REBUTTAL TESTIMONY OF GEORGE GREER, M.D. IN DEA HEARING ON SCHEDULING OF MDMA UNDER THE CONTROLLED SUBSTANCES ACT

REBUTTAL TO TESTIMONY OF DR. JOHN DOCHERTY

Dr. Docherty addresses my study as if it were an experiment to scientifically determine the efficacy of MDMA as an adjunct to psychotherapy for mental disorders. It is not and never was intended to be such a study. In the first paragraph of my report, "MDMA: A New Psychotropic Compound and Its Effects in Humans," I state:

> The information gathered here is limited because the primary purpose of the sessions conducted with MDMA was therapeutic rather than investigative. Consequently, only the therapists' observations and the subjects' reports are available for analysis. Independent psychological evaluations with testing before and after sessions [Docherty's point #3] , control group data [point #1] with double-blind assessment, vital signs during sessions (except in 2 subjects), pre- and post-session laboratory testing of organ and metabolic functions, etc., were not done.

Most people did not have diagnosable mental disorders [point #2] because this was a pilot study of the potential therapeutic use of MDMA in primarily normal and healthy subjects who simply wanted to learn from the experience. The procedure

[point #4] and setting [point #5] was intentionally varied as was the involvement of the facilitators [point #6] for the purpose of examining the potential of using MDMA in various ways. I conclude that my data supports the conclusion that MDMA does have therapeutic potential that is yet to be scientifically proven through double-blind studies.

I would like to draw a distinction here between a scientifically proven effective treatment and a medically acceptable treatment. Many treatments, especially in psychiatry, are accepted by many practitioners, but have not been proven to be effective to the satisfaction of all scientists in the field. The efficacy of psychotherapy itself, with its myriad techniques, has yet to be scientifically proven to be effective to the satisfaction of many psychiatrists and psychologists. Yet it is considered to be medically accepted treatment. It is my clinical judgment, and that of my peer review committee, that, based on my clinical experience, the use of MDMA is a medically accepted part of the treatment approach I use.

The drug is not a treatment in itself, as is the case with most drugs used in psychiatry today, but is part of a treatment program. The condition for which this program is useful is a fear of emotional injury that prevents the person from correctly judging unnecessarily self-limiting beliefs and from communicating to others certain thoughts and feelings in a

direct and open way. This condition, in the patients for whom I prescribe and administer MDMA, is rarely debilitating in terms of their being able to work and function socially, but it does restrict their potential for self-actualization and self-satisfaction. In the final analysis, their own reports stand as evidence that this conclusion is valid. Only they are in a position to determine what their goals for self-actualization and personal satisfaction are and, therefore, to what extent these goals are achieved. Treatment of such a fear-induced inhibition to learning how to achieve personal goals has been an important part of the therapy that many of my patients have sought in coming to me as a psychiatrist.

REBUTTAL TO TESTIMONY OF PROFESSOR RONALD SIEGEL

My primary criticism of Professor Siegel's testimony is that he reports no method of determination of the identity of the drugs that his informants are taking. Street drugs often contain impurities as well as other psychoactive drugs. (See the enclosed letter from Dr. Alexander Shulgin.) Mr. Sapienza's testimony [on page 10] states that a sample of MDMA obtained in the Bronx also contained PCP, a powerful and dangerous hallucinogenic drug known to cause severe adverse psychotic reactions in some people. It is possible and even likely that the samples of MDMA that were reported by Professor Siegel's subjects to cause effects "similar to effects from LSD" [point #4 on page 3] contained MDA, PCP or other substances. Outside of

one brief and highly unusual idiosyncratic reaction in one of my 76 patients, I know of no report of the effects of samples proven to be pure MDMA which have been shown to produce hallucinogenic effects. Of course, MDA does cause hallucinations at high doses, and samples purported to contain only MDMA have contained MDA [Shulgin letter]. Therefore, Professor Siegel may well be basing all of his conclusions on the abuse potential of MDMA on data contaminated by the fact that some informants unknowingly took MDA or even PCP. This lack of certainty of the drug(s) actually ingested by the informants invalidates Professor Siegel's conclusions.

In point #2, Professor Siegel states, "The full data and reasoning for these opinions is not given here due to the constraints of time." Given the above criticism, the data and reasoning is exactly what is needed in order to make a reasonable determination of MDMA's abuse potential. Without them, no rational assessment can be made, and no official agency can reasonably rely on them.

Even though Professor Siegel was dealing with individuals who may have taken contaminated samples, he reports facts that suggest that whatever substances he is assessing have low abuse potential. In his point #3, he reports that use is most commonly four times per month to less than ten times in a lifetime, which indicates a lack of dependence-producing potential. He reports

that "circumstantial-situational use, whereby users try to work through personal problems [this might be called unsupervised therapeutic use] is escalating as users become aware of claims of medical use," indicating that much of the MDMA taken is not taken to "get high" and escape from personal problems or reality in an abusive way; daily use occurs only in dealers; and compulsive and continuous use, characteristic only of drugs with high abuse potential, has not been reported. Professor Siegel is describing a drug with low abuse potential.

It is very unclear what Professor Siegel is saying in his point #6 when he discusses abuse potential and Schedule I. He certainly provides no basis for comparing MDMA to the other substances he mentions. He does state that MDMA is "a hallucinogen", but, again, gives no evidence for the basis of this opinion. Since his opinion with respect to abuse potential appears to rest on this mistaken assumption, his opinion should not be relied upon in this proceeding.

In point #7, Professor Siegel states MDMA has "no currently proven medical use in treatment." If Professor Siegel means by this statement that there have been no double-blind clinical trials, then his statement is correct. However, it is not at all the same as saying that MDMA has no "accepted" use in treatment, which is the criterion for Schedule I. The difference between these two standards has been discussed above.

Finally, in point #8, Professor Siegel mentions unspecified "untoward physical and psychological reactions ... reported to occur in medical settings." I do not know to which medical settings he is referring. All of the available written reports of the use of MDMA in medical settings have been submitted as part of the testimony of Dr's Downing, Ingrasci, Wolfson and myself. No significant or lasting untoward reactions have been reported in any of these settings.

REBUTTAL TO TESTIMONY OF DR. EDWARD TOCUS

Dr. Tocus' main point is that because no Investigational New Drug Exemptions or New Drug Applications exist for MDMA, it has no accepted medical use in treatment. It is my understanding that IND's and NDA's are filed for the purpose of getting a drug approved for marketing in interstate commerce, and not to establish medically accepted use. As mentioned in my original letter to the DEA in requesting a hearing on this matter, it is my understanding that the Food and Drug Administration has no jurisdiction over the practice of medicine. On page 2 of his testimony, Dr. Tocus states, "Approval of an IND allows the sponsor of a drug to legally administer that drug to humans." This is simply incorrect. The enclosed copy of a page from the FDA brochure on obtaining IND's states, "The FDA has no authority over the practice of medicine and cannot require a physician to prescribe or not to prescribe a drug for a

particular illness." I am not marketing MDMA, but using it only within a program of treatment in my medical practice.

On pages 6 and 7, in point #1, Dr. Tocus states, "The actual or relative potential for abuse of MDMA is evidenced by its chemical and pharmacological similarity to the Schedule I controlled substance MDA." Point #1 of Dr. Lipton's testimony clearly describes the fallacy in assuming that two drugs with similar chemical structure have similar pharmacological effects. The data included in Dr. Nichols' testimony and in the letter by Dr. Shulgin included with my original testimony clearly demonstrates that MDA and MDMA are quite different pharmacologically. Therefore, Dr. Tocus' statement provides no valid evidence that there is a similarity in abuse potential between MDA and MDMA.

In point #4, Dr. Tocus simply states that there is an abuse pattern of MDMA. However, this pattern is one of low abuse given the paucity of DAWN mentions and lack of confirmed deaths, as described in my original testimony. (In regard to the report submitted to the DEA by Dr. Arthur Rivin, M.D., I have called Dr. Rivin to obtain the details of that death, which he said occurred a few years ago. The deceased was a man in his 60's who had a history of coronary artery disease and who had been asymptomatic for quite some time. A psychologist friend had given him a sample of a drug called "Ecstasy", and he died soon afterward.

The friend later called Dr. Rivin to tell him that the drug had been taken. No sample of the drug was ever submitted for analysis, and no drugs were found in his blood on autopsy, though coronary artery disease was found. Therefore, it is impossible to determine whether or not the death was caused by or even involved MDMA.)

In point #6, Dr. Tocus states, "MDMA can produce harm to the public health." He only mentions unnamed animal studies as evidence supporting this statement. Toxicity in humans cannot be extrapolated from animal studies, therefore there is no evidence presented that MDMA can produce harm to the public health.

Point #7 offers no evidence for a dependence liability of MDMA, which underscores its low abuse potential.

I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct. Executed on May 16, 1985 in Santa Fe, New Mexico.

George Greer, M.D.

George Greer. M.D.

CLINICAL TESTING FOR SAFE AND EFFECTIVE DRUGS

INVESTIGATIONAL DRUG PROCEDURES

Before 1962, there was no requirement that the Food and Drug Administration be notified that drugs were being tested on humans.

The 1962 Kefauver-Harris Amendments to the Federal Food, Drug, and Cosmetic Act greatly strengthened the Government's authority over clinical (human) testing of new drugs.

With this new regulatory authority, the Food and Drug Administration has taken steps to:

1. Provide added safeguards for those on whom drugs are tested.
2. Improve reports by drug investigators.
3. Establish investigative procedures to supply substantial scientific evidence that a drug is safe and effective.

First Steps

Before a new drug may be tested on humans, the sponsor (usually a pharmaceutical firm, sometimes a physician) must give the FDA the information specified as a "Notice of Claimed Investigational Exemption for a New Drug" (Forms FD 1571, 1572, and 1573), known as an "IND." Copies of these IND forms may be obtained from:

Document and Records Service Section
(HFD-106)
Bureau of Drugs
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

The IND should include the following information:

a) Complete composition of the drug, its source, and manufacturing data, to show that appropriate standards exist to insure safety.

b) Results of all preclinical investigations, including animal studies. Initially, these should be directed toward defining the drug's safety, rather than its efficacy. The data must demonstrate that there will not be unreasonable hazard in initiating studies in humans. Further animal studies may be conducted concurrently with clinical studies. The Bureau of Drugs will, on request, comment on the adequacy of the proposed animal studies. The FDA generally requires as a minimum: (i) pharmacological profile, (ii) acute toxicity be determined in several species of animals and that the route of administration be that which will be used in the animal trials, (iii) short term studies ranging from two weeks to three months depending upon the proposed use to evaluate toxicity. Additional animal studies are frequently necessary.

c) A detailed outline (protocol) of the planned investigation.

d) Information regarding training and experience of the investigators. (See "Qualifications of Investigators.") Investigators are responsible to the sponsor and are required to submit, to the sponsor (not the FDA), either Form FD 1572 for clinical pharmacology or Form FD 1573 for clinical trials.

e) Copies of all informational material supplied to each investigator. (The type of information is listed in Form FD 1571.)

f) An agreement from the sponsor to notify the FDA and all investigators if any adverse effects arise during either the animal or human tests.

g) The investigator's agreement to obtain the consent of the person on whom the drug is to be tested before the test is made.

h) Agreement to submit annual progress reports and commitments regarding disposal of the drug when studies are discontinued.

Physician-Sponsored IND

When an investigator wishes to act as sponsor for the use of a drug solely as a research tool or for early clinical investigation of a drug of therapeutic or diagnostic potential (clinical pharmacology—phases 1 and 2) a simpler abbreviated form of submission is acceptable. An example would be the study of a drug that no manufacturer is interested in sponsoring. An outline of such a study should provide the following information:

1. The identity of the compound or compounds, together with the facts that satisfy the investigator that the agent may be justifiably administered to man intended.

2. The purpose of the use and the general protocol.
3. Appropriate background information, including a brief statement of the investigator's scientific training and experience and the nature of the facilities available to him.

The physician sponsoring this form of IND deals directly with the FDA. The FDA has no authority over the practice of medicine and cannot require a physician to prescribe or not to prescribe a drug for a particular illness. But physicians are encouraged to submit an IND when they use a drug for purposes other than those approved by the FDA, when the drug was marketed. This enables the FDA to accumulate data on the safety and efficacy of the drug for that kind of treatment and to share the information with other physicians.

The Clinical Investigation

The kind and extent of the investigational drug tests are crucial to producing the substantial scientific evidence of safety and effectiveness needed to approve the drug for marketing. This evidence is obtained in three phases:

Phase I

Pharmacology studies are used to determine toxicity, metabolism absorption and elimination, and other pharmacological actions; preferred route of administration, and safe dosage range. These studies involve a small number of persons and are conducted under carefully controlled circumstances by persons trained in clinical pharmacology.

Phase II

Initial trials are conducted on a limited number of patients for a specific disease treatment or prevention. Additional pharmacological studies performed concurrently on animals may be necessary to indicate safety.

Phase III

Proposals for this phase, involving extensive clinical trials, are in order if the information obtained in the first two phases demonstrates reasonable assurance of safety and effectiveness, or suggests that the drug may have a potential value outweighing possible hazards. The phase III studies are intended to assess the drug's safety, effectiveness and most desirable dosage in treating a specific disease in a large group of subjects. The studies should be carefully monitored, no matter how extensive.

The FDA receives constant reports on the progress of each phase. If the continuation of the studies appears to present an unwarranted hazard to the patients, the sponsor may be requested to modify or discontinue clinical testing until further preclinical work has been done.

30-Day Delay

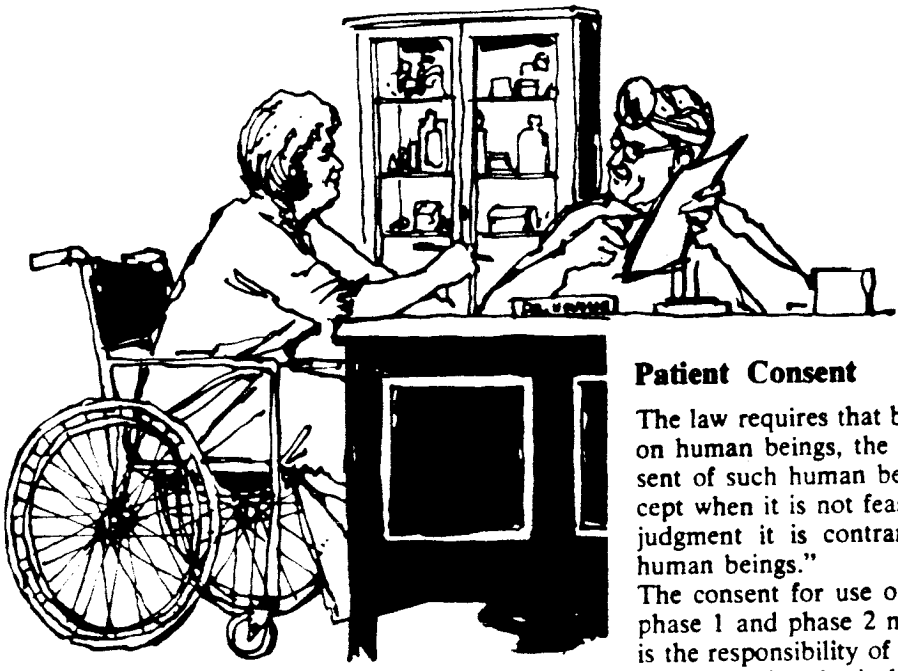
After the sponsor submits his IND, he must wait 30 days before beginning clinical tests. This delay enables the FDA to review the protocol to make certain it contains all of the necessary information and to assure that patients are not exposed to unwarranted risks. The 30-day period may be extended if the FDA feels additional time is needed for the sponsor to correct deficiencies in the protocol. The FDA also may waive the delay requirement if it feels such action is justified.

Sponsors may discuss their protocols at any time either before or during the tests with the Office of Scientific Evaluation, Bureau of Drugs.

Tests in Institutions

Drug tests on persons in hospitals, prisons, research facilities, and other institutions must be carefully supervised by institutional review committees.

The committees must be composed of persons with varying backgrounds, such as lawyers, clergymen or laymen, as well as scientists. They are appointed by the institution involved in the study. The FDA inspects the institutions periodically to determine if the committees are operating properly.



Qualifications of Investigators

The sponsor of an investigational new drug (usually the manufacturer) will ask the clinical investigator to supply the following information on Form FD 1572 (for the clinical pharmacologist engaged in phase 1 or 2 trials) or Form FD 1573 (for the physician engaged in phase 3 clinical trials):

1. A statement of his education, training and experience.
2. Information regarding the hospital or other medical institution where the investigations will be conducted; special equipment and other facilities.

The training and experience needed will vary, depending upon the kind of drug and the nature of the investigation. In phase 1, the investigator must be able to evaluate human toxicology and pharmacology. In phase 2, the clinicians should be familiar with the conditions to be treated, the drugs used in these conditions and the methods of their evaluation. In phase 3, in addition to experienced clinical investigators, physicians not regarded as specialists in any particular field of medicine may serve as investigators. At this stage, a large number of patients may be treated by different physicians to get a broad background of experience.

Obligations of Investigators

The investigator must keep careful records of his study and retain them for at least two years after the NDA is approved. The records must be made available promptly to the drug sponsor and to the FDA when required. Regular progress reports must be sent to the sponsor.

Reports must be sent to the sponsor immediately when dangerous adverse effects are observed, so the FDA and the other investigators can be notified, and the study stopped if the hazard warrants.

The regulations regarding consent of human beings given investigational drugs must be observed.

Patient Consent

The law requires that before using investigational drugs on human beings, the physician must "obtain the consent of such human beings or their representatives except when it is not feasible or when in his professional judgment it is contrary to the best interest of such human beings."

The consent for use of an investigational new drug in phase 1 and phase 2 must be in writing. In phase 3, it is the responsibility of the investigator, taking into consideration the physical and mental state of the patient, to decide when it is necessary or preferable to obtain consent in other than written form.

If written consent is not obtained, the investigator must obtain oral consent except as provided above, and record that fact in the medical record of the person receiving the drug.

Causes for Termination of Investigation

The FDA may direct the sponsor to terminate an investigation at any stage under certain conditions. These include:

Evidence of significant hazard.
Convincing evidence that the drug is ineffective.
Submission of false data.
Omission of material information.
Unsatisfactory manufacturing practices.
Failure to conduct the investigation in accordance with the plan submitted by the sponsor-and approved by the FDA.
Commercialization of the drug. The IND regulations are not intended to provide a way of marketing a drug for profit without an approved NDA.
Failure to submit progress reports at intervals not

exceeding one year.

Failure to report serious or potentially serious adverse reactions.

Failure to meet requirements for patient consent.

The Commissioner may notify the sponsor of any of the above conditions and invite immediate correction. A conference may be arranged. If the corrections are not effected immediately, the Commissioner may require the sponsor to terminate the investigation and recall unused supplies of the drug. The drug in question may not be reintroduced into clinical testing in man until additional data have been submitted to the FDA and the Commissioner has approved the proposed resumption of the study.

The Investigator and "Promotion"

The regulations forbid manufacturers or any persons acting for or on their behalf to disseminate any promotional material concerning a new drug prior to completion of the investigation.

This is not intended to restrict the full exchange of scientific findings in scientific or other communications media. Its purpose is to restrict promotional claims by the sponsor until the safety and effectiveness of the investigational drug have been established. Violation of the regulations by an investigator may result in FDA action to deny him further supplies of the drug. The manufacturer may also jeopardize his right to sponsor the investigation.

Special preclearance before Human Trials

Before starting an investigation in any of the following categories, FDA approval is required for:

a) Substances controlled under Schedule I of the Controlled Substances Act (PL 91-513).

b) Investigations of drugs so toxic that their use may be justified only under special conditions.

c) Substances proposed for treatment of drug dependence.

d) Reinstitution of drug investigations which had been terminated by the Commissioner.

Use of Drugs for Laboratory Procedures

New drugs used only for studies in vitro (test tubes) or in laboratory animals are exempted from the new-drug provisions of the Act provided they are labeled "Caution—Contains a new drug for investigational use only in laboratory research animals, or for tests in vitro. Not for use in humans."

The exemption does not apply, however, for a new drug used in vitro when this use will influence the diagnosis or treatment of disease in a human patient—for example, discs to determine the sensitivity to antibiotics of bacteria in culture, or a stick or strip of paper incorporating a reagent to test for sugar in the urine. Apparent ineffectiveness of an antibiotic sensitivity disc or a false negative test for glycosuria might well lead to an incorrect diagnosis and deprive the patient of appropriate treatment.

Before such a preparation can be marketed there must be certification (in the case of antibiotics) or approval of a New Drug Application (in the case of other drugs). For that reason, it is necessary to submit adequate proof of the effectiveness of these preparations before they can be marketed.

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
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May 17, 1985

Dr. George Greer
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Dear George:

You had asked a few days ago for me to put together some comments concerning what I had found in my various assays of samples which had been called XTC or Adam or even MDMA. I have not kept a log, so the best I can do is give you a feeling for what I have seen.

Many samples called Adam or MDMA have proved to be, in fact, MDMA, usually as the hydrochloride salt. Some have been the undiluted chemical but with varying degrees of purity; others have been diluted with inorganic salts, usually Calcium Phosphate. One had been diluted with Borax. Other samples, however, have proven to be something other than MDMA. The N-demethylated homolog MDA is usually the material present, although a number of samples from the East Coast proved to be the ethyl homolog (MDE). I have also seen trimethoxy-amphetamine (TMA) mixed with something I couldn't identify in a sample which I believe had come from Germany.

An additional point should be mentioned concerning the analysis of MDMA. Many, if not most, toxicology laboratories screen for drugs of this type by a TLC chromatographic assay coupled with a UV spectrum for quantitative evaluation. With most procedures MDMA and MDA are indistinguishable. The Seattle incomplete identification grew out of this uncertainty. And I feel as more and more labs begin looking for MDMA they will believe they have found it, even if it truly is something else. Gas chromatographic analysis can easily tell them apart, but a lot of labs don't bother.

As you had suggested, I am sending a copy of this letter on to Rick Cotton.

Our love to Requa and Autrey.

Sasha