roman Numerals. Compound number I is mescaline; IV is MDA; VIII is MDMA. Of the remaining five drugs (II, III, V, VI, and VII), only one (VII) is scheduled under the CSA. Yet the table on page 300 of Dr. Hardman's paper makes clear that the chemical structural relationships of the 8 drugs are exceedingly close. In particular, by looking at the columns headed "4" and "3" on page 300 of GG-18, one can see that compounds III, IV (MDA), V, and VIII (MDMA) all have the methylenedioxy group added to amphetamine. Yet compound III and compound V are not scheduled drugs.

Like MDMA, compounds III and V differ from MDA only by the addition of a single methyl group (CH_3), yet neither are known to have enough abuse potential to warrant scheduling. Of the total of 32 unique compounds on the HHS list and Dr. Hardman's list, 12 are not controlled substances, and six are scheduled no higher than Schedule IV in either the United States (pemoline) or in the WHO recommendations (fencamfamine, fenproporex, mefenorex, propylhexadrine and pyrobalerone). Therefore, more than

half (18 of 32) of these closely related compounds do not have sufficient abuse potential to be scheduled at all or have only such a low abuse potential that they are appropriately placed in Schedule IV either domestically or internationally.

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]

Pharmacology

The Agency's Proposed Findings of Fact 12 through 19 only suggest that MDMA is a central nervous system (CNS) stimulant. While it is true that MDA and amphetamine are

---

[8] Agency Counsel's Proposed Finding Number 8 is simply a mis-citation of the scientific record. The three sources in the scientific literature cited by the Agency flatly contradict the finding proposed by Agency Counsel. The scientific literature cited by Agency counsel emphasizes the difference between MDMA and MDA. See GG-4 at 193 ("qualitative differences of their actions"; "opposite optical isomers are responsible for their actions"); GG-25 at 842 (comparable potency but "qualitative aspects of the intoxication are altered"); GG-31 at 292 (MDMA qualitatively similar only to "low levels" of MDA). Prof. Nichols, in his direct testimony, goes into tremendous detail on this issue and directly contradicts the Agency's proposed finding. Nichols direct, at 6-8. And the NIH scientists whose study the agency filed late in the proceeding (A.-B24) specifically assessed the literature as reflecting that MDA and MDMA produced "qualitatively different" intoxications. A-B24, at 3. DEA witness Glennon takes the same position. GG-10, at 808 ("qualitive aspects of the intoxication produced by MDMA apparently differ from those produced by MDA").

CNS stimulants, it is also true that an enormous array of other substances are CNS stimulants, including caffeine and six of the eight phenethylamines that are not currently controlled and are not recommended for control by WHO. CNS stimulants may or may not have a potential for abuse. Placing a substance in that general category is of little assistance in attempting to discern whether or not it should properly be considered to have a potential for abuse or what relative degree of abuse potential it has. For example, all eight of the compounds tested by Dr. Hardman had pharmacological effects similar to each other, yet only four are currently controlled substances. GG-18, at Table II.

LD-50

The Agency's Proposed Findings of Fact 22-25 all relate to the LD-50 of MDMA. As Dr. Hardman testified, establishing the LD-50 is a standard toxicological procedure for every drug reviewed by the Food and Drug Administration. Tr. 6, at 18. One could recite countless permutations of what percentage the LD-50 of one drug was of any other. Such an exercise has no significance. It certainly has nothing to do with the abuse potential or the relative safety of a drug. The key variable -- as Dr. Hardman testified -- is the therapeutic index. Tr. 6, at 19. That is, what ratio the LD-50 is to the effective dose. (ED-50). If people are taking doses to achieve the desired effect that are close to the LD-50 dose, then there are obvious safety concerns. (Even then, Dr. Hardman testified that drugs with

an exceedingly low therapeutic index -- such as anesthetics -- can still be safely used and have "accepted safety" under medical supervision. Tr. 6, at 19). As the Agency's own proposed finding (No. 25) notes, the estimated oral LD50 for MDMA is 325 mg/kg. The effective dose is 2 mg/kg. Greer Testimony Regarding Government Exh. B-25, dated November 22, 1985, at 5. If the data on the LD50 of MDMA demonstrates anything, it is that a large margin of safety exists. It says nothing about potential for abuse or relative potential for abuse.

Studies on Rat Neurotransmitter Levels and Nerve Terminals

Agency findings 26 through 31 all relate to the effects of MDMA on neurotransmitter levels and nerve terminals in rats. The human significance of the findings has simply not been established. Humans have not been reported to inject MDMA. They take it orally. MDMA is more than six times as potent when injected compared with its potency taken orally. GG-25, at 1.[9] In the studies referenced by agency counsel, injected doses of 2.5 mg/kg and below demonstrated no neurotoxicity. A.-B24, Table 1A. To translate this into the equivalent of a human oral dose, the injected

[9] Dr. Hardman found that the LD-50 of MDMA when injected into a rat was 49 mg/kg (GG-18, at 301). The study carried out by Intox Laboratories estimated that the LD-50 for MDMA when administered orally to rats was approximately 25 mg/kg. (GG-40). Thus it takes six times the injected dose to achieve the same effect when the drug is administered orally.

dose level must be multiplied by six, to take account of the six-fold difference in potency between injected doses and oral doses. Thus the lowest oral dose level at which any toxic effects would occur would be 15 mg/kg -- more than seven times the therapeutic dosage level and the normal street dosage level of 2 mg/kg.[10]

It should be noted that the four-day course of repeated injections of MDMA which produced the more serious changes in brain chemistry in Dr. Seiden's study was the equivalent of a 110-pound human being taking oral doses of 6,000 mg, 12,000 mg, or 24,000 mg per day for four days consecutively! It is impossible to reach responsible conclusions about the public health significance of Dr. Seiden's findings with respect to MDMA based on these phenomenally high dosage levels.

But, perhaps most importantly, Dr. Seiden and his colleagues admit that the drug fenfluramine produces the biochemical effects in rat brains not at such high dosage levels but rather at the effective dosage levels at which humans use fenfluramine:

> Fenfluramine also produced a long lasting depletion of serotonin in the striatum, hippocampus and rest of brain at a dose (6.25 mg/kg) only 1.25 times the ED_{50} dose for anorexia. In the case of

---

[10] Dr. Seiden's brief letter report on MDMA does not state what dose he used when he gave the rats only one injection. A-B22. It appears that the lowest dose he used was 10 mg/kg -- or the equivalent of an oral dose of 60 mg/kg. Dr. Seiden's report notes that with one injection, the effect of MDMA on his animals even at this enormously escalated level was only "mildly positive." Id.

> the other anorectics, the minimum dose necessary to produce a prolonged neurochemical effect varied from 10 (DEP) to 40 (mazindol) times the ED_{50} dose. It would thus appear that fenfluramine is a significantly more toxic drug than the other anorectics tested. This conclusion is in accord with previous findings by Harvey (1978).

GG-47, at 276.

Fenfluramine is approved for daily use on a chronic basis by the Food and Drug Administration.[11] Dr. Seiden specifically testified that the FDA was made aware in the 1970's that fenfluramine caused these effects and the FDA has taken no action. Tr. 3, at 90. Given the FDA's failure to take fenfluramine off the market or add any warnings or precautions in connection with its use, one cannot conclude that the preliminary results cited by agency counsel with respect to gargantuan doses of MDMA justify any conclusion with respect to a health hazard. This is obviously an area that should be researched more. But its significance at the present time is quite limited.

Drug Discrimination Studies

The point of animal drug discrimination studies is to attempt to predict whether drugs will have an abuse potential in humans. Obviously predictions sometimes turn out to be wrong. One of the Agency's own witnesses, Dr. Glennon, has made precisely this point in his writings:

---

[11] Physician's Desk Reference 1657-58 (39th ed. 1985).

> Nevertheless, unless a particular compound has been tested in humans, one cannot be certain that all the structure-activity relationships described in this chapter will apply in the clinical situation. Based on our collective experience, it is likely that the most common error found in animal models is the identification of "false positives." That is, the models may indicate a compound to be active, whereas actual testing in humans reveals inactivity. It is clear that no present animal models correlate with the qualitative differences between hallucinogens observed in humans.

GG-26, at 96-97.

Even then, the drug discrimination studies cited by agency counsel simply do not prove anything with respect to abuse potential. The studies cited by agency counsel were all assessed by NIDA in 1984 when NIDA specifically declared, "the direct evidence that MDMA has any abuse potential in animals is not substantiated, based on the data DEA provided." GG-55. With all due respect, the agency is flogging a dead horse. These studies only demonstrate that animals recognize MDMA as a CNS stimulant. We have discussed above the inadequacy of such evidence to demonstrate abuse potential or relative abuse potential. These studies do, however, unequivocably show that test animals do not recognize MDMA as an hallucinogen. GG-10, at 811.[12]

---

[12] In this connection, one misstatement in the Agency's brief should be noted. Their proposed finding 39 misinterprets the study they cite. Their proposed finding is directly contradicted by their own witness. DOM is a known hallucinogen against which other drugs are tested. The authors of the document cited by Agency Counsel (one of whom is the Agency's witness Dr. Glennon) specifically interpreted the data cited by Agency Counsel as denoting a lack of generalization, not partial generalization as agency counsel attempts to claim:

(Footnote continued)

The Agency attempts to make capital out of the fact that animals trained to recognize MDA also recognize MDMA. But that fact is highly misleading. MDA is unique among chemicals in being recognized by animals who are trained to recognize hallucinogens and also by animals trained to recognize stimulants. The agency's own witness established this fact in the scientific literature. A-A6. MDMA does not share this dual response characteristic of MDA. GG-10, at 810-811. The dual character of MDA means that animals trained to recognize MDA who also respond to MDMA are simply responding to the CNS stimulant characteristic of MDMA.

In any event, the evidence in the record on the qualitative differences in humans between MDA and MDMA is uncontradicted. Dr. Alexander Shulgin, a leading researcher who has researched the effects in humans of both MDA and MDMA, and Dr. Richard Yensen, a clinical psychologist who has carried out experiments with humans with MDA and who is familiar with MDMA, both submitted information on the different effects in humans of MDA and MDMA. GG-30, at 1-3; Yensen Rebuttal at 1-2. The scientific literature overwhelming supports this view. See fn. 8, supra.

(Footnote 12 continued from previous page)

> The lack of generalization between (±)-DOM and the N-monomethyl derivatives of MDA [meaning MDMA] is also consistent with the report that the qualitative effects of these derivatives in man are different from those produced by (±)-MDA.

GG-10, at 811.

Self-Administration Studies

The two self-administration studies submitted into the record -- at the last minute -- by the Agency in fact undermine agency counsel's case, not support it. Dr. Harris, in his submission (A.-B23), reports that his tests indicated that MDMA was only "one-third to one-fourth as potent as d-amphetamine in stimulating locomotor activity"; and that MDMA "does not produce physical dependence." A.B23, at 2-3. With respect to reinforcing properties, Dr. Harris reported on three monkeys. One monkey self-administered MDMA "robustly." A second monkey "could not satisfy our demanding criteria for concluding that they [the doses of MDMA] were serving as reinforcers." One monkey "did not self-administer MDMA at any dose tested." A.-B23, at 3.

We respectfully submit that, viewed objectively, Dr. Harris' data suggests that MDMA has less of a potential for abuse rather than more.

Dr. Griffiths' study involved an effort to measure whether three baboons would self-administer MDMA. One baboon did not self-administer; one did self-administer, but at levels of self-administration "below those maintained by cocaine, d-amphetamine and phencycladine in previous experiments," and one baboon apparently self-administered erratically. When Dr. Griffiths originally submitted his paper, his conclusion was that the preliminary results of his experiment indicated that "MDMA has moderate reinforcing effi-

cacy." A.-B21A (Emphasis added). We submit that the results of Dr. Griffiths' experiment, again if viewed objectively, are in fact highly ambiguous. In comments submitted on his study, we noted a number of severe methodological problems that, in our judgment, demonstrate that the data reported is not reliable and may not be scientifically reproducible. Response to Agency Exhibits B-21, B-22, and B-23 by Drs. Grinspoon, et al., Nov. 4, 1985, at 2-6. But even accepting Dr. Griffiths' original evaluation of his results, he concluded that MDMA had only "moderate" reinforcing efficacy.

These inconclusive and highly ambiguous results from these animal studies hardly prove anything. They certainly cannot compare in probative value to the evidence in the record about the actual relatively low level of MDMA use "on the streets," or to the testimony of psychiatrists who have administered the drug and who have professional opinions about the drug's low potential for abuse based on direct clinical observations. See supra, pp. 35-47.

B. Accepted Medical Use in Treatment in the United States

The second criterion specified by the CSA for determining whether a substance goes into Schedule I or another Schedule is whether the substance has an "accepted medical use in treatment in the United States." Drs. Greer, Grinspoon, et al., submit that the phrase "accepted medical use in treatment" 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 Agency contends -- 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 approval to ship a drug on an interstate basis -- lack of financial return is the most obvious and the most frequent in actual practice.

Drs. Grinspoon, Greer, et. al., submit that their 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). The consequence of the so-called "plain meaning" rule has been stated as follows:

> "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. If the language is plain, unambiguous and uncontrolled by other parts of the act or other acts upon the same subject, the court cannot give it a different meaning."

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

Drs. Greer, Grinspoon, et al., respectfully submit that the agency cannot make any showing that would justify a departure from clear statutory language. Indeed, all the factors cited by the Sutherland treatise reinforce the plain meaning. To depart from the plain meaning requires ignoring legislative history, ignoring other provisions of the CSA, contradicting long-standing interpretations of the federal Food, Drug and Cosmetic Act, ignoring the rights of individual States to approve the intra-state marketing of drugs, and ignoring the responsibilities of States to regulate medical practice.

In the present case, the Controlled Substances Act is perfectly clear. The Act refers to "accepted medical use in treatment." That phrase is clear. It refers to what is "accepted" in a "medical" setting for "treatment." What is relevant to that determination is evidence of medical opinion with respect to whether the use of a particular sub-

stance in medical treatment is accepted within the medical community as an appropriate course of treatment. Such evidence is familiar in the law of medical malpractice and the law of medical licensing and discipline within the various states of the United 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. It would have been an exceedingly simple matter for the Congress to provide such a criterion.

The Congress knows how to write such a provision, as numerous cross-references in the CSA to the Food, Drug and Cosmetic Act demonstrate. For example, the Congress in the Controlled Substances Act defined the term "drug" by specific reference to the Food, Drug and Cosmetic Act, see 21 U.S.C. § 802 (12); excluded non-narcotic over-the-counter drugs from the statutory scheduling scheme by specific reference to the Food, Drug and Cosmetic Act, see 21 U.S.C. § 811(g)(1); specifically referred to the investigational new drug provisions of the Federal Food, Drug and Cosmetic Act in § 307(c)(2)(A) and in § 307(e) of the Controlled Substances Act, 21 U.S.C. §§ 827(c)(2)(A), 827(f),* imposed

---

* In the compilation of the Controlled Substances Act into U.S.C. and U.S.C.A. references to "The Federal Food, Drug and Cosmetic Act" in the original Act have been changed to references to "this title." See Comprehensive Drug Abuse Prevention and Control Act of 1970, Pub. L. 91-513, 84 Stat. 1236, 1970 U.S. Code Cong. & Ad. News 1464-65, 1461, 1466.

labeling and packaging requirements based on specific references to the provisions of the Federal Food, Drug and Cosmetic Act, see §§ 305(a), 305(b) of the Controlled Substances Act, 21 U.S.C. §§ 825(a), 825(b);* and imposed obligations with respect to dispensing by prescriptions by references to specific determinations under the Federal Food, Drug and Cosmetic Act, see §§ 309(a), 309(b) of the Controlled Substances Act, 21 U.S.C. §§ 829(a), 829(d).*

But the Congress plainly chose not to refer to determinations under the Food, Drug and Cosmetic Act when it required findings to be made about "accepted medical use."

2. Legislative History

Agency counsel references only one instance in the legislative history of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (Pub. L. 91-513) in which the definition of the term "accepted medical use" was discussed: testimony by Dr. John Jennings, then Acting Director of the Bureau of Drugs, Food and Drug Administration. The Agency selectively -- and unfortunately therefore misleadingly -- quotes from Dr. Jennings' testimony.

More importantly Agency counsel omits any reference to numerous more extensive and more important passages in testimony by Administration witnesses to the Congress. That testimony demonstrates beyond any legitimate question that the determination of "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.

Dr. Jennings' testimony on this subject was, in full, as follows:

> Q: Let me ask one question: when a drug is under investigation pursuant to investigational new drug applications, is the drug considered to have an accepted medical use?
>
> Dr. Jennings: Usually not, although it might.
>
> Q: Could you enlarge on that?
>
> Dr. Jennings: Yes, sir. The exemption for investigational use is usually granted for a drug for which the medical use has not been established, so in most cases that would be so, there would not be an accepted medical use.
>
> However, drugs that have one or maybe several accepted medical uses might be under investigation for additional medical uses.
>
> Q: But in the great majority of the cases --
>
> Dr. Jennings: It would be true that the accepted medical use would not have been established.

House Hearings, at 343.

Much more important testimony, however, was given by three Administration witnesses -- all more senior than Dr. Jennings -- testifying before the Subcommittee on Public Health and Welfare of the House Committee on Interstate and Foreign Commerce -- the subcommittee which ultimately drafted the bill that became the Controlled Substances Act. 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;

and Dr. Roger Egeberg, Assistant Secretary of HEW. The relevant portions of their testimony were as follows:

> Mr. Sonnenreich: [Criterion] Two [no accepted medical use] is a factual determination and normally where we get such information is through the AMA or WHO. You don't have to be a doctor to find out whether or not it has an accepted medical use in the United States or not. So the fact that you are asking whether it has got accepted medical use is something that a lawyer can find out as well as a doctor.

House Hearings, at 165 (emphasis added).

> 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 have no legitimate medical use in the United States.

House Hearings, at 678 (emphasis added).

> Mr. Roger: 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).

Several observations are appropriate about the testimony set out above of Messrs. Ingersoll and Sonnenreich, and Drs. Egeberg and Jennings. First, it is clear that Dr. Jennings did not testify that the issuance of an NDA determined whether or not a drug had "accepted medical use." Specifically, Dr. Jennings responded to a question as to whether a drug "under investigation" was "considered to have" an accepted medical use. Dr. Jennings' response was that an investigational drug would "usually not" have an accepted medical use, "although it might." Dr. Jennings never spoke to the question of how one would determine whether a drug had an "accepted medical use." And Dr. Jennings specifically emphasized that it was possible that some drugs under investigation "might" have an "accepted medical use."

Second, the testimony of the other three Administration witnesses all speaks much more directly to the issue of the meaning of "accepted medical use." Mr. Sonnenreich, who earlier in this proceeding was cited by the Agency as a leading authority on the CSA, makes clear that the Department of Justice would look to the American Medical Association and to the World Health Organization to provide information on "accepted medical use." He further emphasized that the determination as to whether a drug has a medical use was to be made "by the medical community," and specifically not by "by any part of the federal government."

Plainly, neither the Administration witnesses nor the Congressmen asking the questions believed that the Food and Drug Administration was to determine "accepted medical use" exclusively on the basis of whether the FDA had issued an NDA to the manufacturer of a drug. To the contrary, Mr. Sonnenreich, representing the Department of Justice and testifying before the House Subcommittee which ultimately drafted the bill which became law, specifically informed the Committee that "accepted medical use" as used in the definition of Schedule I substances was to be "determined by the medical community," and "not by the Federal government."[5]

---

[5] Agency counsel and Mr. Joranson cite materials prepared by the Commissioners on Uniform Laws pertaining to various interpretations of phrases in the Controlled Substances Act. We respectfully submit that it is the statutory language of the Controlled Substances Act and the intent of Congress as reflected in the relevant legislative history that control the interpretation of the statutory

(Footnote continued)

It is difficult to imagine a clearer statement that agency counsel's current position is wrong.

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 marihuana, it would then have to apply to DEA to reschedule the drug. We think it not inappropriate for NORML to apply first for rescheduling under the CSA. (citations omitted).

(Footnote 5 continued from previous page)
phrases at issue. We have a further problem with Mr. Joranson's survey. On cross-examination, Mr. Joranson acknowledged that his survey was directed to the Controlled Substances Boards of the various states. Tr. 6, at 52-53. He acknowledged that he had not surveyed the medical licensing authorities in each of the fifty states, nor had he sought the views of state or national medical associations. Tr. 6, at 61. We respectfully submit that it is the medical licensing boards of the various states who are really the most appropriate state officials to speak to the proper interpretation of state laws having to do with "accepted medical use" and "accepted safety for use under medical supervision."

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 in the course of the practice of medicine. It is to that subject that we now turn.

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] In explaining this proviso, the committee reports emphasized that the bill was "not intended as a medical practices act, and [would] not interfere with the practice of the healing art by chiropractors and others in the States where they are licensed by law to engage in such practice."[8] While the definition of "drug" as ultimately enacted did not include this proviso (see U.S.C. 721(g)), the legislative history nonetheless

---

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

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

[8] S. Rep. No. 361, 74th Cong., 1st Sess. 3 (1935); S. Rep. No. 646, 74th Cong., 1st Sess. 1 (1935).

makes it very clear that Congress did not intend the Act to apply to the state-regulated practice of medicine -- a proposition that both the FDA and the courts have recognized as set out below.

Moreover, Congress has in several other respects specifically provided for deference to state law under the FDC Act. The drug provisions of the Act do not apply, for example, to drugs wholly in intrastate commerce. 21 U.S.C. §§ 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. § 353(b). Further, the Act generally defers to state law in areas that do not directly conflict with it.[9]

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. This issue has most frequently arisen when the FDA

---

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

> Nothing in the Amendments made by this Act to the Federal Food, Drug, and Cosmetic Act shall be construed as invalidating any provision of state law which would be valid in the absence of such amendments unless there is a direct and positive conflict between such Amendments and such provision of state law.

has considered 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 labeling.[10] In 1972, the agency summed up its view of this subject when, in the preamble to a proposed rule on drug labeling, it stated:

> If an approved new drug is shipped in interstate commerce with the approved package insert and neither the shipper nor the recipient intends it be used for an unapproved purpose, the requirements of section 505 of the Act are satisfied.
>
> Once the new drug is in a local pharmacy after interstate shipment, the physician may, as part of the practice of medicine, lawfully prescribe a different dosage for his patient, or may otherwise vary the conditions of use from those approved in the package insert, without informing or obtaining the approval of the Food and Drug Administration.
>
> This interpretation of the Act is consistent with congressional intent as indicated in the legislative history of the 1938 Act and the drug amendments of 1962. Throughout the debate leading to enactment, there were repeated statements that Congress did not intend the Food and Drug Administration to interfere with medical practice and references to the understanding that the bill did not purport to regulate the practice of medicine as between the physician and the patient. Congress recognized a

---

[10] Under the FDC Act, the labeling of any prescription drug, whether subject to approval or not, must be adequate for the drug's intended purposes. In the case of prescription drugs (as opposed to "over-the-counter" drugs available without a prescription), the requirements are met by conditioning availability on a practitioner's prescription, and on there being labeling directions for physicians and pharmacists (as opposed to laymen) as to the proper prescribing, dispensing, and administration of the drug. 21 C.F.R. § 201.100.

> patient's right to seek civil damages in the courts if there should be evidence of malpractice, and declined to provide any legislative restrictions upon the medical profession.

37 Fed. Reg. 16503 (1972).

Subsequently, in 1975, the Food and Drug Administration wrote as follows:

> The comments recommended that the proposed regulations be revised to require an appropriate statement in package inserts that, in addition to the conditions of use which the manufacturer may recommend to physicians in compliance with the law and Food and Drug Administration regulations, there are other conditions of use for which the drug may be regarded as safe and effective on the basis of the experience of critical physicians using the drug in the practice of medicine over a period of years.
>
> The Commissioner stated in a separate notice of proposed rulemaking published in the Federal Register of August 15, 1972 (37 Fed. Reg. 16503), concerning the use of a drug for conditions not included in its labeling, that the labeling does not intend either to preclude the physician's use of his best judgment in the interest of the patient or to impose liability if he does not follow the package insert. The Commissioner clearly recognizes that the labeling of a marketed drug does not always contain all the most current information available to physicians relating to the proper use of the drug in good medical practice. 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 1979, the Food and Drug Administration once more reiterated this view:

> Good medical practice and patient welfare require that physicians remain free to use drugs according to their best knowledge and judgment. . . .

44 Fed. Reg. 37435-36 (1979).

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

> Although no final rule has been issued on this subject, the Agency has continued to apply the principle set forth in the preamble to the 1972 proposal. In FDA's Drug Bulletin of April 1982, the Agency sought to clarify and reiterate the position that the Act does not 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. In the course of its argument in the 1983 case, the FDA emphasized the

> commonly recognized exception to the Act's broad and protective coverage: the practice-of-medicine' exemption. FDCA's legislative history expresses a specific intent to prohibit FDA from regulating physicians' practice of medicine. According to the Commissioner, FDCA does not regulate physicians in their practice because physicians are licensed by the states. Letter from the Commissioner at 3, JA 88.

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. 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. Drs. Grinspoon, Greer, et al., specifically submitted, as their Exhibits 15 and 38, opinions of the Legislative Counsel of the State of California and the California State Attorney General. These opinions made clear that, as a legal matter, doctors within the State of California are 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. §§ 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 §§ 26670(b)-26676; N.Y. Educ. Law, Art. 137, § 6817(b)-(c) (McKinney 1985). Drugs which are legally manufactured within a particular state, available to physicians within that 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" for the treatment of patients suffering from a rare disease when the drug of choice for treating the disease has not been approved for marketing. 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:

> For a variety of reasons, the most prominent being the lack of financial return, many orphan drugs never have their human clinical tests completed and a new drug application for approval submitted to FDA. For those orphan drugs for which tests are completed, the period of testing is often substantially longer than for drugs for common diseases.
>
> During the testing period, drugs for a rare disease, as are other drugs, are often placed in what is commonly called "compassionate IND status." (IND status stands for investigational new drug and is the period during which human clinical trials are conducted.) 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.

The survey of the Subcommittee on Health and the Environment found that since 1970 pharmaceutical companies have had 24 drugs for rare diseases in "compassionate IND status." The survey results show that the average time for human clinical testing for 20 of the 24 compassionate IND drugs was 8.5 years, as compared with 5.1 years for the 47 orphan drugs which have been approved and marketed since 1970. In fact, one drug was in compassionate IND status for 19 years. Even at 5.1 years, the period of testing is significantly longer than that for drugs for common diseases.

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.

The Committee's bill, in section 526, requires FDA to notify the public of the designation of a drug for a rare disease or condition. One reason for this notice is to advise the appropriate health professionals and voluntary disease organizations of the testing which will begin or is being conducted on the drug. This notice, plus the broader and more efficient distribution possible through open protocols, will increase the availability of orphan drugs during the lengthy testing period.

Report of the House Committee on Energy and Commerce on the Orphan Drug Act, 97th Cong., 2d 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. FDA wrote as follows:

> This Section codifies a special procedure authorizing the "treatment use" of investigational drugs in an investigational context.
>
> When reports in the medical literature begin to appear that a new investigational drug shows promise for a serious disease, a demand for the drug for the benefit of patients frequently develops. FDA has responded to this demand by permitting physicians to obtain investigational drugs for treatment use either under physician-sponsored IND's or under protocols that are part of commercially sponsored IND's. . . .
>
> Although the Agency has for many years permitted selected investigational drugs to be distributed primarily for treatment use under these circumstances, the current IND regulations do not specifically authorize the practice. The proposed revisions would expressly authorize this use of investigational drugs. . . .
>
> FDA has been criticized for not adequately informing the medical community about the availability of certain

> investigational drugs for treatment use. The proposal is intended to improve physician (and patient) access to these investigational drugs. . . .
>
> For some of the most promising investigational drugs, requests for the drug for treatment of individual patients can extend into the hundreds. The regulation would encourage drug companies to accommodate such requests. . . .

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

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 long standing 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 it is also inconsistent with the recognition that many drugs become accepted as treatment by the medical community long before an NDA is finally approved.

(iii) HHS Secretary Bowen

In this connection, it is instructive to note the experience of the new Secretary of the Department of Health and Human Services, Dr. Otis Bowen. In a 1981 speech to an American Medical Association meeting, Secretary Bowen stated that he had administered to his wife, who was at the time dying of cancer, DMSO and "another helpful medication I had

to get from France"[11] because it was not approved for marketing in the United States by the FDA. Speaking of the DMSO, Dr. Bowen told his AMA audience, "Why can't a dying person with severe pain have easy prescription access to it? . . . The container said 'for horses only'".[12] In short, the Secretary administered to his wife both a veterinary preparation as well as an unapproved drug which he obtained from a foreign country.

What the Secretary did was not a violation of the Food, Drug and Cosmetic Act. And the reason it was not is that the Act does not regulate the practice of medicine. 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 simple fact is that the Federal Food, Drug and Cosmetic Act does not govern either the propriety or the "accepted" or "nonaccepted" nature of that medical practice.

The Federal Food, Drug and Cosmetic Act licenses commercial companies to market products about which therapeutic claims are made. 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

---

[11] American Medical News, Nov. 22/29, 1985, p. 37.

[12] N.Y. Times, Nov. 8, 1985, at B6.

Federal Food and Drug Act. But, as long as the physician is practicing medicine within his or her practice, it is exclusively the views of the relevant medical community that determine whether or not that physician is practicing "accepted" medicine. From a legal point of view 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 "accepted medical use in treatment."

4. 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:

> Congress did not intend the Food and Drug Administration to interfere with medical practice as between the physician and the patient. Congress recognized the patient's right to seek civil damages in the courts if there should be evidence of malpractice and declined to provide any legislative restrictions upon the medical profession. . . . Congressional intent set out in 37 Fed. Reg. 16503 (1972) indicates the Congress did not intend the Food and Drug Administration to interfere with medical practice and that the bill did not purport to regulate the practice of medicine as between the physician and the patient.

453 F. Supp. at 1149. The Court in United States v. Evers also points out:

> ". . . the physician can ascertain from medical literature and from medical meetings new and interesting proposed uses for drugs marketed under package inserts not including the new proposed usages. . . . New uses for drugs are often discovered, reported in medical journals and at medical meetings, and subsequently may be widely used by the medical profession. . . . The manufacturer may not have sufficient commercial interests or financial wherewithal to warrant following the necessary procedures to obtain FDA approval for the additional use of the drug. When 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 consenting 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. The mention of a requirement that licensed doctors must prescribe, treat 'within state sanctioned alternatives' raises the specter

> of medical stagnation at the best, statism, paternalistic big brother at worst. It is by the alternatives to orthodoxy that medical progress has been made. A free, progressive society has an enormous stake in recognizing and protecting this right of the physician.

People v. Privitera, 141 Cal. Rptr. 764, 774 (Cal. App. 1977).

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 within the medical community may have different but equally "acceptable" views with respect to particular medical practices. In determining what constitutes "accepted" medical practice, the courts have evolved a test 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.

* * *

> . . . 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, § 166 (3d ed.).

D. Louisell & H. Williams, Medical Malpractice, ¶ 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.

In sum, it is our position that the phrase "accepted medical use in treatment in the United States" means that the use of a particular drug is accepted by reputable physicians. Those physicians need not constitute the majority, but they must be reputable physicians who constitute at least a respectable minority of practitioners within the medical community.

6. Evidence in the Record With Respect to the Accepted Medical Use of MDMA and Proposed Findigs 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 summary, during the nine years of practicing psychiatry in New Mexico, I have become well acquainted with the academic community, rural and private practice standards of psychiatric evaluation and treatment. I have been involved at all levels of developing and maintaining quality medical treatment of psychiatric patients in this state -- in the political and government agency area, in the grassroots community level, and in the private profit and not-for-profit hospitals. . . .
>
> 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 4-7. Both further testified that for appropriate patients with appropriate indications use of MDMA in psychotherapy was considered

good medical practice and accepted medical practice within their community of physicians. Tr. 2, at 70, 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 Ingrasci, a psychiatrist in private practice in Massachusetts 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 one way or the other about whether MDMA use by other psychiatrists would be accepted in specific circumstances by reputable psychiatrists. Dr. Docherty did specifically testify, however, 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 about the proper treatment to utilize for their patients. 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. And Dr. Kleinman also testified that the decision by physicians to employ a particular medical procedure or treatment, including use of a drug, based on a variety of evidence but without the benefit of a controlled clinical trial would in many circumstances constitute acceptable medical practice. Tr. 5, at 184-85, 187-88. Dr. Kleinman specifically testified that the judgment by a clinician to use a particular medical procedure or to use a drug involved a risk/benefit analysis. Tr. 5, at 188-90.

7. Conclusion

On the basis of the evidence in this record, we submit agency counsel has not met their burden of proving that the careful use of MDMA for appropriately screened patients for appropriate conditions does not constitute accepted medical practice. To the contrary, we believe the testimony establishes that reputable psychiatrists regard appropriately limited use of MDMA in the course of a psychotherapeutic practice to be an accepted medical use of MDMA in treatment.

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.

Our starting point for interpreting this provision is an elementary maxim of statutory constructions -- which is to give effect to each provision of a statute.

> 'It is an elementary rule of construction that effect must be given, if possible, to every word, clause and sentence of a statute.' A statute should be construed so that effect is given to all its provisions, so that no part will be inoperative or superfluous, void or insignificant, and so that one section will not destroy another unless the provision is the result of obvious mistake or error.

Sutherland Stat Const § 46.06 (4th ed.) (footnotes omitted.)

The Agency'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). Under the "elementary" rule of statutory construction cited above, the Agency's approach must be rejected.

What, then, is the proper interpretation of the third criterion for including a substance in Schedule I? The starting point for our analysis must focus on how "accepted medical use in treatment" differs from "accepted safety for use under medical supervision." The key to the difference is to recognize that, in order for a drug or any medical procedure to be accepted in "treatment," reputable physicians must make <u>two</u> judgments. They must reach a conclusion that a drug (or other medical procedure) is (1) safe <u>and</u> (2) effective.

Plainly, there can be circumstances where reputable physicians are withholding judgment as to whether a drug is effective. Under these circumstances, there would not be an "accepted medical use in treatment." But it is still possible that reputable physicians would have concluded, based on existing information, that a drug could be safely used under medical supervision. This is not a hypothetical situation. Given the need for extensive and lengthy clinical testing in order for a drug to win FDA approval for

interstate marketing, such a situation exists during much of the early clinical testing of many drugs.

We submit 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. But, if a drug has not been around very long, reputable physicians may not yet have reached any conclusion about its effectiveness in treatment. 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. Such a case might involve a drug that was in widespread use in another country. The foreign data might be sufficient to justify a conclusion by reputable physicians that the drug can be safely used under medical supervision. But the foreign evidence might not be sufficient to justify a conclusion that the drug is effective and therefore that it has an accepted medical use in treatment. 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. In all of these circumstances, reputable physicians could properly and reasonably conclude that a drug was safe to use under medical supervision long before a judgment was made whether it was effective.

In sum, the second and third statutory criteria for placing drugs in Schedule I clearly identify different

questions and different issues that must be decided before a substance may be placed in Schedule I. Even if a substance does not have an "accepted medical use in treatment," the substance must also be shown to have "no accepted safety for use under medical supervision." This criterion asks whether sufficient information exists to support a judgment by reputable physicians that a substance can be safely used under medical supervision in either a research or experimental treatment context.

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

In considering the evidence of the safety of MDMA, it is critical to remember how MDMA is utilized by psychiatrists. 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.

As reflected in the record, MDMA has been administered to animals in a number of different studies. GG-18; GG-40; GG-10; GG-12; GG-13. The injection LD-50 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, 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. Ingrasci has reported on his clinical observations in administering the drug to nearly 100 individuals over 5 years. Ingrasci 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.

In addition, other psychiatrists have been using MDMA in their practices over the past 10 years. Because MDMA cannot be patented, no pharmaceutical company has had the financial incentive to carry out the extensive animal and clinical tests required by the FDA for approval to market the drug on an interstate basis. But 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]

---

[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 known, 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. See Mills v. Rogers, 457 U.S. 291, 293 n.1 (1982) (antipsychotic drugs carry a significant risk of adverse side effects described as "disabling" in their most severe forms). With a drug like MDMA in which there have been essentially no reports of any long-term side effects, reputable physicians can and have concluded that MDMA is safe for use under medical supervision, taking into account both possible risks and possible benefits.

Under these circumstances, MDMA has "accepted safety for use under medical supervision" and cannot be properly placed in Schedule I.

D. Restrictions That Would Apply to MDMA Schedule III

Because MDMA has not been approved for interstate shipment and sale by the Food and Drug Administration, 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. First, no one could manufacture MDMA legally without approval from the Drug Enforcement Administration. Second, no researcher of any kind could obtain MDMA from another source without obtaining an IND from the Food and Drug Administration. To obtain an IND would require FDA review and approval of the research protocol. Third, if MDMA were placed in Schedule III, a physician could not legally manufacture MDMA for use in his or her own practice. The physician would have to seek approval from the DEA to manufacture it, even if the physician sought to manufacture MDMA exclusively for use in her or his own practice. Specifically, a physician would have to register with DEA to conduct research on MDMA as a Schedule III substance. Then, as part of his or her application for registration with the DEA, the physician would have to seek the permission of the DEA to manufacture the amount of MDMA needed for the research. 21 C.F.R. § 1301.22(b)(5).

There is no obligation on the part of the DEA to approve the manufacture of MDMA under such circumstances. If the DEA refused to approve such manufacture, then the physician would have to obtain MDMDA from another source. To do so the physician would have to obtain an IND, in order to allow the drug to be shipped to him. If the DEA did approve the manufacture of the drug as part of a physician's research protocol, the DEA could condition its approval of an individual researcher's right to manufacture MDMA on the researcher/physician obtaining an IND from the Food and Drug Administration to cover the research.

In short, placing MDMA in Schedule III would only remove obstacles to research created by the effects of Schedule I -- it would not permit anyone to utilize MDMA in any setting without formal and explicit government approval.

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

The determination by the Secretary of Health and Human Service (HHS) whether a substance has an accepted medical use or accepted safety under medical supervision is binding on the Attorney General 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 has been satisfied.

A. The June 6, 1984 HHS Transmittal

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

The relevant staff member of the Department of Health and Human Services, Dr. Edward Tocus, reviewed the DEA Control Recommendation proposing that MDMA be placed in Schedule I. It is important to set out two sets of facts -- one set relevant to medical issues and the other set relevant to abuse potential.

Medical

The record in this proceeding reflects the fact that Dr. Greer had previously written to the Assistant Secretary for Health about Dr. Greer's therapeutic work with MDMA, and that Dr. Greer had also written to an FDA staff member (Mr. Contrera) who worked for Dr. Tocus about Dr. Greer's work with MDMA. Tr. 3, at 14; Letter of George Greer to DEA Administrator, August 22, 1984.

Dr. Tocus testified that at the time he reviewed the DEA 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 had to have been approved by the Food and Drug Administration for interstate shipment and sale. Tr. 9, at 66-67. Further, Dr. Tocus testified that, based on his understanding of the law, if HHS came to the conclusion that a drug should be

scheduled but it had not been approved for interstate shipment and sale, "that 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 testified that he did not take any action to make inquiries about medical opinion on MDMA even though he had been told on a hearsay basis that there was some therapeutic interest in MDMA. Id. Dr. Tocus further testified that the Department of HHS did not refer the issue of the appropriate scheduling of MDMA to the FDA's Drug Abuse Advisory Committee. Tr. 98, at 117.

Dr. Tocus made six typographical corrections to the DEA document. These corrections are set out in GG-59. Dr. Tocus then prepared a one-and-one-half page analysis of the scheduling recommendation of the DEA. A.-B4; Tr. 9, at 35-36.

The memorandum that Dr. Tocus prepared does not mention that Dr. Tocus had been informed orally that there was therapeutic interest in MDMA, or that Dr. Greer had previously communicated his interest in MDMA both to the Assistant Secretary for Health and to the FDA. A.-B4.

The memorandum prepared by Dr. Tocus never mentions the phrase "accepted medical use in treatment" and never mentions the phrase "accepted safety for use under medical supervision." Id. The memorandum contains a single

line asserting that "there is no known legitimate use of MDMA in humans." Id.

Dr. Tocus testified that he forwarded his one-and-one-half page memorandum (A.-B3, B4) and the DEA's evaluation (GG-56) to the Commissioner of FDA and thence to the Assistant Secretary for Health. Tr. 9, at 35-36.

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, noting that there have been some reports of MDMA use outside the medical context, 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. Dr. Tocus testified that he was aware of the views of NIDA prior to receiving the NIDA memorandum, and that he shared those views. Tr. 9, at 48. But those judgments were not reflected in the materials that Dr. Tocus forwarded to the Commissioner of Food

and Drugs or to the Assistant Secretary for Health. Tr. 9, at 48. None of the underlying documents prepared at the Department of HHS ever reached the conclusion that MDMA had a "high" potential for abuse. The one-and-one-half page memorandum prepared by Dr. Tocus notes on page one that DEA has concluded that MDMA has a high potential for abuse. But the HHS memorandum itself never so concludes.

Moreover, the DEA document created false and misleading impressions in the following ways:

> (1) The DEA document attached three letters from law enforcement agencies in mid-1979 indicating that these agencies had detected MDMA in various amounts in submissions to their laboratories. The DEA failed, however, to inform HHS that the DEA had sought information on MDMA trafficking and synthesis from 17 law enforcement agencies in mid-1979; that five agencies had written that they had not detected any MDMA; and that nine of the 17 had not replied at all. Tr. 5, at 42.
>
> (2) Further, the DEA memorandum provided HHS with three written communications from law enforcement agencies in 1982 indicating that those agencies had detected samples of MDMA in submissions to their laboratories. A.-B2. But DEA wholly failed to inform HHS that those three communications were received in response to a notice seeking information published in DEA's Microgram which goes to some 1,400 forensic laboratories and law enforcement agencies in this country and internationally. Tr. 5, at 48-49.
>
> (3) The DEA document provided HEW with information on seizures of MDMA by law enforcement agencies during the 1972-1983 time period. But the DEA document wholly failed to provide HHS with any comparative data, showing the total number of seizures during the period in question; the relative amounts of other

> drugs seized or other similar drugs seized during the same period; or in any way to provide a basis for HEW to draw any reasoned conclusions as to the significance in relative terms of the amount of MDMA seized as reflected in the DEA document. A.-B2.

Finally, based on this record, the Commissioner of Food and Drugs forward the package on to the Assistant Secretary of Health. The Commissioner wrote that it was his conclusion only that "MDMA has a significant potential for abuse," with no mention being made of any higher level of abuse potential. GG-54.

HHS Action is Not Valid

Drs. Greer, Grinspoon, et al., respectfully submit that HHS's review and analysis of the questions whether MDMA had an accepted medical use in treatment in the United States or whether MDMA had an accepted safety for use under medical supervision was not 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]

---

[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

(Footnote continued)

Second, the FDA failed to consider "all relevant factors" by failing to consult with relevant medical organizations to determine whether there was, in fact, interest in the therapeutic utility of MDMA, whether there was "accepted medical use in treatment," and whether there was "accepted safety for use under medical supervision."[15] This failure demonstrates the arbitrary and capricious nature of the agency's decision and is particularly egregious in light of the fact that Dr. Tocus was on notice that there might be some interest, and that a member of his staff had received information from Dr. Greer.

Third, the recommendations of the Department of HHS are further invalid because the responsible official, the Assistant Secretary for Health, wholly failed to exer-

---

(Footnote 14 continued from previous page)
to agency expertise does not apply to erroneous conclusions of law, which require reversal of agency's decision).

[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 Mutual 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 failed 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 failing 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).

cise the discretion that he was obligated to exercise to make the judgments required of him under the Act. This failure developed because HHS staff 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] Therefore, the Assistant Secretary for Health never had the opportunity to exercise the discretion that, under the statute, he was obligated to exercise.

The recommendations and conclusions contained in the June 6, 1984 HHS transmittal with respect to the issue of whether MDMA had a "high potential for abuse" are also invalid as arbitrary and capricious. First, the responsible deciding official was not informed that the National Institute on Drug Abuse had concluded that the animal studies cited at great length by the Drug Enforcement Administration in the memorandum that was forwarded to the Assistant Secretary for Health did not substantiate abuse liability of MDMA. Second, the DEA itself withheld from the Department of Health and Human Services critical information and data which had an important bearing on making the assessment as to whether MDMA had a high potential for abuse or some lesser potential for abuse.

---

[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).

Finally, Drs. Grinspoon and Greer respectfully submit that the conclusion contained in the June 6, 1984 transmittal from the Assistant Secretary for Health to DEA stating that HHS had concluded that MDMA had a high potential for abuse is arbitrary and capricious because there is no explanation 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. If the Assistant Secretary for Health was to come to a different conclusion than that reached by the Commissioner of Food and Drugs, in order to fulfill the Agency's obligation to prepare a reasoned explanation for its decision, the Assistant Secretary for Health was obligated to explain why he had come to a different conclusion than the Commissioner.[17]

Furthermore, the Department of Health and Human Services did not follow its own procedures in reaching a conclusion on its recommendation with respect to MDMA. In 1975, in an article prepared by the legal staff of the Office of the General Counsel of the Department of Health, Education and Welfare, and reviewed and approved by the

---

[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 Mutual 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.

Deputy Chief Counsel of the Drug Enforcement Administration, the procedures followed by HEW were described:

> This request [from the DEA] is filed with the Commissioner of FDA, who has the responsibility for coordination of activities within HEW. The Commissioner solicits evaluations and recommendations from the affected bureaus within FDA. (E.G. Bureau of Drugs, Bureau of Veterinary Medicine), from the National Institute of Drug Abuse, and from the Controlled Substances Advisory Committee. There is no statutory requirement that HEW receive comments from, or provide a hearing to, interested parties in preparing its evaluation and recommendations. A reason for creating this advisory committee, however, is to provide a forum whereby HEW can hear from interested persons, the medical and scientific community in the public.

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

Subsequently, in 1985, the DEA published another article describing the procedures to be followed by the DEA and by the Department of Health and Human Services in scheduling drugs. That description is as follows:

> Once DEA has collected the necessary data, the Administrator of DEA (by authority of the Attorney General) requests from HHS a scientific and medical evaluation and recommendations as to whether the drug or other substance should be controlled or removed from control. This request is filed with the Assistant Secretary for Health of HHS; HHS solicits information from the Commissioner of FDA, who is responsible for coordinating activities within HHS. The Commissioner solicits evaluations and recommendations from the National Institute on Drug Abuse, and the scientific and medical community at large.

Drug Enforcement Administration, Drugs of Abuse, at 7 (1985).

Reflecting this procedure, the charter of the Drug Abuse Advisory Committee of the Department of Health and Human Services 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 Deparmtent of Health and Human Services with regard to marketing, investigation, and control of such drugs or other substances.

GG-62 (emphasis added). The Charter of the Advisory Committee, signed by the Secretary of HHS, reflects the obligation of the Commissioner to seek the advice of the advisory committee on all drug abuse matters. The purpose of this procedure is to obtain the advice of the scientific and medical community at large.

It is elementary administrative law that an agency is obligated to follow its own procedures.[18] Drs. Grinspoon, Greer, et al. respectfully submit that the failure of the Department of Health and Human Services to obtain comments from its Drug Abuse Advisory Committee -- and

---

[18] See, e.g., Morton v. Ruiz, 415 U.S. 199, 235 (1974) (it is incumbent upon agencies to follow their own procedures); Ogala Sioux Tribe v. Andrus, 603 F.2d 707 (8th Cir. 1979) (agency's failure to follow its own procedure requires remand to agency).

through it from the medical community at large and the public -- represents arbitrary and capricious agency conduct.

For all the above reasons, Drs. Greer, Grinspoon, et al., respectfully submit that the June 6, 1984 transmittal from HHS constitutes arbitrary and capricious agency action which cannot properly form any part of the basis for a scheduling decision under the Controlled Substances Act.

The June 6, 1984 transmitted 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 was the case 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 6, 1984 transmittal were not as obviously arbitrary and capricious as it is, that transmittal could not properly, in the present circumstances, be held to be binding on any issue with respect to the scheduling decision to be made by the Administrator of the DEA.

During the course of the present proceeding, very substantial amounts of evidence relevant to the three statutory criteria (e.g., medical use, medical safety, potential for abuse, dependency potential) have been received into evidence. The Government has submitted the results of numerous additional animal studies and Drs. Greer, Grinspoon, et al., have submitted one animal study. Drs. Greer, Grinspoon, et al., have submitted the testimony of twelve

psychiatrists and other expert witnesses. The Agency has called its own set of expert witnesses which have been cross-examined by counsel for Drs. Greer and Grinspoon, et al. Virtually all of this evidence has direct bearing on the scientific and medical issues that the Department of HHS transmittal of June 6, 1984 purported to comment upon. 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]

Under those circumstances, the Administrator cannot take the position that he will 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 as to those issues and therefore precludes consideration of them. To take this position, would mean that the Administrator's action would plainly be arbitrary and capricious and not based on substantial evidence, since by definition the Administrator would be ruling out at least 60 percent to 70 percent of the evidence put into the record by both the Agency and Drs. Greer, Grinspoon, et al., in this proceeding.

---

[19] See 5 U.S.C. § 706(2).

C. Required Action

Drs. Greer, Grinspoon, et al., respectfully submit that the Agency has only two courses of action open to it. Either the Administrator can review all evidence in the record and reach a decision based on the entire record on all issues that have been at issue in the proceeding. The other alternative would be for the Administrative Law Judge to prepare his recommended findings of fact and conclusions of law, and for the Administrator to forward that recommended decision to the Department of Health and Human Services for its review and comment on the scientific and medical issues as they have been developed in the course of the hearing. Once HHS has reviewed and filed its comments and recommendations back with the DEA, the parties have had a chance to comment upon those recommendations, and the Administrative Law Judge has revised his recommended decision to any extent he believes warranted on the basis of the comments of the Department of HHS, then the Administrator would be in a position to make a final decision on the scheduling of MDMA, giving the statutorily directed binding effect on medical and scientific issues to the views expressed by the Department of HHS.

Under the procedure outlined above, however, the "binding" views of HHS would have been expressed on the basis of a full record and not on the basis of the egregiously inadequate record that was before HHS in June, 1984, and without ignoring the extensive new evidence introduced

both by Agency Counsel and by Drs. Greer and Grinspoon, et al., into the present proceeding.

D. Summary

In sum, the Administrative Procedure Act prohibits any effort to give "binding effect" to the views expressed in the June, 1984 transmittal from HHS. That transmittal, in the first instance, is of no force and effect because it represents in itself arbitrary and capricious Agency action. Even if it did not, it was not based on highly relevant and probative evidence submitted by both sides to this proceeding, and any effort by the Administrator of DEA to reach a decision on the scheduling of MDMA which did not take account of all evidence in the record would be equally invalid.

V. THE LEGAL EFFECT OF THE INTERNATIONAL SCHEDULING OF MDMA

As reflected by the record in this proceeding, the Expert Committee on Drug Dependents 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. Placing MDMA in Schedule III domestically under the CSA is entirely consistent with scheduling in Schedule I internationally.

Substantial confusion is generated by the fact that the Convention on Psychotropic Substances of 1971 uses the term "Schedule I" to refer to a set of control requirements which do not in any sense translate automatically into

the legal restrictions imposed by "Schedule I" under the Controlled Substances Act. The DEA itself has recently recognized that the United States can meet its treaty obligations with respects to substances placed in Schedule I internationally by the use of schedules under the CSA other than Schedule I. The DEA took this precise position in DEA's recent proposal to move a THC formulation from Schedule I to Schedule II of the Controlled Substances Act, even though THC is in Schedule I internationally. See 50 Fed. Reg. 42184-86 (1985), 50 Fed. Reg. 42186-87 (1985).

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 requirements of Article 7 of the Convention are recited in the Federal Register notices cited above with respect to THC. We have set out earlier at pages 94 to 95 of this brief the severe restrictions that would exist on the manufacture, distribution and possession of MDMA if it were placed in Schedule III, given the dual effects of the Food, Drug and Cosmetic Act and the Controlled Substances Act.

The combined effect of the provisions of those two Acts by their own force and effect, in our judgment, satisfy the requirements of Article 7 of the Convention of Psychotropic Substances. Unlike the situation where a drug has

been licensed for interstate shipment and sale by the Food and Drug Administration, by placing MDMA in Schedule III the government through the DEA and the FDA would have total control over who can manufacture it and in what amounts, who can possess it and in what ways, who can distribute it and to whom, and for what purposes it can be distributed. Under those circumstances, there is simply no doubt that the DEA and the FDA can exercise their authority to meet the obligations of the Convention of Psychotropic Substances with MDMA in Schedule III under the Controlled Substances Act.

VI. CONCLUSION

For the reasons set out above, Drs. Grinspoon, Greer, et al., respectfully submit that MDMA should be placed in Schedule III under the Controlled Substances Act. Placing MDMA in Schedule III is the only scheduling decision consistent with the criteria for the various schedules set out in the Controlled Substances Act. Further, it will allow needed research into MDMA's psychotherapeutic potential to continue instead of obstructing it. Schedule III will still give the DEA and the FDA complete authority to review and control the use of MDMA. Finally, Schedule III will meet the obligations of the United States under the Convention of Psychotropic Substances in the event that MDMA is placed in Schedule I internationally.

Respectfully submitted,

Richard Cotton

Dewey, Ballantine, Bushby,
Palmer & Wood
1775 Pennsylvania Avenue, N.W.
Washington, D.C. 20006
(202) 862-1000

Attorney for
Drs. Greer and Grinspoon,
Professors Bakalar and Roberts

January 15, 1986

CERTIFICATE OF SERVICE

I certify that on January 15, 1986, a copy of the foregoing Brief, Including Proposed Findings of Fact and Conclusions of Law, on Behalf of Drs. Greer and Grinspoon, Professors Bakalar and Roberts was mailed, postage prepaid, to the following:

Stephen E. Stone, Esq.
Charlotte A. Johnson, Esq.
Office of Chief Counsel
Drug Enforcement Administration
1405 I Street, N.W.
Washington, D.C. 20537

Robert T. Angarola, Esq.
Robert A. Dormer, Esq.
Hyman, Phelps & McNamara, P.C.
1120 G Street, N.W.
Washington, D.C. 20005

David E. Joranson
State of Wisconsin Department of
Health and Social Services
1 West Wilson Street
P.O. Box 7851
Madison, WI 53707

Lyn B. Ehrnstein, Esq.
257 Wetherly Drive
Beverly Hills, CA 90211

Richard Cotton