No. 20-71433

In the United States Court of Appeals for the Ninth Circuit

SUZANNE SISLEY, M.D.; SCOTTSDALE RESEARCH INSTITUTE, LLC; BATTLEFIELD FOUNDATION, DBA FIELD TO HEALED; LORENZO SULLIVAN; KENDRICK SPEAGLE; GARY HESS,

Petitioners,

v.

U.S. DRUG ENFORCEMENT ADMINISTRATION; WILLIAM BARR, ATTORNEY GENERAL; TIMOTHY SHEA, ACTING ADMINISTRATOR, DRUG ENFORCEMENT ADMINISTRATION,

Respondents

EXCERPTS OF RECORD
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A HANDBOOK ON THE 1970 FEDERAL DRUG ACT

SHIFTING THE PERSPECTIVE

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PART I

INTRODUCTION

CHAPTER 1

DEVELOPMENT OF THE ACT

The Comprehensive Drug Abuse Prevention and Control Act of 1970 is considered by many to be a major advance in bringing some coherence and rationality into a highly diffuse area, criminal and regulatory laws dealing with federal response to drug use and control. It was designed to be sufficiently flexible to deal with the ever-changing drug scene as well as the ever-changing social conditions which require federal intervention. However, like all laws, whatever their original intent, some of the Act's provisions fall short of the mark, either in terms of need or because of lack of sufficient implementation.

Like most legislation, the Federal Drug Act was evolved with the intention to benefit the public, assist law enforcement, and bring some consistency to regulatory controls in this area. However, as is often the case with such legislation, this law was too altered by vested interests inside and outside government seeking to modify its force to suit preconceived positions. Those provisions in the Act in which the public interest was compromised are fairly obvious to the interested reader. Since this book is not intended to be an exposé, but rather a commentary on the Act itself, the activities of vested interests will be dealt with only when they are necessary to increase understanding as to the evolvement of a particular provision. The main purpose of the material presented here is to complement and explain the language of the Comprehensive Drug Abuse Prevention and Control Act of 1970.[1]

To provide better understanding of the Comprehensive Drug Abuse Prevention and Control Act of 1970, this introduction will present some of the pertinent history that led to drafting the law

1. 21 U.S.C. §§801-966.

and some of the highlights of the legislative history concerning particular provisions of the law. Following this discussion, an analysis of the Act, section by section, will be undertaken.

SETTING THE STAGE

The logical forerunner to the reform of criminal drug laws was the uniting of major parts of drug law enforcement functions. Investigation of drug offenses flows logically into the prosecution of the offender. Until 1968, law enforcement functions were scattered among the Federal Bureau of Narcotics, the Bureau of Customs, the Bureau of Drug Abuse Control (BDAC) in the Department of Health, Education and Welfare (HEW), and the Immigration and Naturalization Service of the Department of Justice. Prosecution of all drug cases was handled through the United States Attorney's Offices of the Department of Justice. The need for some reorganization was apparent to most thoughtful observers.

The first important recommendations dealing with this problem came from the First Hoover Commission in 1949.[2] Both the First (1947-49) and the Second (1953-55)[3] Hoover Commissions were established as a "Commission on Organization of the Executive Branch of the Government." Their purpose was to study and investigate organization and methods of operation of the Executive Branch and to recommend organizational changes to promote economy, efficiency and improved services; theirs was a broad mandate. One of the many areas studied by the First Hoover Commission was that of federal drug law enforcement. The Commission felt that, since there was duplication of effort by the Federal Bureau of Narcotics and the Department of Justice in their relationships with state and local law enforcement agencies, the fight against narcotic crimes would be facilitated if the Federal Bureau of Narcotics was placed in the Department of Justice. Therefore, the Commission recommended that the

2. The Commission was officially entitled the Commission on Organization of the Executive Branch of the Government. It was established and approved on July 7, 1947 by Pub. L. No. 162, 80th Congress.

3. Pub. L. No. 108, 83rd Congress, 1st Sess., 1953.

regulatory and law enforcement functions of the Federal Bureau of Narcotics, in the Treasury Department, be transferred to the Department of Justice.[4] No action was taken on this recommendation.

In contrast to the Hoover Commission, the establishment of the Prettyman Commission[5] in 1963 was for the purpose of reviewing and evaluating federal drug law enforcement and prevention functions and of recommending a program to prevent the abuse of narcotic and dangerous drugs and to provide rehabilitation to habitual drug users.

The Prettyman Commission submitted its report in November, 1963. Its recommendations were similar to those of the First Hoover Commission. "The Commission recommends that the functions of the Bureau of Narcotics relating to the investigation of the illicit manufacture, sale, other distribution, or possession of narcotic drugs and marihuana be transferred from the Department of the Treasury to the Department of Justice."[6]

The Prettyman Commission stated that the Bureau of Narcotics was an anomaly in the Department of the Treasury, because the great majority of the Bureau's activities concerned law enforcement, not taxation. The Commission recognized that taxation was only a guise for law enforcement and regulation. It felt that top Treasury officials were diluting their productivity by having to be concerned with criminal investigations when their expertise lay in financial matters. The Department of Justice was the natural haven for the Bureau of Narcotics.[7]

This recommendation, in addition to the others of the Prettyman Commission, was given greater consideration by the Administration and the Congress than the recommendations of the Hoover Commission, mainly because the times were different and there were different considerations to review. Misuse of drugs (dangerous drugs), other than narcotics and marihuana was ap-

4. Final report of the President's Advisory Commission on Narcotic and Drug Abuse, November 1963, at 33.

5. Final report of the President's Advisory Commission on Narcotic and Drug Abuse, November, 1963.

6. *Id.* at 32.

7. *Id.* at 32-33.

parently increasing, and drug abuse was spreading from the ghettos to middle class suburbia. Legislators, law enforcement and the judiciary were receiving more and more pressure to do something about drug abuse.

The misuse of dangerous drugs was of particular concern. Prior to 1951, there was no federal statute specifically prohibiting the distribution of dangerous drugs for other than medical purposes. However, federal health authorities who could not condone such activities, utilized some legal fictions to overcome the lack of specific statutory authority. For example, those accused of illicit distribution were charged with having "misbranded" the drugs, not having labeled them as required by law.[8]

Although until 1951 there was comparatively little illicit traffic in dangerous drugs, a small number of manufacturers, distributors, physicians and pharmacists were allegedly diverting these drugs into illicit channels. In that year, Congress passed the Durham-Humphrey amendment[9] to the Federal Food, Drug and Cosmetic Act, aimed at this group, which prohibited the dispensing of dangerous drugs without the prescription of a licensed practitioner. Despite the creation of this specific statutory authority, the procedures required to enforce this provision still presented a legal anomaly. Although there now existed a statutory prohibition against the act of illegally dispensing dangerous drugs, the violation charged was still the misbranding of the drugs.[10]

Throughout the early and mid 1950's, the efforts of the Food and Drug Administration concerning illicit traffic in dangerous drugs were almost solely against physicians and pharmacists. In the late 1950's and early 1960's it was discovered that, in increasing numbers, truck drivers involved in or the cause of highway

8. 21 U.S.C. §§333 (k), 352 (f), See *Sullivan v. United States,* 332 U.S. 689 (1947). This case involved the prosecution of a pharmacist for illicitly distributing dangerous drugs. Since it was prior to the Durham-Humphrey Amendment, the charge was that the pharmacist removed the labeling from the drugs and in dispensing them in this condition had misbranded them. As tortuous as the path was to obtain convictions in these kinds of cases, it is obvious that, since they were obtained, the courts were assisting in the fight against flagrant distribution of dangerous drugs.

9. Pub. L. No. 215, 82nd Cong., 1st Sess., H.R. 3298, 1951.

10. See *United States v. Carlisle,* 234 F.2d 196 (1956).

accidents were under the influence of amphetamines or barbiturates (to bring them down from amphetamines) or had these drugs in their possession. In that period, FDA's focus expanded to include the illicit distribution of dangerous drugs to truckers. Despite a growing traffic, FDA's former enforcement policy continued to exist; i.e. investigators were not to go out to seek persons violating the law but were to await the receipt of complaints and conduct follow-up investigations. This policy diminished the number of cases investigated and thereby precluded obtaining a realistic estimate of the extent of the problem.

The early 1960's also saw the public discovery of the properties of hallucinogenic substances, particularly LSD, and a growth in their usage, first in academic circles and later by "street" people. With demand for amphetamines, barbiturates and now hallucinogens, FDA's enforcement personnel began encountering a more sophisticated trafficker who was better organized to meet the demands for these drugs. FDA personnel did not have the experience in criminal investigations of this nature nor the statutory authority (i.e. to make arrests, execute search warrants or carry weapons) necessary to cope with the increasing traffic or the more businesslike criminal.

After analyzing the above mentioned setting, the Prettyman Commission recommended the following:

> The Commission recommends that the responsibility for the investigation of the illicit traffic in dangerous drugs be transferred from the Department of Health, Education and Welfare to the Department of Justice.[11] The Commission recommends that the functions of the Bureau of Narcotics relating to the investigation of the illicit manufacture, sale, other distribution, or possession of narcotic drugs and marihuana be transferred from the Department of the Treasury to the Department of Justice.[12]

The main difference between Hoover Commission and the Prettyman Commission concerned the placement of regulatory control over licit drug importation, exportation, manufacturing and distribution. The Prettyman Commission felt that regula-

11. *Supra* note 4, at 35.

12. *Supra* note 4, at 32.

tory control over licit activity involving dangerous drugs should *remain* in the Department of Health, Education and Welfare and that "the functions of the Bureau of Narcotics relating to the regulation of the legitimate importation, exportation, manufacture, sale and other transfer of narcotic drugs and marihuana be *transferred* from the Department of the Treasury to the Department of Health, Education and Welfare."[13]

The major reason set forth for the recommended transfer of functions was that it was no longer necessary to rely on Congress' taxing powers to control narcotics and marihuana;[14] therefore, the Treasury Department was an inappropriate repository for these duties. The Commission recommended that the transfer of functions be accomplished by new legislation utilizing Congress' authority to regulate interstate commerce.[15]

Valid arguments can be and have been made for both uniting regulatory and law enforcement functions in one department and for dividing such functions among two departments. Regardless of the acuity of the arguments, the most imposing obstacle was the entrenchment of the agencies concerned within their parent organizations. The most prominent argument given really rested on a desire to maintain the *status quo,* coupled with uncertainty as to new department procedures should a change occur. A major argument for unification was the overlap between joint functions, as when a legitimate drug dealer, controlled under the regulatory scheme, engages in criminal activity, such as the manufacture of prohibited substances or the diversion of dangerous drugs into illicit channels. In fact, the drafters of the Comprehensive Drug Abuse Prevention and Control Act relied on this position after a BNDD (Bureau of Narcotics and Dangerous Drugs) study revealed that 92 percent of all stimulant and depressant drugs on the illicit market had been diverted from legitimate manufacturers.[16] A companion recommendation to be discussed later, was that a specialized unit be formed in the

13. *Supra* note 4, at 35 and 36.
14. *Supra* note 4, at 36.
15. *Supra* note 4, at 36.
16. Internal BNDD memorandum (1969).

Department of Health, Education and Welfare to conduct the regulatory control of narcotic and dangerous drugs.[17]

In the ensuing years, only a portion of these recommendations were followed. The first step taken was the passage of the Drug Abuse Control Amendment of 1965.[18] This law created criminal sanctions for illegal activities involving dangerous drugs including hallucinogenic substances. It also empowered persons enforcing the law to carry firearms, execute search warrants and make arrests.[19] However, enforcement of the law was placed under the auspices of the Department of Health, Education and Welfare instead of the Treasury Department. To carry out this mandate, the Bureau of Drug Abuse Control was created within the Food and Drug Administration. The recommendation of the Prettyman Commission was put into effect; however, instead of reducing the number of agencies involved in similar tasks, the creation of BDAC created one more agency working on drug abuse problems.

To a great extent, the Drug Abuse Control Amendments reflected the philosophical convictions of health law officials rather than conventional law enforcement agencies. To demonstrate, unauthorized possession of the drugs for one's own use was not prohibited, and illicit manufacture and sale carried only misdemeanor penalties. Further evidence is that possession of a drug such as LSD, quickly becoming an emotional concern in the public mind, was not prohibited, while the majority of law enforcement officials believed that the two-to-ten-year minimum-mandatory penalty for possession of any amount of marihuana was justified.

Despite criticism from some quarters that the new law was not strong enough, it was the most important piece of legislation in the fight against the abuse of dangerous drugs in a decade. It was

17. Controversy in this area still exists today. Just recently the Department of Justice reclassified those agents who conducted regulatory operations to the status of a general investigator rather than criminal investigator. It would not be surprising to see next an attempt to transfer the entire function to the Department of Health, Education and Welfare.
18. Pub. L. No. 89-74, H.R. 2, July 15, 1965 (21 U.S.C. §3602).
19. 21 U.S.C. §372.

no longer unclear whether the manufacture and sale of dangerous drugs for other than medicinal purposes was proscribed. Control was obtained over hallucinogenic substances, and it became mandatory for all handlers of dangerous drugs to register and maintain records of the manufacture and distribution of these drugs.

The new law was quickly implemented by the Bureau of Drug Abuse Control in the Food and Drug Administration. Misuse of dangerous drugs was growing so rapidly, however, that the new law was almost immediately subject to reexamination. Public pressure began to mount to increase the penalties for dangerous drug violations and to make simple possession of such drugs unlawful. The pressure was in part due to the lurid stories of LSD "trips" and "speed freaks" dutifully reported and exploited by the media. A sense of crisis seemed to invade government at all levels. In response, Congress, with little debate in committee or on the floor of both houses, amended the Drug Abuse Control Amendments in 1968 to make simple possession of amphetamines, barbiturates, and hallucinogens a misdemeanor, and the penalty for illegal sale and manufacture increased from a misdemeanor to up to five years.[20]

Despite strong public opposition from medical and scientific groups, Congress made possession for personal use unlawful as a concession to law enforcement. Law enforcement argued that the penalty served both as a deterrent and as a warning to young people that these drugs were dangerous. It was claimed that because there was previously no penalty for use, young people felt that the drugs were not dangerous. Another argument advanced was that, in cases when undercover agents could not make a purchase from a peddler, it was often difficult to obtain sufficient evidence to successfully prosecute. With the availability of a possession offense, this difficulty was surmounted. Subsumed within this argument was the unspoken reason for wanting a possession offense—the added leverage it gives law enforcement. It is much easier to extract information from an individual who has the

20. Pub. L. No. 90-639, 1968.

threat of a prison sentence hanging over his head than one who doesn't. According to the argument, the same individual can be turned into a useful informant by continuing the threat. In most cases small-time peddlers or possessors of small amounts of drugs for their own use are not the type of criminal in which federal law enforcement professes interest. Federal agents would not focus attention on them without a possession penalty; however, with a possession penalty, it is argued, they provide a convenient first rung up the ladder to big dealers.

As a consolation to the medical and scientific communities for having provided law enforcement with this possession offense, Congress included an innovative provision in the Amendments. It stated that anyone charged with simple possession, who had not been previously convicted of a violation of dangerous drug laws, could, within the discretion of the court, be placed on probation for one year with certain conditions, usually rehabilitative in nature, set by the court; if, after the period of probation, the defendant meets all conditions of this probation, the court may then set aside his conviction.[21] This provision was aimed at the numerous youthful offenders who were being arrested and forever burdened with a criminal record. Congress' inclusion of first offender treatment for simple possession was another step in the growing recognition that illegal possession of a drug for one's own use is an offense markedly different from possession of a drug for purposes of illegal distribution or manufacture.[22]

In addition to the penalty provision of the Drug Abuse Control Amendments of 1965, the Secretary of Health, Education and Welfare was authorized to investigate and then to designate drugs that, having a potential for abuse because of their depressant or stimulant effect on the central nervous system or because of their hallucinogenic effect, should be under the control of the Drug Abuse Control Amendments.[23] This delegation of authority to the Secretary of Health, Education and Welfare was

21. 21 U.S.C. §333 (b) (3) (B).
22. H.R. Rep. No. 1609, 90th Cong., 2d Sess. (1968) at 4-6.
23. 21 U.S.C. §321 (v).

both practical and realistic; it gave him the administrative discretion to place drugs under control without having to return to Congress each time a new drug capable of abuse was discovered or presented a problem.[24]

The authority to designate drugs for control was transferred to the Attorney General by Reorganization Plan No. 1 of 1968, which moved the Federal Bureau of Narcotics and the Bureau of Drug Abuse Control to the Justice Department and combined them to form the Bureau of Narcotics and Dangerous Drugs (BNDD). In its report on the Amendments to the Drug Abuse Control Amendment, the Senate Committee on Labor and Public Welfare expressed its concern over the transfer of the subject authority with the following comment:[25]

> Since the Committee recognizes the expertise, experience, and responsibility of the Department of Health, Education and Welfare in the field of public health and drug evaluation, it directs the Department of Justice to consult with and act in conjunction with the Department of Health, Education and Welfare before designating a drug as a depressant or stimulant drug in accordance with Section 201 (v) of the Federal Food, Drug and Cosmetic Act, as amended.[26]

This statement was a forerunner of a major controversy which would develop over the same issue when the Drug Abuse Prevention and Control Act of 1970 was being considered.

The second step taken in following the recommendations of the Prettyman report was a major one. On April 8, 1968, Reorganization Plan No. 1 of 1968 created the Bureau of Narcotics and Dangerous Drugs in the Department of Justice.[27] The President's message accompanying the plan specifically stated that the move was in the direction recommended by the 1949 Hoover

24. This authority was the precursor to the scheduling system authority utilized in the 1970 Act.

25. H.R. Doc. No. 249, 90th Cong., 1st Sess., 1968. Prepared by President Lyndon B. Johnson and submitted to the Congress February 7, 1968, pursuant to Chapter 9 of Title 5 of the United States Code (5 U.S.C. §906).

26. *Supra* note 22, at 6.

27. *Supra* note 25.

Commission and the 1963 Presidential Advisory Commission on Narcotic and Drug Abuse. The new Bureau was a merger of the Federal Bureau of Narcotics and the Bureau of Drug Abuse Control. The laws to be enforced were, of course, the conglomeration of narcotic and marihuana laws, criminal and regulatory, and the Drug Abuse Control Amendments of 1965.

Some ancillary background leading to the reorganization plan is worth noting. At the time the reorganization was being considered by President Johnson, the Federal Bureau of Narcotics had a reputation for employing more than a few agents of questionable integrity. This integrity issue was further compounded by the fact that many of the agents in the new Bureau of Drug Abuse Control had been recruited from the Bureau of Narcotics. It was well known and accepted that the new organization's first priority was to be a major housecleaning. One propounded solution, to place the new Bureau of the Justice Department within the Federal Bureau of Investigation, was adamantly rejected by J. Edgar Hoover. He felt that such a move would tarnish the image of the FBI with the inevitable publicity that would occur in such a cleanup. His subterfuge argument was that drug investigations were of an initiatory nature whereas the FBI investigated crimes after the fact and that the two basic differences in investigation technique could not be resolved. Thus, the proposed integration of drug law enforcement into the larger federal law enforcement responsibility never got off the ground, and the administration decided to proceed with a reorganization which would create a brand new bureau. The housecleaning took place shortly after the Bureau was formed, evidenced by numerous resignations, adverse personnel actions and prosecutions. Internal investigations are still continuing, but the major violators have apparently been eliminated from the Bureau.

A surprising factor in the history of the reorganization is that almost a majority of the House of Representatives opposed it. At the hearings held by a Subcommittee of the Committee of Government Operations to consider the reorganization, House Resolution 1101, stating that the House of Representatives did

not favor the reorganization, was also considered.[28] There was almost total agreement about transferring the Bureau of Drug Abuse Control to the Federal Bureau of Narcotics. The controversy concerned whether to place the merged Bureau in the Department of Justice or in the Treasury Department. The main argument for the Treasury Department was that disassociating the Federal Bureau of Narcotics from drug law enforcement performed by the U.S. Customs Agency was inefficient and impractical and would cause a deterioration in the cooperation then enjoyed by the two agencies. The countervailing argument in favor of the Department of Justice was that closer cooperation with the prosecuting arms of the federal government, all housed in the Justice Department would result, and the interface with the Organized Crime Section of the Criminal Division would be facilitated. Final vote on House Resolution 1101, opposing the reorganization into the Department of Justice, indicates how close it came to being defeated; on April 2, 1968, the House rejected that resolution by a vote of 200 to 190.

All government officials affected by or concerned with the reorganization had to follow administration policy and come out in favor of the reorganization. However, there was strong internal opposition to the Plan, especially in the Treasury Department. Depending upon your point of view, it was fortunate or unfortunate that opposing government officials were not aware nor had expected that the vote would be so close. To quote a ranking official of the former Bureau of Narcotics, "If we had only known that it would have taken only six phone calls, we wouldn't be here now."

Reorganization Plan No. 1 of 1968 closed a large organization gap. Almost all federal law enforcement efforts against illegal drug activities, except for the Bureau of Customs, were now

28. Reorganization Plan No. 1 of 1968 and H. Res. 1101, Subcommittee of the Committee on Government Operations, 90th Cong., 2d Sess., March 19, 20 and 21, 1968.

being directed by the agency whose primary concern is federal law enforcement—the Department of Justice.[29]

The stage was now set for the inevitable reformation of the drug laws. On July 14, 1969, President Richard Nixon sent a message to the Congress containing ten specific steps for combatting drug abuse.[30] Proposal number one announced the following:

> To more effectively meet the narcotic and dangerous drug problems at the Federal level, the Attorney General is forwarding to the Congress a comprehensive legislative proposal to control these drugs. This measure will place in a single statute, a revised and modern plan for control. Current laws in this field are inadequate and outdated.
>
> I consider the legislative proposal a fair, rational and necessary approach to the total drug problem. It will tighten the regulatory controls and protect the public against illicit diversion of many of these drugs from legitimate channels. It will insure greater accountability and better recordkeeping. It will give law enforcement stronger and better tools that are sorely needed so that those charged with enforcing these laws can do so more effectively. Further, this proposal creates a more flexible mechanism which will allow quicker control of new dangerous drugs before their misuse and abuse reach epidemic proportions. I urge the Congress to take favorable action on this bill.

The administration's bill had been authorized and drafted by the Office of the Chief Counsel of the BNDD. It was begun during the Johnson Administration and ultimately introduced after Mr. Nixon took office. It had been subjected to drafting and re-

29. Enforcement of the laws against smuggling of drugs is still conducted by the U.S. Bureau of Customs. However, at the time of this writing, President Nixon has presented a reorganization plan which would place 500 Customs agents who investigate drug violations, BNDD, the Office of Drug Abuse Law Enforcement and the Office of National Narcotics Intelligence in a newly formed Drug Enforcement Administration in the Department of Justice.

Also, see the second report of The National Commission on Marihuana and Drug Abuse, *Drug Use in America: Problem in Perspective* (1973) which goes further and recommends the establishment of a single, independent agency incorporating all federal efforts in science, education, law enforcement, etc.

30. H.R. Doc. No. 138, 91st Cong., 1st Sess. (1969). The message dealt with 10 specific areas as follows: I. Federal Legislation, II. State Legislation, III. International Cooperation, IV. Suppression of Illegal Importation, V. Suppression of National Trafficking, VI. Education, VII. Research, VIII. Rehabilitation, IX. Training Program, X. Local Law Enforcement Conferences.

drafting and had taken over a year to complete. In the latter part of this period, Senator Thomas J. Dodd fashioned his own bill on one of the numerous drafts he had obtained and introduced it on April 18, 1969, as S. 1895.[31]

On July 15, 1969, the Attorney General submitted to the Congress the final draft of "The Controlled Dangerous Substances Act of 1969." He said that the bill:

> . . . attempts to synthesize the existing controls into one body of organic law. This had been made particularly desirable as a result of the recent governmental reorganization in which the Bureau of Narcotics of the Treasury Department and the Bureau of Drug Abuse Control of the Department of Health, Education and Welfare were merged into a single agency within the Department of Justice. These agencies formerly administered separate bodies of statutory law, one based upon the taxing power, and the other upon the commerce clause. The statutes relate to different drug classifications and provide differing regulatory mechanisms and penalty structures. In many cases, they are inconsistent with each other and cannot easily be made to coalesce in either logic or practice.[32]

The Bill was introduced by Senators Dirksen and Hruska on behalf of the Administration and, although action on it began almost immediately, it did run into some procedural difficulties. The following is a summary of the course it navigated:

> The measure was introduced in the Senate on July 16, 1969 as S. 2637, the proposed Controlled Dangerous Substances Act. In the House, however, because the Ways and Means Committee had traditional jurisdiction over narcotics and marihuana through its taxing power and because the Interstate and Foreign Commerce Committee had jurisdiction over stimulant and depressant drugs through its power to regulate interstate commerce, the proposal was introduced as two bills. H.R. 13742, the proposed Controlled Narcotic Drug Act, was introduced on September 11, 1969 and referred to the Ways and Means Committee. H.R. 13743, the proposed Controlled Depressant and Stimulant Drugs Act, was introduced the same day and referred to the Interstate and Foreign Commerce Committee.[33]
>
> Hearings were held on H.R. 13742 and H.R. 17463 (a bill combining the provisions of H.R. 13742 and H.R. 13743) on July 20, 21, 22, 23 and 27.
>
> Thereafter the Committee on Ways and Means decided to consider only the provisions relating to imports and exports of narcotic drugs, marihuana and depressant and stimulant drugs and recommended to the Interstate and Foreign Commerce Committee an amendment to H.R. 18583 which is incorporated in the Bill as Title III thereof. The reported bill is based upon the provisions of the legislation heretofore discussed; the form in which the bill is reported is designed to preserve the jurisdiction of the Ways and Means Committee over future amendments to this legislation that relate to imports and exports of drugs covered by the bill.[34]
>
> The Senate Judiciary Subcommittee on Juvenile Delinquency began hearings on S. 2637 on September 15, 1969. On December 16, 1969, the Senate Judiciary Committee favorably reported S. 3246, a clean version of the Controlled Dangerous Substances Act, and on January 28, 1970, the Senate passed S. 3246 by a vote of 80 to 0. Upon receipt of this Bill by the House of Representatives, it was retained at the Speaker's desk pending resolution of the jurisdictional difficulties which had led to the original bifurcation of the measure (on) September 11.[35]

The House of Representatives version of the bill was reported out by the Committee on Interstate and Foreign Commerce as H.R. 18583 on September 10, 1970. It passed the House by a vote of 341-6 on September 24, 1970. The bill was then sent to the Senate where it was amended and passed by a vote of 54-0 on October 7, 1970.

Because of the amendments made by the Senate, a Committee of Conference was convened to reach a compromise on the differences. The Committee reached accord and its results were re-

31. S. 1895, 91st Congress, 1st Session. A bill to reorganize and coordinate control of the narcotic and drug abuse laws under the Bureau of Narcotics and Dangerous Drugs, Department of Justice (1969).

32. Letter from John N. Mitchell to the Speaker of the House of Representatives, uly 15, 1969.

33. Letter from Richard G. Kleindienst, Deputy Attorney General to Representative Wilbur Mills, Chairman, Committee on Ways and Means, July 20, 1970.

34. House Comm. on Interstate and Foreign Commerce, Report to Accompany H.R. 18583, The Comprehensive Drug Abuse Prevention and Control Act of 1970, H.R. Rep. No. 1444 (Part 1), 91st Cong., 2d Sess. (1970).

35. *Supra* note 33.

ported on October 13, 1970.[36] On October 14, 1970, both sides of the Congress agreed to the conference report and it was sent to the President. It was signed into law by President Nixon on October 27, 1970.[37]

36. H.R. Rep. No. 1603, 91st Cong., 2d Sess. (1970).
37. *Supra* note 1.

CHAPTER 2

GETTING THE BILL THROUGH CONGRESS

On September 15, 1969, Attorney General John N. Mitchell was the first witness to testify at hearings before the Senate Subcommittee to Investigate Juvenile Delinquency of the Committee on the Judiciary.[38] The Subcommittee was considering, *inter alia* S. 2637, the Administration's Controlled Dangerous Substances Act of 1970. Attorney General John Mitchell summarized the need for the legislation as follows:

> The overall purpose of this bill is to consolidate and rationalize the patchwork of existing legislation and to bring about much needed change so that our basic Federal statutory tool is as effective and as up-to-date as possible.
>
> Currently, there are two completely separate bodies of legislation dealing with these problems. Each legislative concept has differing authorizations for administrative control, law enforcement and penalties.
>
> The Harrison Narcotic Act, which is the primary law controlling narcotic drugs, was passed in 1914. It was based on a complex regulatory and prohibitive scheme employing the Government's power to tax. This body of law was administered by the former Bureau of Narcotics of the Treasury Department. It was added to in 1937 by the passage of legislation controlling marihuana. Like the Harrison Narcotic Act, the marihuana laws are also based on the taxing power.
>
> During the postwar years, the abuse of new classes of drugs—the barbiturates, amphetamines and hallucinogens—became a national problem. Recognition of a new agency for the purpose of enforcing a new set of drug laws.
>
> This agency was the former Bureau of Drug Abuse Control within the Department of Health, Education and Welfare. It administered

38. Hearings on S. Res. 4, S. 1895, S. 2590, S. 2637 before the Subcomm. to Investigate Juvenile Delinquency of the Comm. on the Judiciary, 91st Cong., 2d Sess. (1969) at 210.

a body of law based upon the power of the Federal Government to regulate interstate commerce. In 1968, as a result of a governmental reorganization, these two agencies were merged into a single Bureau within the Department of Justice, known as the Bureau of Narcotics and Dangerous Drugs.[39]

Bringing the problem up to date, Attorney General Mitchell stated:

> At the present time, the new Bureau still administers these two distinct systems of legislation inherited from its predecessor Bureaus. This has resulted in a great deal of confusion in the regulation of the lawful manufacture of controlled drugs and in inconsistencies in the punishment of illicit drug activities. Under the existing regime, the lawful manufacturers and distributors of drugs and the scientific and medical community must comply with two dissimilar regulatory schemes, thus imposing undesirable and unnecessary burdens.
>
> One system of regulation is based on the alternatives of either the treaty power or an informal administrative proceeding.
>
> The other system, based on the Drug Abuse Control Amendments of 1965, provides a much more formal administrative proceeding to contest Governmental promulgated regulations to control dangerous drugs.
>
> Also, the current regulatory scheme has certain loopholes. For example, under the drug abuse control amendments, persons who wish to conduct research need not register, while those wishing to do research in marihuana and narcotics must.
>
> In addition, there are a number of cases in which penalties for essentially similar violations are vastly different.[40]

Focusing on the proposed legislation, the Attorney General set forth the basic system of the Act in the following manner:

> Our proposed law is aimed at eliminating the present inconsistencies which exist in regard to the administrative control of drugs. The drugs which are currently controlled under both sets of statutes have been divided into four separate schedules on the basis of: (1) the need for legitimate access to them and (2) the relative dangers and extent of abuse.[41]
>
> The main distinctions between these four categories are increasingly tough levels of Federal registration requirements and administrative control, such as the use of detailed order forms and the establishment of quotas.
>
> Perhaps the greatest advantage to this approach is that drugs may be moved from one schedule to another as scientific information and law enforcement problems come to light. The moving of a drug from schedule III, for example, to schedule I will only be done by the Attorney General upon advice in writing of a scientific advisory committee and of the Secretary of the Department of Health, Education and Welfare.
>
> By giving the Attorney General this discretion, the Congress will permit a quick response to the ever-changing problem based upon relative harm and relative abuse potential of existing drugs and newly discovered drugs.
>
> The present system requires new legislation to meet every major new drug problem.
>
> Considering the complexity of the drug problem, it would appear advisable for Congress to give the Attorney General the authority to quickly tailor the Federal approach to the then existing threat.[42]

39. *Id.* at 211, 212.
40. *Id.* at 212.
41. *Id.* at 212.

This latter provision raised a great hue and cry in the scientific community. The general feeling was that lawyers and law enforcers were not sufficiently knowledgeable in medicine and pharmacology to make the determination as to which substances should be controlled, and, if so, at what level of control.

One faction strongly opposed to the provision had originally stated its position at the time of the reorganization when jurisdiction over the Drug Abuse Control Amendments and, thereby, the authority to designate "depressant and stimulant" drugs, was transferred from the Secretary of Health, Education and Welfare to the Attorney General. The American Psychiatric Association stated the following at that time and is still of the same opinion:

> There is, however, objection to the transfer of the functions of the Department of Health, Education and Welfare. Pending some convincing reassurance to the contrary, it is our sense that the medical contribution to the national program to combat addiction and drug abuse in the form of expanded research, training and treatment in the field will be better nourished under the aegis of the Department

42. *Id.* at 214, 215.

> of Health, Education and Welfare than under the Department of Justice. The former is traditionally oriented toward the unfortunate; the latter is traditionally oriented toward the punishment of offenders. Both have their place and it is in the national interest that neither one is in the position administratively to determine the relative emphasis to be given the other in a total national effort to cope with the menace.[43]

In response, the Department of Justice pointed out that the determination to bring any particular drug under control is not simply a medical, enforcement or legal question. The criteria which must be considered before placing a drug under control have as many legal implications as medical ones. The determination to control a drug is a policy determination made after an evaluation of all available scientific and medical information and after consideration of any problems posed from either the legal or law enforcement standpoint. The Department of Justice contended that the Attorney General is the best qualified to make such a policy determination as he had the enforcement authority and manpower at his disposal to back up the policy decision and it is his responsibility to implement such a decision in terms of enforcing the regulatory and penal controls.

A further argument presented was that both the Secretary of Health, Education and Welfare and the Attorney General are Cabinet appointees who are generally chosen for the administrative abilities rather than their medical or legal acumen. Each relies on the advice and expertise of specialists in the various areas under their jurisdiction. Presented with the medical and scientific evidence regarding the proposed control or transfer of a substance, the Attorney General would be capable of making a final determination. The Department of Justice further pointed out that the procedure provided in S. 2637 was balanced, in that it required the Attorney General to "request the advice in writing from the Secretary of Health, Education and Welfare" and from a special Scientific Advisory Committee as to whether or not a substance should be added, deleted or rescheduled as a controlled substance. Thus, the Attorney General would be assured

43. *Supra* note 28, at 98.

of receiving medical and scientific input in his decision-making process.

This provision was not entirely acceptable to the Department of Health, Education and Welfare nor to many members of the medical community including the American Medical Association and the American Psychiatric Association. A compromise had to be made and one was worked out. It provided for the Attorney General to initiate control proceedings (1) on his own motion, (2) at the request of Health, Education and Welfare, or (3) on the petition of any interested party. However, before a substance could be removed from or placed under control, the Attorney General must request a scientific and medical evaluation of the substance and its effects and request recommendations from the Secretary of Health, Education and Welfare. If the Secretary recommends that a substance not be controlled, the Attorney General may not move to control the substance.[44]

In a sense, this was a hollow concession to the scientific community. In light of the emotional atmosphere and concern surrounding drug misuse, it is difficult to envision a Secretary of Health, Education and Welfare refusing to place under control a substance which the Attorney General has submitted as having a potential for abuse or as currently being abused. Through 1972, no request for control initiated by the Department of Justice has been denied by the Secretary. Further, amphetamines, Ritalin® and Preludin®, have been moved from Schedule III to Schedule II since passage of the Act, and naloxone, an antagonist, has been decontrolled and removed from the schedules.

An additional provision of the Administration's Bill was that the Attorney General need not seek the advice of the Secretary of Health, Education and Welfare if he found that control of a substance was required by United States obligations under international treaty, conventions or protocols.[45] This "end run" attempt to eliminate the Secretary of Health, Education and Welfare from rendering any decision if a particular substance was

44. This compromise was included in the final Bill and appears in 21 U.S.C. §811 (b).

45. 21 U.S.C. §811(d).

covered under the Single Convention or any future international agreement was countered by the House of Representatives. Its accepted version of the Bill (H.R. 18583) provided that the Attorney General must seek the evaluation and recommendation by the Secretary of Health, Education and Welfare in the case of any future obligations but that he need not if the control of a substance is required by existing international obligation.[46] Therefore, the Single Convention on Narcotics, 1961, and the drugs contained therein, are subject to unilateral action by the Attorney General but the proposed Psychotropic Convention of Vienna, dealing with stimulants, depressants and hallucinogens, which is presently pending before the Congress is not.[47] Despite the compromises and concessions, the infighting and intrigue—when the smoke cleared, pragmatic control over "control" remained with the Attorney General and the Department of Justice.

The concept of differentiating among drugs by placing them individually in schedules was evolved only after the expenditure of a great deal of time and energy. Government draftsmen arrived at the theory behind the schedules in a unique fashion. Industry was invited initially to submit its comments on various proposed provisions and then to sit down with government attorneys and law enforcement officers to reach a mutually agreeable manner in which to deal with the juxtapositioning of the various drugs in the various schedules and to establish the criteria by which drugs were to be distinguished. At first the scheduling

46. In a further attempt to exclude the Secretary of Health, Education and Welfare from determinations regarding substances to be controlled, Senator Hruska introduced S. 3118 in the Senate on February 3, 1972. This Bill would have amended Section 201 of the Comprehensive Drug Abuse Prevention and Control Act of 1970 so that the Attorney General could, upon his own findings, control, or except from control, any substance so provided for in the Convention on Psychotropic Substances signed by the U.S. in Vienna on February 21, 1971. (The House version of this Bill was introduced by Representative Staggers as H.R. 12875 on February 2, 1972.)

Neither the Senate or House Bill gained any support and both were not acted upon in 1972. There is currently an unintroduced version of both Bills circulating in Congress, but no action has been taken upon it to date.

47. Second report of the Commission on Marihuana and Drug Abuse, *Drug Use in America: Problem in Perspective* (March, 1973).

system appears rather mundane, but careful examination points up its importance in permitting flexibility in terms of control.

Schedule I differs from all other schedules in two major respects. First, it is not intended to be part of the sequence of the other schedules that were constructed to contain drugs in their decreasing order of relative danger. Second, it houses all drugs which have no legitimate medical use. One reason for establishing this schedule is that the segment of industry which manufactured and distributed "legitimate" drugs was very sensitive about having its products classified with illicit drugs having no legitimate medical use, such as heroin, marihuana and the hallucinogens, the most important drugs in Schedule I.

Placing heroin and marihuana in the same schedule was another source of controversy. Under the prior law marihuana was treated the same, and considered by many to be in the same category of danger, as heroin and cocaine. Offenses involving marihuana yielded the same minimum-mandatory sentences as those involving heroin and cocaine. Although the old federal law did not classify marihuana as a "narcotic," many states, which fashioned their drug laws after the federal law, placed marihuana in the statutory definition of a narcotic and made no differentiation between penalties for the drugs. With increasing evidence that marihuana was not as dangerous as many people had formerly believed, and certainly not as dangerous as the opiate drugs and cocaine, strong feelings were growing against associating them.

One alternative suggested, to have separate schedules for illicit narcotics and for hallucinogens including marihuana, was opposed for fear that increasing the number of schedules would make the law unwieldy and that similar breakdowns would be requested for drugs in other schedules. These requests would be made by manufacturers wishing to disassociate their products from other products having reputations for abuse. The matter was finally resolved through the penalty distinctions. Marihuana and heroin were kept in Schedule I; however, the penalty for importation, exportation, manufacture or distribution of heroin was set at not more than fifteen years imprisonment or a fine of

not more than $25,000 or both.[48] The penalty for the same offenses involving marihuana and all other nonnarcotic drugs was set at not more than five years imprisonment or not more than a $15,000 fine, or both.[49] This penalty scheme for marihuana and the hallucinogens in reality becomes the same as for Schedule III substances.

The intent of the scheduling system and its greatest value is its practicality and ability to adjust the regulatory framework. The criteria which must be met to qualify a drug for a particular schedule are arranged in decreasing order of relative danger from Schedule II through Schedule V. This system provides a ready-made structure for allotting penalties and regulatory controls equivalent to the criteria in the same descending order. The following is an example of how this system is organized:

Schedule No.	*Main Distinguishing Criteria*	*Penalties*	*Regulatory Control*
I.	High potential for abuse; no currently accepted medical use.	Narcotics Max. 15 yrs. $25,000	Quotas on amounts imported and manufactured Individual registration required to manufacture or distribute a specific substance
	Same	Nonnarcotics Max. 5 yrs. $15,000	Distribution only pursuant to an order form Not available through prescription
II.	High potential for abuse; has currently accepted medical use; may lead to severe psychological or physical dependence	Narcotics	Same as above, except drugs may be obtained upon *written* prescription, but may not be refilled
	Same	Nonnarcotics Max. 5 yrs. $15,000	
III.	Potential for abuse less than in Schedules I & II; may lead to moderate or low physical dependence or high psychological dependence	All drugs Max. 5 yrs. $15,000	No quotas on amounts imported or manufactured One registration covers all drugs in the schedule No order forms required May be obtained through written *or oral* prescription which may be refilled up to 5 times in 6 months

48. 21 U.S.C. §(b)(1)(A).
49. 21 U.S.C. §(b)(1)(B).

IV.	Low potential for abuse relative to Schedule III substances; limited physical or psychological dependence relative to Schedule III substances	All drugs Max. 3 yrs. $10,000	Same as III
V.	Low potential for abuse relative to Schedule IV substances; limited physical or psychological dependence relative to Schedule IV substances	All drugs Max. 1 yr. $5,000	Same as III except contains over the counter substances available for medical purposes only

Another major point of controversy arose over the administration's penalty provisions in S. 2636. Mr. John E. Ingersoll, Director of the Bureau of Narcotics and Dangerous Drugs, accompanied Mr. Mitchell during his testimony before the Subcommittee to Investigate Juvenile Delinquency.[50] Mr. Ingersoll set forth the recommended penalties as follows:

> The penalty structure in Title V closely parallels existing federal law. With regard to trafficking offense, minimum mandatory sentences are imposed for the first and subsequent offenses of unlawful distribution, importation and manufacture of Schedules I and II substances. For a first offense the range is five to twenty years, and for a subsequent offense the range is ten to forty years. Probation and suspended sentences are not permitted.
>
> No minimum mandatory is imposed for first or subsequent offenses involving distribution, importation or manufacture of Schedules III and IV dangerous substances. First offenses involving Schedule III substances are punishable by up to ten years. As to Schedule IV substances, first offenses are punishable by up to one year imprisonment and second offenses by up to two years.
>
> No minimal mandatory sentences are imposed in first offense possession cases, regardless of the drug involved. Possession of Schedules I and II substances would draw from two to ten years, but with provisions allowing for probation and suspension of schedules. Possession of Schedule III and IV substances is a misdemeanor punishable by imprisonment for up to one year. However, second offense possession of Schedules I and II substances would draw a minimum mandatory sentence of five to twenty years with no provision for probation and suspension of sentence. Second offense possession of Schedule III substances is punishable by up to three years imprisonment, and second

50. *Supra* note 38, at 218.

offense possession of Schedule IV substances would be punishable by up to two years.[51]

Any criminal penalty structure to be effective, must be acceptable to the courts, the prosecutors and the public. It must represent a rational, credible approach to the problem and must further be flexible enough to tailor the penalty to the crime and to the person committing it. In drafting any penalty structure, an effort must be made to identify the types of individuals who are engaged in the traffic and use of narcotic and dangerous drugs. To make a penalty structure more credible and directly applicable to individuals violating the laws, three distinct types of persons involved in the drug syndrome must be identified. These three types are 1) the professional criminal who is engaged in the business of supplying these drugs to others for profit; 2) the casual user or intermittent experimenter in drugs, who, for a variety of reasons, starts exploring the drug scene, usually using the nonaddicting variety such as marihuana, LSD, and other hallucinogens; and 3) drug addicts who should be isolated and identified for penalty purposes.[52]

The Administration initially attempted to toe the line on minimum-mandatory sentences. However, it was not insensitive to the fact that there were important factions in the Congress and the Judiciary who were strongly against minimum-mandatory sentences because of the negative effect they had on any possible treatment and rehabilitation of drug users and the discretion they removed from the judiciary. In order to remain flexible on this issue, the Attorney General stated the following:

> I would hope that it would be agreeable to the Committee that after the Committee has taken its full testimony in this area, that the Department be permitted to express its further opinions in the whole area of the penalty structure. I think that we can learn more than we know now, and, if it is the desire of the Committee that they have a more definitive opinion from us on this penalty structure and all of its facets, we would be glad to do so. I think that based upon the testimony that this Committee will receive, we may have further definitive opinions to express.[53]

It did not take long for various Congressional factions to react to the penalty recommendations. Senator Thomas J. Dodd had stated his opposition to minimum-mandatory penalties when he

51. *Supra* note 38, at 231.
52. *Supra* note 38, at 232.
53. *Supra* note 38, at 255.

presented a paper before the 1962 White House Conference on Narcotics. He buttressed his argument with excerpts from a Senate Report[54] which stated: "A study of the effectiveness of the Narcotics Control Act of 1956 is clearly called for. The Act is one of the harshest penal laws ever placed on our statute books, utilizing principles of deterrence and punishment as opposed to parole or probation for defendants convicted on narcotic and marihuana violations. The Act has not been in effect for more than six years. Statistics and other data suggest that it has failed in its deterrent purpose and has been most costly to the government. It has also produced many injustices and has generally had a destructive effect on prison rehabilitation programs." The report further cited statistics showing that a majority of federal prison officials, federal judges, federal probation officers and United States Attorneys were opposed to minimum-mandatory sentences.

The opposition was not only in the Congress. It arose from within the Executive Branch itself. The first voice heard was that of Dr. Stanley F. Yolles, Director, National Institute of Mental Health. He testified on September 17, 1969 before the Subcommittee to Investigate Juvenile Delinquency as follows:

> The principle and the effects of mandatory penalties defeats the whole purpose of treatment and rehabilitation of drug users; it unnecessarily limits the courts and negates the traditional American expectancy that each individual will be heard by a court of law in terms of his intent, the circumstances of his alleged offense, and his potential ability to be rehabilitated.
>
> As a result of my professional experience with drug users sentenced by the courts, I am convinced that the social and psychological damage caused by incarceration is in many cases far greater to the individual and to society than was the offense itself. Each case of drug abuse must be decided separately, from the legal as well as the medical point of view.[55]

Two other scientific notables, Dr. Roger O. Egeberg, Assistant Secretary for Health and Scientific Affairs, Department of

54. S. 1519, 88th Cong., 2d Sess., 1962.
55. *Supra* note 38, at 278.

Health, Education and Welfare[56] and Dr. Sidney Cohen, Director of the Division of Narcotic Addiction and Drug Abuse, National Institute of Mental Health,[57] shared Dr. Yolles' opinion and stated so at the same hearing.

Other than administration policy makers and law enforcement officials, there were few who supported minimum-mandatory sentences. Congress felt very strongly about this provision and soon relayed the word to the Administration. If the sentencing provisions were not softened, action on the drug bill would be dragged out. The impact of the message was not lost; it occasioned the reappearance of Mr. John E. Ingersoll before the Subcommittee to Investigate Juvenile Delinquency on October 20, 1969.[58] He acknowledged that minimum-mandatory sentences were not applicable to all types of offenders and presented three alternative penalty structures for the subcommittee's consideration. He set them forth as follows:

> All alternatives contain a professional criminal penalty of not less than five years nor more than twenty years for first offenders, and not less than ten years nor more than forty years for second offenders. All alternatives provide for up to five years and/or $15,000 for traffickers in hallucinogenic, depressant and stimulant drugs in Schedules I, II and III, with second offenses allowing for imprisonment of up to ten years, a fine of $30,000, or both, for alternatives A and B, and not less than two but not more than ten years for alternative C.
>
> All include a special parole term of two years for first offenders and four years for second offenders. All Schedule IV violations carry a penalty of up to one year, a fine of $5,000, or both. Both imprisonment and fine double for second offenders.
>
> Alternatives A, B and C, all treat possession for one's own use the same, allowing for first offender treatment at the court's discretion and imprisonment of up to one year, a fine of $5,000, or both. Possession with intent to sell is treated in all alternatives as a sale offense and sentenced accordingly as a felony.
>
> As to first offense sales of narcotic drugs in Schedules I and II, alternative A imposes a sentence of up to two years imprisonment, a fine of $25,000, or both, as well as a special parole term of three years. Second offenders are subject of up to 24 years, a fine of $50,000, or both as well as a special parole term of six years.
>
> Under alternative B, first offender sales of narcotic drugs carry a penalty of up to twelve years, and, in addition, a discretionary fine of $25,000. The special parole term is three years. Probation, suspension of sentence and parole are not permitted. Second offenses carry a penalty of not less than five years or more than $50,000. The special parole term is six years. No probation or suspension of sentence is permitted but parole is available.
>
> Alternative C first offender sellers of narcotic drugs are subject to imprisonment for up to twenty years, a fine of $25,000, or both. The special parole term is three years. Second offenders are subject to not less than five nor more than twenty years, with a discretionary fine of $50,000. The special parole term is six years. No probation or suspension of sentence is permitted, but parole is available.[59]

56. *Supra* note 38, at 683.
57. *Supra* note 38, at 289.
58. *Supra* note 38, at 663.

Mr. Ingersoll stated a preference for alternative B because it provided a minimum-mandatory sentence for a second sale offense for narcotic substances. He equated such an offender with a professional criminal engaged in drug trafficking and stated, "I think that when a man or a defendant comes around for the second time for a hard narcotics sales or distribution offense, that he is professionally engaged in this kind of activity."[60]

After much discussion within and between the Administration and the Congress, Mr. Ingersoll's preference was not accepted by the Congress. The Bill which finally passed contained only one minimum-mandatory sentence providing not less than ten years to life imprisonment for an individual engaging in a continuing criminal enterprise involving a continuing series of violations undertaken by him, as an organizer or supervisor, in concert with five or more persons and from which he derives substantial income.[61]

The position of Congress on the penalty structure was aptly stated in House Report No. 91-1444 by the Committee on Interstate and Foreign Commerce which reported on the Comprehensive Drug Abuse Prevention and Control Act of 1970:

59. *Supra* note 38, at 679.
60. *Supra* note 38, at 680.
61. 21 U.S.C. §848.

> The foregoing sentencing procedures give maximum flexibility to judges, permitting them to tailor the period of imprisonment, as well as the fine, to the circumstances involved in the individual case.
>
> The severity of existing penalties involving, in many instances, minimum-mandatory sentences have led, in many instances, to reluctance on the part of prosecutors to prosecute some violations, where the penalties seem to be out of line with the seriousness of the offense. In addition, severe penalties, which do not take into account individual circumstances and which treat casual violators as severely as they treat hardened criminals, tend to make convictions somewhat more difficult to obtain. The committee feels, therefore, that making the penalty structure in the law more flexible can actually serve to have a more deterrent effect than existing penalties, through eliminating some of the difficulties prosecutors and courts have had in the past arising out of minimum-mandatory sentences.[62]

The Administration's Bill happily expanded upon a provision first introduced in the 1968 Amendment to the Drug Abuse Control Amendments. That amendment granted first offender treatment to simple possessors of dangerous drugs not previously convicted for a drug offense. The administration's bill granted the same opportunity to simple possessors of all controlled drugs. Mr. Ingersoll, in his testimony before the Subcommittee presented the provision as follows:

> The new bill also affords first offender treatment in the case of unlawful possession. And this is a significant departure from existing law. Under this provision a person, who pleads guilty or is found guilty of possession of a controlled substance and who has no previous conviction for an offense relating to narcotics, marihuana, stimulants, depressants or hallucinogenic drugs either under federal or state law, is eligible for a conditional discharge and can be placed on probation. Upon fulfillment of the terms and conditions, the court shall then discharge him. No adjudication of guilt is ever entered on record and such a discharge is not deemed a conviction. Such a provision will in no way hamper our enforcement activities since the type of person it is aimed at is not engaged in large scale narcotic or dangerous drug trafficking or distribution.[63]

The provision appeared to present incongruous magnaminity from policy makers who wished to maintain minimum-mandatory sentences. The skeptics of this largesse were, upon close reading, soon justified.

62. *Supra* note 34, at 11.
63. *Supra* note 38, at 231, 232.

In presenting the penalty provisions, it had not been emphasized that the first offender treatment provision was one of two under which a defendant could be charged. The other provision, contained in Section 501 (d), called for a sentence of not less than two years to ten years imprisonment for simple possession of any substance in Schedules I or II. In light of the feelings of law enforcement officers and prosecutors, it is highly doubtful that first offender treatment would have been afforded to eligible defendants. This option was excised from the bill that was finally passed, and first offender treatment is available, at the judge's discretion, to appropriate defendants possessing any substance for their own use.[64]

Congress was particularly sensitive to the feelings of the country with regard to the harshness of marihuana penalties, as evidenced by the following statement from the Report of the Committee on the Judiciary on S. 3246:

> The basic consideration here was that the increasingly longer sentences that had been legislated in the past had not shown the expected overall reduction in drug law violations. The opposite has been true notably in the case of marihuana. Under federal law and under many state laws, marihuana violations carry the same strict penalties that are applicable to hard narcotics, yet the marihuana violations have almost doubled in the last two years alone.
>
> In addition, the severe drug laws specifically as applied to marihuana have helped create a serious clash between segments of the youth generation and the government. These youths consider the marihuana laws hypocritical and unjust. Because of these laws the marihuana issue has contributed to the broader problem of alienation of youth from the general society and to a general feeling of disrespect for the laws and the judicial process.[65]

In addition to the inequities in the marihuana penalties, Congress was greatly concerned over the widespread increase in the use of marihuana and the dearth of knowledge regarding the ef-

64. 21 U.S.C. §844.
65. Senate Comm. on the Judiciary, Report to Accompany S. 3246, S. Rep. No. 613, 91st Cong., 1st Sess. (1969) at 2.

cts of such use. In manifesting this concern, Senator Dodd had cluded in his Bill (S. 1895) a provision establishing a committe to study marihuana.[66] The report of the Senate Committee the Judiciary stated the general feeling as follows:

> The span of arguments on this drug ranges from the death penalty to complete legalization of the drug. The gross ignorance and misunderstanding regarding this problem aggravates it and makes it worse than it already is.
>
> It was determined that an authoritative report from a group of experts on this matter is needed to dispel the irrational fears of the public regarding marihuana and to provide understanding with respect to the substantial dangers associated with this drug.[67]

The Administration's Bill, S. 2637 did not originally call for study on marihuana, but the version reported out by the Senate idiciary Committee (S. 3246) provided for such a study as follws:

> This title authorizes the Attorney General and the Secretary of Health, Education and Welfare to appoint a committee of experts to carry out a study covering all aspects of marihuana use.
>
> The study shall include, but need not be limited to, the following matters:
>
> 1. Identification of existing gaps in our knowledge of marihuana.
> 2. An intensive examination of the important medical and social aspects of marihuana use.
> 3. Surveys of the extent and nature of marihuana use.
> 4. Studies of the pharmacology and effects of marihuana.
> 5. Studies of the relation of marihuana use to crime and juvenile delinquency.
> 6. Studies of the relation between marihuana and the use of other drugs.
>
> The study is to be completed within two years at which time the committee will submit a report of its findings and recommendations to the President and the Congress.[68]

56. *Supra* note 31, at 24. Congressman Edward I. Koch sponsored a separate bill ablishing a commission on marihuana, which was adopted by the House and cluded in their version, H.R. 18583, of the Administration's Bill. Congressman ch's Bill was H.R. 10019, 91st Cong., 2d Sess. (1969).
57. *Supra* note 65, at 2.
58. *Supra* note 65, at 10.

The House version of the Administration's Bill, H.R. 18583 revised the provision by establishing a Commission mandated to report on marihuana within one year, rather than two years, and by requiring a comprehensive study and report on the causes of drug abuse and their relative significance within a second year.[69] The House's provision eventually became Section 601 of the Act.[70]

In addition to containing points of controversy, the Administration's Bill provided law enforcement with new and expanded tools. Agents of the Bureau of Narcotics and Dangerous Drugs were given the authority to make arrests for any offenses committed against the United States.[71] This provision was specifically patterned after the total-spectrum arrest authority possessed by the Federal Bureau of Investigation.[72]

Mr. Mitchell commented on this provision in his testimony before the Subcommittee to Investigate Juvenile Delinquency as follows:

> And I believe it is important for the overall law enforcement aspects of the country that these agents be given these powers as exist in other branches and services of the Government so that they will be available for law enforcement duties as they may arise. And I think that, since we do have this reservoir of manpower, that they should be available for use in emergency situations. As you are probably well aware, I am diametrically opposed to creating any national police force of any type, form or shape, but I do believe that with these general powers these agents in the Bureau could be available on an emergency basis for proper duty.[73]

An additional, much needed authority provided for in the Act was the provision for issuance and execution of administrative-inspection warrants.[74] The warrants were to be utilized in conducting inspections of premises regulated by the new law. Pro-

69. *Supra* note 34, at 5.
70. 21 U.S.C. §801 note.
71. 21 U.S.C. §878.
72. 18 U.S.C. §3052.
73. *Supra* note 38, at 253.
74. 21 U.S.C. §880.

ding for this authority by statute was made necessary by the 967 Supreme Court decisions in *Camara* v. *Municipal Court,* nd *See* v. *Seattle.*[75] The statute requires the same kinds of con- itutional safeguards necessary for the issuance, execution, and turn of a warrant provided for by the Fourth Amendment.[76]

There is no question that the statute satisfied the requirements the *Camara* and *See* cases; however, this point was made moot the Supreme Court's holding in the case of *United States* v. *iswell.*[77] In that case, the Court held that a warrant is not nec- sary to conduct an administrative inspection of required rec- ds and stock, as long as the authority set forth in the statute thorizing the inspection is reasonably restricted in terms of ne, place and scope.[78] Thus, under this new law, there should no need to utilize the warrant section.

An important new provision, that will most likely be employed ore and more often as new areas for its use are discovered, ants the Attorney General broad subpoena power.[79] It provides

5. 387 U.S. 53 (1967) and 387 U.S. 541 (1967), respectively. The court held that, ler the Constitution, in the event of refusal to allow inspection, a warrant was uired by housing authorities to inspect a dwelling unit in a building and by re department inspector to inspect a commercial warehouse.

6. See Sonnenreich and Pinco, "The Inspector Knocks: Administrative Inspection rrants Under an Expanded Fourth Amendment," 24 Southwestern Law Journal (1970).

7. 406 U.S. 311 (1972).

8. Section 880 of the Act requires that inspections be made "at reasonable es" and describes the places which may be inspected as: (1) places where ginal or other records or documents required under this Title are kept or re- red to be kept, and (2) places, including factories, warehouses, or other estab- ments, and conveyances, where persons registered under Section 303 (or ex- pted from registration under Section 302(d)) may lawfully hold, manufacture, or ribute, dispense, administer, or otherwise dispose of controlled substances. he scope of the inspection is limited to the following: (1) to inspect and copy rds, reports, and other documents required to be kept or made under this title: to inspect, within reasonable limits and in a reasonable manner, controlled nises and all pertinent equipment, finished and unfinished drugs and other stances or materials, containers, and labeling found therein, and all other gs therein (including records, files, papers, processes, controls, and facilities) ropriate for verification of the records, reports, and documents referred to in se (1); and (3) to inventory any stock of any controlled substance therein and in samples of any such substance.

9. 21 U.S.C. §876.

that in *any* investigation (criminal and administrative) concern- ing controlled substances, the Attorney General may by subpoena compel the attendance and testimony of witnesses and require the production of any records. Should the subpoenaed person re- fuse to comply, the Attorney General may request the appropri- ate federal court to order compliance with the subpoena. Further refusal to comply could be punished as contempt.

Within constitutional parameters, the scope within which this authority may be utilized is boundless. The section preceding it in the law[80] gives the Attorney General specific subpoena au- thority for use in administrative hearings; therefore, the con- clusion cannot be avoided that the subpoena power granted here was intended by Congress to be employed in criminal investiga- tions. There is virtually no documented legislative history con- cerning this provision; thus, within constitutional boundaries, the Bureau of Narcotics and Dangerous Drugs is free to use the au- thority as it sees fit. To date, the administrative subpoena power has been used several times; however, there has been no necessity as yet to employ the general subpoena authority.

Probably the most controversial provision of this bill was the authorization of "no-knock" search warrants. Under this provi- sion agents of the Bureau of Narcotics and Dangerous Drugs are authorized to enter premises without giving notice of their au- thority and purpose, if there has been a finding by a judge or magistrate that there is probable cause to believe that if the no- tice of authority and purpose were given, either the evidence sought would be quickly disposed of, or that the officers would be placed in danger of physical harm.[81]

The provision created a general impression among civil liber- tarians that the authority would be abused and that, further, it was unconstitutional. The administration argued that no-knock authority was provided for by the common law or statutory law in at least thirty-two states and that the same provision using broader language had recently been passed by the Congress for the District of Columbia. In the District of Columbia Bill the

80. 21 U.S.C. §875.

81. 21 U.S.C. §879.

portion of the probable cause provision, dealing with evidence and danger to the police, states that a no-knock warrant may be granted if evidence "*is likely* to be easily and quickly destroyed or disposed of, or the executing officer" *is likely* to be placed in danger if notice if given, whereas the instant Bill requires that evidence "*will*" be easily and quickly destroyed or disposed of or the agent's life *will* "be placed in danger."[82]

It was further argued that New York State has had a similar statute since 1964[83] and that its constitutionality had been tested in the courts and it had been upheld.[84] The Administration relied heavily on the holding in the case of *Ker* v. *California*.[85] Their position on the *Ker* case is contained in the House Report on H.R. 18583 which states:

> That case upheld unannounced entry and seizure of narcotics without a warrant primarily on the basis of the officers need to prevent destruction of the evidence. The judgment of the exigency of the circumstances was that of the police officers, not of an independent judicial officer; yet the court upheld the search as coming within one of the permissible exceptions of the announcement of authority and purpose requirements. Among the objections of the four dissenters was reliance on the subjective judgment of the police officers.
>
> While decided by a closely divided court six years ago, *Ker* has not been overruled or limited with respect to unannounced entry in subsequent cases. In *La Peluso* v. *California*, 385 U.S. 829 (1966), the Supreme Court refused to reconsider it. *Sabbath* v. *United States*, 391 U.S. 585 (1968), while holding unannounced entry by Federal officers invalid on the basis of 18 U.S.C. §3109, did not disturb the constitutional holdings in *Ker*. (See footnote 2, 391 U.S. at 591.)
>
> In a somewhat related area, the Court has very recently recognized the valid governmental interest in preventing harm to the officer or destruction or concealment of evidence. *Chimel* v. *California*, 395 U.S. 752 (1969), involved the permissible scope of searches incident to the execution of an arrest warrant. It held that "contemporaneous searches" must be limited to the person of the arrested individual and the immediate area under his control. The holding is premised on the concept that warrantless searches are permissible under the Fourth Amendment only for certain limited purposes. As in unannounced entry cases, one of these purposes is the prevention of the destruction of evidence. (See 395 U.S. at 763.)
>
> *Ker* is still controlling law with respect to the constitutionality of unannounced entry and is reinforced by the rationale of *Chimel*. On the basis of *Ker*, it is the view that subsection (b) is constitutional.[86]

82. Sonnenreich and Ebner, "No-knock and Nonsense: An Alleged Constitutional Problem," 44 St. Johns Law Review 626 (1970).
83. N.Y. Crim. Proc. §799 (McKinney, 1964).
84. *People v. DeLage*, 16 N.Y. 2d, 289, 266 N.Y. 2d 353 (1965), cert. denied, 383 U.S. 963 (1966).
85. 374 U.S. 23 (1963).

Interpretation of the *Ker* case was not entirely one-sided. A minority of four Congressmen on the Committee on Interstate and Foreign Commerce strongly disagreed with the majority interpretation of the *Ker* decision.[87] The dissenters on the House side had compatriots in Senators Sam J. Ervin, Jr., and Philip A. Hart of the Committee on the Judiciary who were also firmly against the authorization of "no-knock" search warrants. Both the Congressmen and the Senators felt that the provision was of "doubtful constitutionality" and that it was an "unwise policy" to allow law enforcement officers to enter premises without notice. Senator Ervin's and Senator Hart's dissenting opinion may be found in the "Additional Views of Messrs. Ervin and Hart" in the Report of the Committee on the Judiciary on the Controlled Dangerous Substances Act of 1969.[88]

Senator Ervin was adamant in his opposition to the no-knock provision. His final statements on the matter were eloquent and he offered an amendment striking out the offending provision.[89] His amendment was defeated by a vote of 42 to 20. Despite the efforts of the opposition, and after a great deal of publicity, public reaction and argument on the floor of the Congress, the administration prevailed and efforts to remove the "no-knock" provision from the Bill were defeated.

86. *Supra* note 34, at 25, 26.
87. *Supra* note 34, at 86.
88. *Supra* note 65, at 157.
89. 116 CONG. REC. S. 17405-33 (daily ed. October 7, 1970).

conflicting definitions and statutes. To date, no such guidelines exist.

On December 15, 1972, the Food and Drug Administration promulgated regulations[125] declaring methadone maintenance a treatment for dependence on heroin and other morphine-like drugs and setting up guidelines for the use of methadone.

125. 37 F.R. 26790, December 15, 1972.

CHAPTER 6

TITLE II—CONTROL AND ENFORCEMENT

A—INTRODUCTION

TITLE II IS A SYNTHESIS of earlier versions of the law designated as the Controlled Substances Act or Controlled Dangerous Substances Act,[126] to which much of the Congressional literature and commentary has been directed. It represents, in great part, a radical departure from previous legislation and reflects the changing emphasis in drug control. This Act is a definite movement from strict control and harsh penalties for the drug abuser to a greater concern for control of the sources of supply. It also represents acceptance by legislators that the penalties for marihuana and nonnarcotic psychotropic drugs were inconsistent with their current known effects.[127]

Constitutional Basis in the Commerce Clause

Early federal narcotic legislation was grounded in the taxing power, a decision which rendered later enforcement burdensome and artificial. Subsequent legislation rendered the taxing aspect of enforcement incidental, without actually negating the underlying constitutional basis.[128] The Comprehensive Drug Abuse Prevention and Control Act logically and efficiently makes control of opiates and other dangerous substances subject to federal control on the following Congressional findings:

A major portion of the traffic in controlled substances flows through

126. For earlier drafts of the Act, see S. 2637, introduced July 16, 1969; S. 3246, introduced December 16, 1969; and H.R. 17463, introduced May 6, 1970.

127. *Supra* note 112.

128. Act of Nov. 2, 1951, Ch. 666, 65 Stat. 767; Act of July 18, 1956, Ch. 629, 70 Stat. 567.

interstate and foreign commerce. Incidents of the traffic which are not an integral part of the interstate or foreign flow, such as manufacture, local distribution and possession, nonetheless have a substantial and direct effect upon interstate commerce because:

(A) after manufacture, many controlled substances are transported in interstate commerce;

(B) controlled substances distributed locally usually have been transported in interstate commerce immediately before their distribution; and

(C) controlled substances possessed commonly flow through interstate commerce immediately prior to such possession.

Local distribution and possession of controlled substances contribute to swelling the interstate traffic in such substances. Controlled substances manufactured and distributed intrastate cannot be differentiated from controlled substances manufactured and distributed interstate. Thus, it is not feasible to distinguish, in terms of controls, between controlled substances manufactured and distributed interstate and controlled substances manufactured and distributed intrastate. Federal control of the intrastate incidents of the traffic in controlled substances is essential to the effective control of the interstate incidents of such traffic.[129]

It was expected that the use of the Commerce Clause as a basis for the consolidated domestic provisions would draw a certain degree of litigation and challenge, particularly by attorneys representing defendants in criminal prosecutions under the Act. Indeed, it might be argued that an attorney would have been remiss in not raising the issue at some point in the criminal prosecutions arising after the effective date of the enactment. Nevertheless, the basis in the Interstate Commerce Clause has been validated in the case of *United States* v. *Lopez*,[130] in which the prosecution alleged conspiracy to possess with intention to distribute cocaine and the actual distribution of cocaine and heroin. The defense took the novel position that Congress exceeded its power under the Commerce clause by assuming, and not requiring the government to prove, that the substance in question did in fact affect interstate commerce.

The Fifth Circuit Court of Appeals dismissed the appellant's argument, citing several cases which stand for the proposition

129. 21 U.S.C. §801.
130. 461 F. 2d 499 (1972).

that "it is well settled under the Commerce Clause that the power of Congress extends to those activities intrastate which so affect interstate commerce . . . as to make their regulation an appropriate means to the attainment of a legitimate end. . . ."[131] The Court concluded that "Congress had a rational basis for finding that controlled substances manufactured and distributed on an intrastate basis could not be differentiated from those manufactured and distributed on an interstate basis."[132] Hence, the Court upheld Congress in its determination that the *intrastate* substances must be controlled in order that the *interstate* substances could be controlled.

International Conventions

Section 7 of Title II also specifically incorporates the Single Convention on Narcotic Drugs, 1961 and other international conventions into the Act. Subsequent modifications or amendments to these international treaties would, of course, become controlling as federal law. At the time of drafting this Act, the Congress was aware of the proposed Psychotropic Convention, which deals with those controlled substances not included in the Single Convention. The original drafting of the Act would have placed prospective international treaties in the same category as the Single Convention with respect to negating the requirements for HEW and Department of Justice approval prior to control. After much discussion in Executive Committee meetings of the House Interstate and Foreign Commerce Committee, the exception was permitted only for the Single Convention. The attempt now to circumvent the Act, so that the Psychotropic Convention provisions would be in the same posture for control purposes as those of the Single Convention, is directly contrary to the intent of the Congress and the final position of the Administration.[133]

Definitions

Section 102 contains the operative definitions for Title II which are also incorporated into Title III. However, some defini-

131. *Id.* at p. 4.
132. *Id.* at p. 8.
133. *Supra* note 47, at 230.

tions, notably that of "narcotic addict," are different in Titles I and II. Only those definitions which require comment or emphasis apart from their statement in the Act are discussed. The parenthetical numbers preceding each definition correspond with the appropriate subsection number in Section 102. These include:

(1) "Addict": This term is defined to include any individual who uses any narcotic drug so as to endanger the public morals, health, safety or welfare or who has no power of self-control with reference to his addiction. The definition is strikingly different from that contained in Title I and perpetuates the earlier "addict" designation of opiate addiction, rather than the broader "drug dependent person" definition of the World Health Organization upon which the Title I definition is based. It would seem that the definition is broad enough to encompass psychological as well as physical addiction, thus bringing it within the scope of current medical authority and certain controlled substances, such as amphetamines, that have minimal physical dependency but severe psychological dependency.[134]

(2) "Administer": This term covers the *direct application,* in any manner and by any means, of a controlled substance to the body of a patient or research subject (including animals) by a practitioner or by his authorized agent or by the patient or research subject at the discretion of the practitioner. The definition requires that the application be performed in the presence of the practitioner regardless of who actually administers the drug.

(3) "Agent": This term means an authorized person (including a corporation) lawfully acting for a manufacturer, distributor or dispenser. Common or contract carriers, public warehousemen and their employees are excepted when acting in the usual and lawful course of their business.

(5) "Control": The term is new to drug law terminology, but its definition in the Act is self-explanatory. It refers to the procedure by which a drug is added to, deleted from or moved within five schedules contained in Part B of the Act.

134. *Supra* note 47, at 120.

(6) "Controlled substance": This is a new term of art, replacing opiate-depressant-stimulant drug terminology and covers all substances subject to Title II. Chemical precursors, as well as drugs, fall within this definition.

(7) "Deliver" or "delivery": The definition of these terms covers the actual, attempted or constructive transfer of a controlled substance. It is purposely broad in scope so as to cover every aspect of the transfer of controlled substances from one person to another.

(10) "Dispense": This term covers the delivery of a controlled substance to an ultimate user or research subject by a practitioner or pursuant to his lawful order. The term includes the prescribing and administering and the packaging, labeling or compounding necessary to prepare the substance for delivery. A "dispenser" is a practitioner who delivers a controlled substance to an ultimate user or research subject. The intent and reason for the delivery determines the definition of the transfer for the purposes of the Title and the corresponding legal consequences.

(11) "Distribute": This term means to deliver a controlled substance and includes attempted or constructive delivery. The term does not include administering or dispensing a controlled substance. In other words, distribute *generally* pertains to the illicit delivery of a controlled substance.

(14) "Manufacture": This term covers the production, preparation, propagation, compounding or processing of a drug or other substance from a plant, from other natural sources or by chemical synthesis. By virtue of the definition of the term "production," manufacture also includes the growing of a controlled substance, such as marihuana or peyote.

(15) "Marihuana": The definition for this term is the same as under existing law.

(16) "Narcotic drug": The definition for this term is the same as under existing federal law including the compounds of coca leaves such as cocaine, that are not pharmacologically classified as narcotics.

(17) "Opiate": The definition of this term is the same as under existing federal law.

(20) "Practitioner": This term limits and describes those who can legitimately "administer" and "dispense" under the Title. It encompasses all medical doctors, pharmacies, hospitals or any other person (as defined in 1 U.S.C. §1) permitted under either federal or state law to distribute, dispense, conduct research, administer or use in teaching of chemical analysis a controlled substance in a professional practice or research.

(21) "Production": This includes the manufacturing, planting, cultivating or harvesting of a controlled substance. This definition is an attempt to bring all natural means of growth and synthetic manufacturing of controlled substances within the regulation of the Title and is significant in that it expands the definition of manufacture.

(22) "Immediate precursor": This term is defined as a substance which is the key drug, active ingredient or "immediate chemical intermediary" used or likely to be used in the manufacture of a controlled substance. Under this definition, BNDD has the authority to regulate the intermediate chemicals used in drug manufacture, as well as the final synthesized product. This definition represents a major expansion of the authority to regulate and control various substances. Any "immediate precursor" that is controlled is subject to the same reporting, licensing and regulatory requirements as those for other controlled substances.

(25) "Ultimate user": This term is a modification of an existing definition and is a key term throughout the Act. It refers only to a person who has *lawfully* obtained *and* who possesses a controlled substance for his own use, for the use of a member of his household, or for an animal owned by him or a member of his household. The key word here is "lawful," in that in order for a person to lawfully obtain a controlled substance, it must be dispensed to him pursuant to the lawful order of a practitioner. If the substance is not obtained lawfully, then the person does not fall within the definition of "ultimate user" and thus is not exempt from registration under Section 302. Furthermore, a person who has lawfully obtained a controlled substance, but who possesses it for a purpose other than one spelled out in the definition (i.e. intent to distribute) falls outside the "ultimate user" category and thus is no longer exempt from registration.

PART B—AUTHORITY TO CONTROL: STANDARDS AND SCHEDULES

This portion of the Act was one of the focal points of attention for the House Committee on Interstate and Foreign Commerce. Considerable controversy arose in the Subcommittee on Public Health and Welfare over whether the Department of Justice should have the drug control authority or whether it should be placed in the Department of Health, Education and Welfare.[135]

Originally, the Act gave the Attorney General final authority to determine which substances should be controlled pursuant to Section 811 (a), after consultation with the Secretary of Health, Education and Welfare. Substantial opposition to this provision developed within what might best be called the scientific-medical-pharmacological community. The opposition argued repeatedly that the Justice Department, despite an expanded scientific presence in BNDD, did not possess the requisite scientific expertise nor the desired *scientific* objectivity to effectively perform this function.[136] The Department of Justice maintained that drug control entailed as many legal considerations as medical ones.[137]

Ultimately the question was resolved by compromise. The Attorney General retained the authority to initiate proceedings to control a substance, to move a controlled substance within the schedules, or to delete a substance already controlled; but to the Secretary of HEW was delegated the responsibility of providing medical and scientific evaluation of the substance. Subsection

135. See testimony of Mr. John E. Ingersoll, Director, Bureau of Narcotics and Dangerous Drugs, before Subcommittee on Public Health and Welfare of the House Committee on Interstate and Foreign Commerce, February 3, 1970, March 3, 1970.

136. *Hearings on S. 1895 et al. before the Subcommittee to Investigate Juvenile Delinquency of the Senate Judiciary Committee,* 91st Cong., 1st Sess., pp. 279, 317 (1969), statement of Dr. Henry Brill, Chrmn., Amer. Med. Assoc. Comm. on Alcoholism and Drug Dependence (at 317), and testimony of Dr. Stanley Yolles, Dir., Nat'l. Inst. of Mental Health (at 279).

137. *Supra* note 135.

(a) further provides that the Secretary's evaluations and recommendations are binding on the Attorney General as to medical and scientific matters; and a recommendation by the Secretary that a substance not be controlled is binding on the Attorney General.[138]

Further controversy developed over the question of the number of control schedules in the Act and the criteria to be utilized in placing substances in those schedules. The original legislation contained only four control schedules; the enacted provision established five. Much of the opposition to the four-schedule structure was from industry interests in minor tranquilizers. The position taken by these interests—that many tranquilizers have a potential for abuse which is substantially less than that of the other Schedule IV substances (amphetamines and barbiturates)—eventually prevailed, and a fifth schedule (having minimal controls) was created. Despite strenuous objection by the Justice Department, a five-schedule system was adopted. At the same time, however, more stringent regulatory controls were established for the substances remaining in Schedule IV.

Sec. 811. Authority and Criteria for Classification of Substances

Subsection (a) authorizes the Attorney General, under the rule-making procedures of the Administrative Procedures Act,[139] to add a substance to a schedule or transfer a substance between schedules if he finds that the substance has a potential for abuse and that it fits the criteria of the schedule in which it is to be placed. The Attorney General is also authorized to remove a substance entirely from the schedules if he finds that it no longer fits the requirements for inclusion in any schedule. Action may be initiated at the request of HEW or on the petition of an interested party, as well as by the Attorney General.

Regulations implementing these procedures are now effective

138. *Supra* note 48.

139. 5 U.S.C. §551 *et seq*.

and provide for a full administrative hearing before a hearing examiner appointed by the Civil Service Commission.[140] By being able to operate under these rule-making procedures, BNDD is able to avoid many of the cumbersome features of the control procedures of Section 701 (e) of the Federal Food, Drug and Cosmetic Act, which it had been operating under for some two years.[141] The most significant difference is that under the Comprehensive Act, once the hearing is completed and the rule issued, the drug is automatically controlled and no stay of the control order pending judicial review need be granted. Under the old 701 (e) procedures, a stay was customary pending judicial review.

Subsection (b) sets out the procedures which the Attorney General must follow prior to initiating control proceedings. After gathering necessary data, he must request from the Secretary of Health, Education and Welfare a medical and scientific evaluation and his recommendation as to whether or not the substance should be controlled. The Secretary's evaluation and recommendations must take into account such things as the drug's pharmacological effects, the state of scientific knowledge regarding the drug, the public health risk and the drug's psychic or physiological dependence liability. The Secretary must also consider, from a medical and scientific standpoint, the drug's actual or relative abuse potential, its current pattern of abuse and the scope and significance of its abuse.

In addition to recommending whether or not the drug should be controlled, the Secretary must give his recommendations as to the schedule in which the drug should be placed. If the HEW recommendation is against control, the Attorney General is

140. See generally 21 CFR §308.41. These rulemaking procedures have already been implemented in transferring the amphetamines from Schedule III to Schedule II (36 F.R. 12734).

They will be further utilized in the upcoming transfer of short-acting barbiturates from Schedule III to Schedule II and the anticipated controlling of methaqualone.

141. 21 U.S.C. §371.

barred by that recommendation from further proceedings, since all medical and scientific findings are binding upon the Attorney General. This provision was designed to prevent the Attorney General's conducting his own research in the event he was dissatisfied with HEW's scientific and medical evaluation. However, the Attorney General is not bound by a recommendation from HEW that a drug *should* be controlled.

Subsection (c) sets out other factors which the Attorney General must consider with respect to any substance he proposes to control. The factors set out are substantially similar to those the Secretary of Health, Education and Welfare must consider.

Subsection (d) provides that where control of a substance is required under international treaties, protocols or conventions, in effect on October 27, 1970, the Attorney General is authorized to control them without regard to the findings and procedures required in Sections 811 and 812. This Subsection will generally apply only to those substances designated as narcotics by the World Health Organization and brought within the purview of the Single Convention on Narcotic Drugs, 1961.[142]

Subsection (e) permits the Attorney General to control an immediate precursor and place it in the same schedule as the substance of which it is a precursor or in a schedule with a higher numerical designation. Again, control of immediate precursors is without regard to the findings and procedures required by Sections 811 and 812.

Subsection (f) provides a procedure which will give the Attorney General advance notice of new drugs coming on the market which may have a potential for abuse. Any time a new drug application is submitted to the Federal Food and Drug Administration for any depressant, stimulant or hallucinogenic drug, such information must be forwarded to the Attorney General if it appears that the drug has an abuse potential. This will enable the Attorney General to initiate control proceedings, and, in many

142. *Supra* note 47, at 120.

instances, actually control the drug before it comes on the market.[143]

To date, this procedure has not always been successful. In one instance, FDA failed to notify BNDD of an approved new drug application for the drug *Tranxene®*, a tranquilizer which FDA felt had a potential for abuse, until three months after the drug had begun to be marketed. Steps have been taken to prevent another such occurrence.[144]

Subsection (g) preserves the functions of the Federal Food and Drug Administration in regulating nonnarcotic drugs which may be sold over the counter without a prescription by requiring the Attorney General to exclude any of these drugs from the schedules.

Sec. 812. Schedules of Controlled Substances

This Section contains the five schedules in which all substances subject to control are listed. Each schedule has its own criteria for drug placement, such as the degree of abuse potential and the degree of psychological or physical dependence liability. With the exception of Schedule I, the criteria for each schedule are relative to one another. The major dividing line comes between Schedules I and II in that no drug listed in Schedule I has

143. BNDD has established its own early warning system called Drug Abuse Warning Network (DAWN). The purpose of the DAWN operation is: 1. The identification of drugs currently being abused and/or associated with harm to the individual and society. 2. To the extent feasible, determination of existing patterns of drug abuse and observation of changing trends including detection of new abuse entities and new combinations. 3. Provision of data for the assessment of the relative hazards to health and the relative abuse potential for substances with current human experiences. 4. Provision of data needed for rational control and scheduling of drugs of abuse, both new and old.

Information is obtained from the following five sources which BNDD feels provide the greatest input in fulfilling their purposes: 1. Inpatient units of nonfederal, short-term general hospitals (as defined by the American Hospital Association). 2. Emergency departments, located in nonfederal, short-term general hospitals. 3. County medical examiners or county coroners. 4. Student health centers. 5. Crisis intervention centers not directly affiliated with colleges and universities.

144. Dextromethorphan is specifically excluded from any schedule by Section (g)(2).

a currently accepted medical use in treatment in the United States. The drugs in all the other schedules have currently accepted treatment uses in the United States.

Schedule I contains certain opium derivatives and opiates which have no medical use in the United States. None have ever received a New Drug Application under the Federal, Food, Drug and Cosmetic Act;[145] thus they cannot be marketed in interstate commerce. Schedule I also contains a number of hallucinogenic drugs, including marihuana and the tetrahydrocannabinols. The hallucinogens are listed in Schedule I purely for regulatory purposes since they have no accepted medical use in this country. This raises an interesting speculation. Despite any moral bias with regard to marihuana, if it proves successful in treatment, such as in reducing intraoccular eye pressure in glaucoma, then it must be rescheduled to a lower schedule because of its medical use. The same would be true of LSD in the treatment of terminal cancer patients and heroin dependence, should it ever be used as a maintenance regimen.

Schedule II contains opium, coca leaf derivatives, the Class "A" narcotics, such as methadone and morphine, and the amphetamines. Liquid methamphetamine was inserted into Schedule II as a compromise measure during the House-Senate conference on the Act.[146]

The Act passed the House with amphetamines and amphetamine-like substances in Schedule III, but the Act was amended in the Senate to list all these drugs in Schedule II. An attempt was made to compromise, with the result that all liquid injectible forms of methamphetamine were listed in II and all other amphetamines were left in III.[147] BNDD's position at that time was that there were too many varieties of amphetamines and amphetamine compounds to be considered to arbitrarily and immediately transfer all of them from Schedule III to Schedule II. They stated that they would move administratively to effect this transfer

145. 21 U.S.C. §505.
146. *Supra* note 111.
147. *Supra* note 111, at 9.

as soon as due consideration was afforded the drugs involved. They acted almost immediately after the Act was approved and the transfer was made uncontested on July 7, 1971.[148]

Schedule III contains the short-acting barbiturates and the Class "B" narcotic drugs, such as empirin and codeine preparations. Paregoric is also listed in Schedule III. As noted earlier, BNDD is presently seeking to move all the short-acting barbiturates into Schedule II.

Schedule IV, which was the new fifth schedule added in the House, contains certain major and minor tranquilizers and the long-acting barbiturates. Schedule V lists all the exempt narcotic preparations which may be sold over the counter without a prescription.

The most notable feature of the scheduling scheme is that it directly relates to the regulatory system and the penalty structure. The degree of regulatory control imposed over a given drug depends upon the schedule in which the drug is listed. The penalty imposed for a violation involving a given drug will depend upon the schedule in which the drug is placed and whether it is classified as a narcotic or a nonnarcotic. This becomes extremely important in light of the fact that drugs can be moved up and down within the schedules administratively. When a substance is moved from Schedule III to II, for example, the regulatory controls tighten drastically; however, the penalties for a violation involving that substance may or may not change, depending on whether it is a narcotic or nonnarcotic.

As a result of this approach, the Federal Government finally has the statutory structure which will permit greater responsiveness to the dynamics of the nation's use of drugs and other chemical substances and from which it can respond with greater accuracy and propriety to the varying crises which, from time to time, may arise. At the same time, the regulatory scheme can be used to loosen as well as tighten controls if time or scientific fact show that present regulation is too severe or is exacting too many social costs. The true test of this system will be in loosening re-

148. 36 F.R. 12734, July 7, 1971.

straints when justified. A scheme that is directed only towards tighter and tighter controls will, in time, lose its most important attributes, flexibility and the capacity to adjust to changing social circumstances.

PART C—REGISTRATION OF MANUFACTURERS, DISTRIBUTORS AND DISPENSERS OF CONTROLLED SUBSTANCES

Part C of Title II establishes the statutory framework by which the federal government seeks to regulate the use of controlled substances in approved circumstances. Among other things, it provides for registration of manufacturers, distributors, researchers and dispensers; authorizes inspections of establishments utilized by registrants and applicants for registration; establishes minimum labeling and packaging requirements; directs that the Attorney General establish production quotas for Schedule I and II substances; and establishes prescription regulations for dispensing controlled substances. This portion of the Act received careful attention throughout the development of the legislation because of its necessarily significant impact upon the pharmaceutical industry and medical and research professions.

Section 821. Rules and Regulations

This Section authorizes the Attorney General to promulgate rules and regulations necessary for the implementation of the regulatory provisions contained in the Act. It also authorizes him to charge "reasonable" fees relating to the registration of manufacturers, distributors and dispensers under the Act.[149] These fees are not intended to cover the entire cost of industry regulation by BNDD, but rather are intended to offset some of the expenses incurred in the handling and processing of registration forms and applications.

Section 822. Persons Required to Register

Subsection (a) requires all persons manufacturing, distributing or dispensing controlled substances, or intending to manufacture, distribute or dispense controlled substances, to annually register with the Attorney General. The annual, as opposed to permanent, registration requirement is intended to give the Attorney General the means of reviewing a given registrant's activities during the year and, if circumstances warrant, the means of denying annual renewal of registration.

149. Registration fees are: Manufacturers, $50.00; Distributors, $25.00; Dispensers, $5.00; Researchers, $5.00; Instructors, $5.00.

Subsection (b) specifically authorizes registrants to manufacture, distribute, dispense, possess or conduct research with controlled substances to the extent authorized by their registration. This Section was inserted to make clear that persons registered were lawfully entitled to handle controlled substances.

Subsection (c), which exempts such persons as agents and employees of registrants, common or contract carriers, warehousemen, and ultimate users from registration, was incorporated primarily to insure that a given establishment was registered and that the employees working within that establishment would not have to register. An example is the case of the chain drug store where pharmacists are rotated from store to store. Insurmountable problems would arise in the record-keeping and inventory procedures if each individual pharmacist were required to register since it is the registrant who is responsible for the records and inventories. But where the actual pharmacy is registered, there is no need to register the employee pharmacists since the "establishment" itself will be responsible for conforming with the regulatory requirements.

Section (d), which permits the Attorney General to waive the registration requirements for a given person, is in reality a carryover from previous law. Under previous law, such persons and places as Veterans Administration hospitals, Civil Defense personnel and military personnel were exempted from registration.[150]

Subsection (e) requires a separate registration for each principal place of business or professional practice where controlled substances are manufactured, distributed or dispensed. The reasons for this separate registration requirement are many. One is to insure that BNDD knows all plants where controlled sub-

150. 26 U.S.C. §4772.

COMMERCE, JUSTICE, SCIENCE, AND RELATED AGENCIES APPROPRIATIONS FOR FISCAL YEAR 2019

WEDNESDAY, APRIL 25, 2018

U.S. SENATE,
SUBCOMMITTEE OF THE COMMITTEE ON APPROPRIATIONS,
Washington, DC.

The subcommittee met at 2:32 p.m., in room SD–192, Dirksen Senate Office Building, Hon. Jerry Moran (Chairman) presiding.

Present: Senators Moran, Shelby, Alexander, Murkowski, Collins, Graham, Boozman, Capito, Lankford, Kennedy, Shaheen, Leahy, Feinstein, Coons, Schatz, Manchin, and Van Hollen.

U.S. DEPARTMENT OF JUSTICE

STATEMENT OF HON. JEFF SESSIONS, ATTORNEY GENERAL

OPENING STATEMENT OF SENATOR JERRY MORAN

Senator MORAN. Good afternoon. I call the hearing to order.

Mr. Attorney General, welcome to the committee, the Committee on Commerce, Justice, Science Appropriations Subcommittee. We're here to examine the Department of Justice's fiscal year 2019 budget request.

I am pleased to welcome you to this subcommittee. My colleagues and I are very much interested in hearing from you in your—hearing your testimony, considering your testimony today. Your input is not only helpful, but necessary, as we review the President's spending priorities for the Justice Department.

While this hearing is about the Department's fiscal year 2019 budget request, I would suspect that you will hear about a number of other issues unrelated to the Department's resource and funding needs. My focus in this hearing is to better understand your top funding priorities and to emphasize those that are important to our Nation.

The Department of Justice is responsible for, and involved in, many important national priorities. Arguably, the greatest responsibility includes keeping Americans safe, which carries a new meaning, given the growing national security threats of today, and upholding the rule of law. This requires that Congress adequately fund our Nation's law enforcement efforts, including counterterrorism and cybersecurity initiatives.

Attorney General SESSIONS [continuing]. Be free to discuss it.

Senator SCHATZ. My final question. The DEA, in August of 2016, called for applications to produce more federally-approved research-grade marijuana. Since then, the Department of Justice has received 25 applications, but none of them have been responded to either with an approval or denial. What is the status of those applications?

Attorney General SESSIONS. We are moving forward, and we will add—fairly soon, I believe, the paperwork and reviews will be completed, and then we will add additional suppliers of marijuana under the controlled circumstances. But, there is—a lot of people didn't know, I didn't know—a treaty—international treaty of which we are a member, that requires certain controls in that process. And the previous proposal violated that treaty. We've now gotten language I believe complies with the treaty and will allow this process to go forward.

Senator SCHATZ. If the Chair will indulge me, one final comment.

We're all evolving on this issue, some quicker than others, maybe some too quick. And I really believe that we have to do this in the proper way. I think there are good civil rights reasons for decriminalizing and for pursuing a Federalist approach around this. But, if we're narrowly addressing the question of whether or not this is medicine, then we do need the Department of Justice, the FDA, and everybody to work together to pursue that question, double-blind studies and all. And I also think that we need to understand we are in a humanitarian crisis when it comes to the opioid epidemic, which means that we may have to cast aside some of the things that we've believed all of our lives as it relates to other drugs and look at harm reduction. I appreciate you keeping an open mind along those lines.

Thank you.

Attorney General SESSIONS. Thank you, Senator Schatz.

Senator MORAN. Senator, thank you.

Senator from Oklahoma, Senator Lankford.

Senator LANKFORD. Thank you, Mr. Chairman.

Let me add to that conversation a little bit before we—before I jump into a line of questions.

MEDICAL MARIJUANA

I am one of the skeptical individuals that, so far, has not evolved on this issue of marijuana. I have a hard time believing that, if only more of our parents smoked more marijuana, our kids would be so much better and our families would be so much better, and employment would be so much better if more of our employees smoked more marijuana. I just have a hard time believing that.

And, as far as medicinal issues, this is an area the NIH has done active work on. And NIH is—currently has several billion dollars that the Appropriations Committee has allocated to them to be able to study pain medications that are nonaddictive, to try to address that. And that was entirely appropriate to do. We have an opioid epidemic. I'd rather not swap an opioid epidemic with addiction to marijuana and just say we solved the problem. We didn't solve the problem, long term.

Congress of the United States
Washington, DC 20515

September 28, 2018

The Honorable Uttam Dhillon
Acting Administrator
Drug Enforcement Administration
8701 Morrissette Drive
Springfield, VA 22152

The Honorable Jeff Sessions
Attorney General
United States Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530

Dear Acting Administrator Dhillon and Attorney General Sessions:

Considering the recent decision by the Drug Enforcement Administration (DEA) to approve the importation from Canada of marijuana for research, we write with deep concern and with questions over the delay in approving additional approved domestic manufacturers of cannabis for this same purpose.

Cannabis offers breakthrough possibilities to help alleviate suffering and disease, but more research is needed. Currently, there is only one legal domestic supplier of marijuana for research purposes. Many have raised concerns about the cannabis it manufactures, however, such as the quality of the product. In August 2016, DEA adopted a new policy so as to increase the number of domestic manufacturers in order to increase the amount of cannabis supply and facilitate research.

Further, on October 18, 2017, you, Attorney General Sessions, testified before the Senate Judiciary Committee. In response to a question from Senator Orrin Hatch about federally-approved manufacturers of research cannabis, you stated "I think it would be healthy to have some more competition in the supply." We agree. Fortunately, over two dozen American companies have filed applications to manufacture cannabis products for research purposes.

Unfortunately, in the two years since DEA's new policy, no additional manufactures have been approved. There have been several unsuccessful attempts to ascertain the cause of this delay, most recently a July 25, 2018 letter from a bipartisan group of Senators and an August 31 letter from a bipartisan group of Representatives.

The need for additional domestic manufacturers of marijuana for research purposes was illustrated a few days ago by DEA. On Tuesday, September 18, it granted approval to the University of California San Diego's *Center for Medical Cannabis Research* to import capsules of THC and CBD from a Canadian company, Tilray Inc., for purposes of medical research. The one manufacturer in the U.S. does not offer capsules of cannabis compounds. If there were other domestic manufacturers, they might offer this option.

On April 18, 2017, President Trump issued an executive order to "Buy American and Hire American." Despite the Department of Justice (DOJ) and DEA possessing over two dozen applications from qualified domestic manufacturers, however, DEA approved the importation of cannabis products from Canada. Adding insult to injury, one application to produce research

cannabis was submitted by a campus within the University of California system — and one campus of that system will be the eventual recipient of Tilray, Inc.'s THC and CBD products.

We should note that just recently the House Judiciary Committee approved by voice vote the *Medical Cannabis Research Act*. This bill would require there be at least three domestic suppliers of cannabis for research purposes. There is strong and bipartisan interest in Congress in increasing the number of manufacturers in the U.S. of cannabis for research. While Congress will act if the Administration does not, the Administration could make this goal a reality much more quickly if it approved some of the pending applications.

With that in mind, and considering the news of the need to import cannabis products from Canada for U.S. research, we would like answers to the following questions, some of which have been asked by some of us previously:

1. What is the current status of the twenty-six cannabis manufacturer applications? How long has each been pending before DOJ and DEA?

2. What steps have the DEA and DOJ taken to review the cannabis manufacturer applications currently pending? What are the reasons these applications have not been approved?

3. When do you estimate the DEA and DOJ will complete their review of all of the cannabis manufacturing applications and begin approving some as new manufacturers?

4. In the past twelve months, excluding Schedule I Bulk Manufacturer registrations for cannabis, how many other DEA registrations has DOJ reviewed?

We look forward to working with the Administration to see that our domestic need for cannabis for research can be met by American institutions. Your prompt response would be greatly appreciated. Thank you for your time and consideration.

Sincerely,

Matt Gaetz
Member of Congress

Eric Swalwell
Member of Congress

Cc: Dr. Nora D. Volkow, Director, National Institute on Drug Abuse

Earl Blumenauer
Member of Congress

Steve Cohen M.C.
Member of Congress

Peter DeFazio
Member of Congress

Pramila Jayapal
Member of Congress

Zoe Lofgren
Member of Congress

Seth Moulton
Member of Congress

Eleanor Holmes Norton
Member of Congress

Jimmy Panetta
Member of Congress

Chellie Pingree
Member of Congress

Jared Polis
Member of Congress

Dana Rohrabacher
Member of Congress

Darren Soto
Member of Congress

OVERSIGHT OF THE U.S. DEPARTMENT OF JUSTICE

HEARING

BEFORE THE

COMMITTEE ON THE JUDICIARY HOUSE OF REPRESENTATIVES

ONE HUNDRED SIXTEENTH CONGRESS

FIRST SESSION

FEBRUARY 8, 2019

Serial No. 116–3

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I want to talk about another policy matter with respect to cannabis. I represent the State of Colorado. In Colorado, recreational use of marijuana was legalized in 2014. Today, more than half the States have legalized either the recreational or medical use of marijuana.

Researchers at the University of Colorado, which I am proud to represent, are working hard to understand the health effects. They are studying promising approaches that use marijuana to relieve chronic pain and the symptoms of Parkinson's disease.

In August of 2016, I understand this is before you were at the Department of Justice, Mr. Attorney General, the DEA took a big step towards improving scientific research on marijuana when it submitted a request in the Federal Register for applications to produce federally approved research-grade marijuana. Several institutions have submitted an application but have yet to receive a response. What is the status of those applications, if you might know, and do you know if the Department of Justice and the DEA intend to support legitimate cannabis research that could help protect the health and safety of our citizens?

Mr. WHITAKER. For the 3 months that I have been the Acting Attorney General, this is an issue that I have been aware of, and I have actually tried to get the expansion and the applications out. We have run into a very complicated matter regarding a treaty that we are trying to work around. We have some international treaty obligations that may not allow the way the marijuana has to be handled from the research facilities to the researchers—or the grow facility to the researchers. So it is something that I am very aware of. It is something I am trying to push. Unfortunately, I have 6 days left in this chair at the most. I don't know if I am going to successfully get to it, but I understand the concern and know that we are trying to make it work.

Mr. NEGUSE. I appreciate that and applaud that. And if I could get your assurances that, within the 6 days, if you could just follow up with the Department staff to follow up with our office in writing, it would be incredibly helpful for us as folks reach out.

Mr. WHITAKER. We will try to get an answer as to the current status, but my recollection where I last found it is that——

Mr. NEGUSE. That is sufficient. Thank you, Mr. Attorney General.

You mentioned earlier that the public essentially learned that Attorney General Sessions was fired on November 7, 2018, by tweet. And you were appointed via that same tweet. When did you first learn that Mr. Sessions was fired, would be fired?

Mr. WHITAKER. I learned on November 7th, if that is your question. I mean, I, you know——

Mr. NEGUSE. It is.

Mr. WHITAKER. Yeah, okay.

Mr. NEGUSE. So you learned by virtue of that same tweet that we all learned.

Mr. WHITAKER. Yes. I would suggest—the only point I would put on that, Congressman—I am sorry to interrupt—is that Mr. Sessions resigned, you know, sent in his resignation letter.

Mr. NEGUSE. Understand. Did you have any conversations with folks at the White House prior to November 7, 2018, about Attor-

this application must be received not later than July 23, 1982.

B. **Secretary, Board of Governors of the Federal Reserve System,** Washington, D.C. 20551:

A. *Colorado National Bankshares, Inc.*, Denver, Colorado; to acquire 100 percent of the voting shares or assets of The Exchange National Bank of Colorado Springs, Colorado Springs, Colorado. Comments on this application must be received not later than July 23, 1982.

Board of Governors of the Federal Reserve System, June 23, 1982.

Dolores S. Smith,

Assistant Secretary of the Board.

[FR Doc. 82-17496 Filed 6-28-82; 8:45 am]

BILLING CODE 6210-01-M

Formation of Bank Holding Companies

The companies listed in this notice have applied for the Board's approval under section 3(a)(1) of the Bank Holding Company Act (12 U.S.C. 1842(a)(1)) to become bank holding companies by acquiring voting shares and/or assets of a bank. The factors that are considered in acting on the applications are set forth in section 3(c) of the Act (12 U.S.C. 1842(c)).

Each application may be inspected at the offices of the Board of Governors, or at the Federal Reserve Bank indicated for that application. With respect to each application, interested persons may express their views in writing to the address indicated for that application. Any comment on an application that requests a hearing must include a statement of why a written presentation would not suffice in lieu of a hearing, identifying specifically any questions of fact that are in dispute and summarizing the evidence that would be presented at a hearing.

1. **Federal Reserve Bank of New York** (A. Marshall Puckett, Vice President) 33 Liberty Street, New York, New York 10045:

1. *Chemical First State Corporation*, Wilmington, Delaware; to become a bank holding company by acquiring 100 percent of the voting shares of Chemical Bank (Delaware) Wilmington, Delaware. Comments on this application must be received not later than July 23, 1982.

B. **Federal Reserve Bank of Atlanta** (Robert E. Heck, Vice President) 104 Marietta Street, N.W., Atlanta, Georgia 30303:

1. *City Bancorp, Inc.*, New Iberia, Louisiana; to become a bank holding company by acquiring 100 percent of the voting shares of City Bank & Trust Company, New Iberia, Louisiana. Comments on this application must be received not later than July 23, 1982.

C. **Federal Reserve Bank of Chicago** (Franklin D. Dreyer, Vice President) 230 South LaSalle Street, Chicago, Illinois 60690:

1. *Crete Bancorporation, Inc.*, Crete, Illinois; to become a bank holding company by acquiring 80 percent of the voting shares of United Bank of Crete-Steger, Crete, Illinois. Comments on this application must be received not later than July 23, 1982.

D. Federal Reserve Bank of Kansas City (Thomas M. Hoenig, Assistant Vice President) 925 Grand Avenue,, Kansas City, Missouri 60198:

1. *Perry Bancshares, Inc.*, Perry, Oklahoma; to become a bank holding company by acquiring 100 percent of the voting shares of Exchange Bank and Trust Company, Perry, Oklahoma. Comments on this application must be received not later than July 23, 1982.

E. **Federal Reserve Bank of Dallas** (Anthony J. Montelaro, Assistant Vice President) 400 South Akard Street, Dallas, Texas 75222:

1. *Dallas Guaranty Bancshares, Inc.*, Dallas, Texas; to become a bank holding comapny by acquiring at least 80 percent of the voting shares of Guaranty Bank, Dallas, Texas. Comments on this application must be received not later than July 23, 1982.

2. *Lower Rio Grande Valley Bancshares*, La Feria, Texas; to become a bank holding company be acquiring 80 percent of the voting shares of The First National Bank of La Feria, La Feria, Texas; The First National Bank of Mercedes, Mercedes, Texas; and Valley National Bank, Harlingen, Texas, a proposed new bank. Comments on this application must be received not later than July 23, 1982.

Board of Governors of the Federal Reserve System, June 23, 1982.

Dolores S. Smith,

Assistant Secretary of the Board.

[FR. Doc. 82-17495 Filed 6-28-82; 8:45 am]

BILLING CODE 6210-01-M

Bank Holding Companies; Notice of Proposed de Novo Nonbank Activities

The bank holding companies listed in this notice have applied, pursuant to section 4(c)(8) of the Bank Holding Company Act (12 U.S.C. 1843(c)(8)) and section 225.4(b)(1) of the Board's Regulation Y (12 CFR 225.4(b)(1)), for permission to engage *de novo* (or continue to engage in an activity earlier commenced *de novo*), directly or indirectly, solely in the activities indicated, which have been determined by the Board of Governors to be closely related to banking.

With respect to each application, interested persons may express their views on the question whether consummation of the proposal can "reasonably be expected to produce benefits to the public, such as greater convenience, increased competition, or gains in efficiency, that outweigh possible adverse effects, such as undue concentration of resources, decreased or unfair competition, conflicts of interest, or unsound banking practices." Any comment on an application that requests a hearing must include a statement of the reasons a written presentation would not suffice in lieu of a hearing, identifying specifically any questions of fact that are in dispute, summarizing the evidence that would be presented at a hearing, and indicating how the party commenting would be aggrieved by approval of that proposal.

Each application may be inspected at the offices of the Board of Governors or at the Federal Reserve Bank indicated for that application. Comments and requests for hearings should identify clearly the specific application to which they relate, and should be submitted in writing and received by the appropriate Federal Reserve Bank not later than July 22, 1982.

A. Federal Reserve Bank of New York (A. Marshall Puckett, Vice President) 33 Liberty Street, New York, New York 10045:

1. *Citicorp*, New York, New York (consumer finance and credit-related insurance activities; Illinois): To expand the activities and service areas of existing offices of its subsidiaries, Citicorp Person-to-Person Financial Center, Inc. and Citicorp Person-to-Person Financial Center of Illinois, Inc., located in Schaumburg, Illinois, and to establish a *de novo* office of Citicorp Homeowners, Inc. at the same Schaumburg, Illinois, location. The new activities in which the offices of Citicorp Person-to-Person Financial Center, Inc. and Citicorp Person-to-Person Financial Center of Illinois, Inc. propose to engage *de novo* are: the making, acquiring and servicing, for its own account and for the account of others, of extensions of credit to individuals secured by liens on residential or non-residential real estate; and the sale of mortgage life and mortgage disability insurance directly related to extensions of mortgage loans. The proposed service area for the aforementioned proposed activities shall be comprised of the entire state of Illinois. The proposed expanded service area of the Citicorp Person-to-Person Financial Center, Inc. office shall be the

entire state of Illinois for a portion of its previously approved activities, specifically, the making or acquiring of loans and other extensions of credit, secured or unsecured, for consumer and other purposes; the sale of credit related life and accident and health or decreasing or level (in the case of single payment loans) term life insurance by licensed agents or brokers, as required; the sale of consumer oriented financial management courses; and the servicing, for any person, of loans and other extensions of credit. The proposed expanded service area of the CPTP-Illinois office shall be the entire state of Illinois for a portion of its previously approved activities, specifically, the making or acquiring of loans and other extensions of credit, secured or unsecured, for consumer and other purposes; the sale of credit related life and accident and health or decreasing or level (in the case of single payment loans) term life insurance by licensed agents or brokers, as required; the extensions of loans to dealers for the financing of inventory (floor planning) and working capital purposes; the sale of consumer oriented financial management courses; and the servicing, for any person, of loans and other extensions of credit. The activities in which the proposed *de novo* office of Citicorp Homeowners, Inc. will engage are: the making or acquiring of loans and other extensions of credit, secured or unsecured, for consumer and other purposes; the sale of credit related life and accident and health or decreasing or level (in the case of single payment loans) term life insurance by licensed agents or brokers, as required; the sale of consumer oriented financial management courses; the servicing, for any person, of loans and other extensions of credit; the making, acquiring and servicing, for its own account and for the account of others, of extensions of credit to individuals secured by liens on residential or non-residential real estate; and the sale of mortgage life and mortgage disability insurance directly related to extensions of mortgage loans. The proposed service area of Citicorp Homeowners, Inc. shall be comprised of the entire state of Illinois for all the aforementioned activities. Credit related life, accident, and health insurance Company, an affiliate of Citicorp Person-to-Person Financial Center, Inc., Citicorp Person-to-Person Financial Center of Illinois, Inc. and Citicorp Homeowners, Inc.

2. *Citicorp*, New York, New York (consumer finance and credit-related insurance activities; Georgia): To expand the activities and service area of an existing office of its subsidiary, Citicorp Person-to-Person Financial Center, Inc., located in Morrow, Georgia, and to establish a *de novo* office of Citicorp Homeowners, Inc. at the same Morrow, Georgia, location. The new activities in which the Citicorp Person-to-Person Financial Center, Inc. office proposes to engage *de novo* are: the making, acquiring and servicing, for its own account and for the account of others, of extensions of credit to individuals secured by liens on residential or non-residential real estate; and the sale of mortgage life and mortgage disability insurance directly related to extensions of mortgage loans. The proposed service area for the aforementioned proposed activities shall be comprised of the entire state of Georgia. The proposed expanded service area of Citicorp Person-to-Person Financial Center, Inc. shall be comprised of the entire state of Georgia for a portion of its previously approved activities, specifically, the making or acquiring of loans and other extensions of credit, secured or unsecured, for consumer and other purposes; the sale of credit related life and accident and health or decreasing or level (in the case of single payment loans) term life insurance by licensed agents or brokers, as required, the sale of consumer oriented financial management courses; and the servicing, for any person, of loans and other extensions of credit. The activities in which the *de novo* office of Citicorp Homeowners, Inc. proposes to engage are: the making or acquiring of loans and other extensions of credit, secured or unsecured, for consumer and other purposes; the sale of credit-related life and accident and health or decreasing or level (in the case of single payment loans) term life insurance by licensed agents or brokers, as required; the sale of consumer oriented financial management courses; the servicing, for any person, of loans and other extensions of credit; the making, acquiring and servicing, for its own account and for the account of others, of extensions of credit to individuals secured by liens on residential or non-residential real estate; and the sale of mortgage life and mortgage disability insurance directly related to extensions of mortgage loans. The proposed service area of *de novo* office of Citicorp Homeowners, Inc. shall be comprised of the entire State of Georgia for all the aforementioned proposed activities. Credit related life, accident, and health insurance may be written by Family Guardian Life Insurance Company, an affiliate of Citicorp Person-to-Person Financial Center, Inc. and Citicorp Homeowner, Inc.

3. *Citicorp*, New York, New York (consumer finance and credit-related insurance activities; Louisiana): To expand the activities and service areas of three existing offices of its subsidiary, Citicorp Person-to-Person Financial Center, Inc. and to establish three *de novo* offices of Citicorp Homeowners, Inc. at the same locations. The new activities in which the offices of Citicorp Person-to-Person Financial Center, Inc. propose to engage *de novo* are: the making, acquiring and servicing, for its own account and for the account of others, of extensions of credit to individuals secured by liens on residential or non-residential real estate; and the sale of mortgage life and mortgage disability insurance directly related to extensions of mortgage loans. The proposed service area of each of the Citicorp Person-to-Person offices for the aforementioned proposed activities shall be comprised of the entire state of Louisiana. The proposed expanded service areas of the Citicorp Person-to-Person offices shall be the entire state of Louisiana for a portion of their previously approved activities, specificially, the making or acquiring of loans and other extensions of credit, secured or unsecured, for consumer and other purposes; the extension of loans to dealers for the financing of inventory (floor planning) and working capital purposes; the purchasing and servicing for its own account of sales finance contracts; the sale of credit related life and accident and health or decreasing or level (in the case of single payment loans) term life insurance by licensed agents or brokers, as required; the sale of consumer oriented financial management courses; and the servicing, for any person, of loans and other extensions of credit. The activities in which the proposed *de novo* offices of Citicorp Homeowners, Inc. will engage are: the making, acquiring, of loans and other extensions of credit, secured or unsecured, for consumer and other purposes; the sale of credit related life and accident and health or decreasing or level (in the case of single payment loans) term life insurance by licensed agents or brokers, as required; the sale of consumer oriented financial management courses; the servicing, for any person, of loans and other extensions of credit; the making, acquiring and servicing, for its own account and for the account of others, of extensions of credit to individuals secured by liens on residential or non-residential real estate; and the sale of mortgage life and mortgage disability

insurance directly related to extensions of mortgage loans. The proposed service areas of the *de novo* offices of Citicorp Homeowners, Inc. shall be comprised of the entire State of Louisiana for all the aforementioned activities. Credit related life, accident, and health insurance may be written by Family Guardian Life Insurance Company, an affiliate of Citicorp Person-to-Person Financial Center, Inc. and Citicorp Homeowners, Inc. The aforementioned activities will be conducted from the following three locations: 9029 Mansfield Road, Suite 103, Shreveport, Louisiana; 3621 Veterans Memorial Boulevard, Metairie, Louisiana; Aurora Village, 4132 General DeGaulle Drive, New Orleans, Louisiana.

4. *Citicorp,* New York, New York (consumer finance and credit-related insurance activities; Georgia and Florida): To expand the activities of an existing office of its subsidiary, Citicorp Person-to-Person Financial Center of Florida, Inc., located in Jacksonville, Florida, and to establish a *de novo* office of Citicorp Homeowners, Inc. at the same Jacksonville, Florida, location. The activities to be engaged in at this location by Citicorp Person-to-Person Financial Center of Florida, Inc. and Citicorp Homeowners, Inc. will include: the making or acquiring of loans and other extensions of credit, secured or unsecured, for consumer and other purposes; the making, acquiring, and servicing for its own account and for the account of others, of extensions of credit to individuals secured by liens on residential or nonresidential real estate; the sale of credit related life and accident and health of decreasing or level (in the case of single payment loans) term life insurance by licensed agents or brokers, as required; the sale of mortgage life and mortgage disability insurance directly related to extensions of mortgage loans; the sale of consumer oriented financial management courses; and the servicing, for any person, of loans and other extensions of credit. The proposed service area of Citicorp Person-to-Person Financial Center of Florida, Inc. and Citicorp Homeowners, Inc. at this location shall be comprised of the entire states of Florida and Georgia for all the aforementioned activities. Apart from this notification, Citicorp Person-to-Person Financial Center of Florida, Inc. will also continue to engage in the previously approved activity of the sale of credit-related property and casualty insurance protecting real and personal property subject to a security agreement with Citicorp Person-to-Person, Inc., and to the extent permissible under applicable state insurance laws and regulations in its previously approved service area of Georgia. Credit related life, accident, and health insurance may be written by Family Guardian Life Insurance Company, and affiliate of Citicorp Person-to-Person Financial Center of Florida, Inc. and Citicorp Homeowners, Inc.

5. *Citicorp,* New York, New York (consumer finance and credit-related insurance activities; Florida): To expand the activities and service area of an existing office of its subsidiary, Citicorp Person-to-Person Financial Center of Florida, Inc., located in Fort Lauderdale, Florida, and to establish a *de novo* office of Citicorp Homeowners, Inc. at the same Fort Lauderdale, Florida, location. The new activities in which the office of Citicorp Person-to-Person Financial Center of Florida, Inc. proposes to engage *de novo* are: the making, acquiring and servicing, for its own account and for the account of others, of extensions of credit to individuals secured by liens on residential or non-residential real estate; and the sale of mortgage life and mortgage disability insurance directly related to extensions of mortgage loans. The proposed service area for the *de novo* activities shall be comprised of the entire state of Florida. The proposed expanded service area of Citicorp Person-to-Person Financial Center of Florida, Inc. shall be comprised of the entire state of Florida for a portion of its previously approved activities, specifically, the sale of credit-related life and accident and health or decreasing or level (in the case of single payment loans) term life insurance by licensed agents or brokers, as required. The activities in which the *de novo* office of Citicorp Homeowners, Inc. proposes to engage are: the making or acquiring of loans and other extensions of credit, secured or unsecured, for consumer and other purposes; the making, acquiring, and servicing for its own account and for the account of others, of extensions of credit to individuals secured by liens or residential or nonresidential real estate; the sale of credit related life and accident and health or decreasing or level (in the case of single payment loans) term life insurance by licensed agents or brokers, as required; the sale of mortgage life and mortgage disability insurance directly related to extensions of mortgage loans; the sale of consumer oriented financial management courses; and the servicing, for any person, of loans and other extensions of credit. The proposed service area of the *de novo* office of Citicorp Homeowners, Inc. shall be comprised of the entire state of Florida for all the aforementioned proposed activities. Credit related life, accident, and health insurance may be written by Family Guardian Life Insurance Company, and affiliate of Citicorp Person-to-Person Financial Center of Florida, Inc. and Citicorp Homeowners, Inc.

6. *Citicorp,* New York, New York (consumer finance and credit-related insurance activities; Florida): To expand the activities and service area of an existing office of its subsidiary, Citicorp Person-to-Person Financial Center of Florida, Inc., located in Tampa, Florida and to establish a *de novo* office of Citicorp Homeowners, Inc. at the same Tampa, Florida location. The new activities in which Citicorp Person-to-Person Financial Center of Florida, Inc. proposes to engage *de novo* are: the making, acquiring and servicing, for its own account and for the account of others, of extensions of credit to individuals secured by liens on residential or non-residential real estate; and the sale of mortgage life and mortgage disability insurance directly related to extensions of mortgage loans. The proposed service area for the aforementioned proposed activities shall be comprised of the entire state of Florida. The proposed expanded service area of Citcorp Person-to-Person Financial Center shall be comprised of the entire state of Florida for a portion of its previously approved activities, specifically, the sale of credit-related life and accident and health or decreasing or level (in the case of single payment loans) term life insurance by licensed agents or brokers, as required. The activities in which the *de novo* office of Citicorp Homeowners, Inc. proposes to engage are: the making or acquiring of loans and other extensions of credit, secured or unsecured, for consumer and other purposes; the sale of credit related life and accident and health or decreasing or level (in the case of single payment loans) term life insurance by licensed agents or brokers, as required; the sale of consumer oriented financial management courses; the servicing, for any person, of loans and other extensions of credit; the making, acquiring and servicing, for its own account and for the account of others, of extensions of credit to individuals secured by liens on residential or non-residential real estate; and the sale of mortgage life and mortgage disability insurance directly related to extensions of mortgage loans. The proposed service area of the *de novo* office of Citicorp Homeowners, Inc. shall be comprised of the entire State of Florida for all the aforementioned proposed activities.

Credit related life, accident, and health insurance may be written by Family Guardian Life Insurance Company, an affiliate of Citicorp Person-to-Person Financial Center of Florida, Inc. and Citicorp Homeowners, Inc.

7. *Citicorp*, New York, New York (consumer finance and credit-related insurance activities; Kansas and Missouri): To expand the activities and service area of an existing office of its subsidiary, Citicorp Person-to-Person Financial Center, Inc., located in Overland Park, Kansas, and to establish a *de novo* office of Citicorp Homeowners, Inc. at the same Overland Park, Kansas, location. The new activities in which the Citicorp Person-to-Person Financial Center, Inc. office proposes to engage *de novo* are: the making, acquiring and servicing, for its own accountant and for the account of others, of extensions of credit to individuals secured by liens on residential or non-residential real estate; and the sale of mortgage life and mortgage disability insurance directly related to extensions of mortgage loans. The proposed service area for the aforementioned proposed activities shall be comprised of the entire states of Kansas and Missouri. The proposed expanded service areas of the Citicorp Person-to-Person Financial Center, Inc. office shall be the entire states of Kansas and Missouri for a portion of its previously approved activities, specifically, the making or acquiring of loans and other extensions of credit, secured or unsecured, for consumer and other purposes; the sale of credit related life and accident and health or decreasing or level (in the case of single payment loans) term life insurance by licensed agents or brokers, as required; the sale of consumer oriented financial management courses; and the servicing, for any person, of loans and other extensions of credit. The activities in which the proposed *de novo* office of Citicorp Homeowners, Inc. will engage are: the making or acquiring of loans and other extensions of credit, secured or unsecured, for consumer and other purposes; the sale of credit related life and accident and health or decreasing or level (in the case of single payment loans) term life insurance by licensed agents or brokers, as required; the sale of consumer oriented financial management courses; the the servicing, for any person, of loans and other extensions of credit; the making, acquiring and servicing, for its own account and for the account of others, of extensions of credit to individuals secured by liens on residential or non-residential real estate; and the sale of mortgage life and mortgage disability insurance directly related to extensions of mortgage loans. The proposed service area of Citicorp Homeowners, Inc. shall be comprised of the entire States of Kansas and Missouri for all the aforementioned activities. Credit related life, accident, and health insurance may be written by Family Guardian Life Insurance Company, an affiliate of Citicorp Person-to-Person Financial Center, Inc. and Citicorp Homeowners, Inc.

Board of Governors of the Federal Reserve System, June 23, 1982.

Delores S. Smith,

Assistant Secretary of the Board.

[FR Doc. 82-17498 Filed 6-28-82; 8:45 am]

BILLING CODE 6210-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 82N-0162]

Proposed Recommendations to the Drug Enforcement Administration Regarding the Scheduling Status of Marihuana and Its Components and Notice of a Public Hearing

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) announces (1) its proposed recommendations, including scientific and medical evaluations, on the appropriate scheduling of marihuana plant materials under the Controlled Substances Act and (2) that the proposed recommendations will be the subject of a public legislative-type hearing to be held on September 16, 1982. The proposed recommendations are published to give interested persons the opportunity to comment on the recommendations and on the scientific and medical evaluations. FDA will consider these comments as well as the information gathered from the public hearing in preparing its final recommendations and scientific and medical evaluations of the marihuana plant materials before transmitting them to the Assistant Secretary for Health, Department of Health and Human Services (DHHS). The Assistant Secretary for Health is responsible for making the DHHS recommendation to the Drug Enforcement Administration (DEA).

DATES: Comments on the proposed recommendations by October 1, 1982. Notice of participation in the public hearing by August 27, 1982. Public hearing to be held September 16, 1982.

ADDRESSES: Written comments on the proposed recommendations to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857. Written or oral notice of participation along with the text or comprehensive outline to the Division of Neuropharmacological Drug Products (HFD-120), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-3800.

FOR FURTHER INFORMATION CONTACT: Edwin V. Dutra, Jr., Bureau of Drugs (HFD-30), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-6490.

SUPPLEMENTARY INFORMATION:

I. Background

The plant, *Cannabis sativa*, commonly known as marihuana, contains hundreds of chemical compounds. Sixty-one of the chemicals that have been identified in the plant—the cannabinoids—are specific to connabis. Ten are now routinely quantified in identifying cannabis samples (Ref. 1).

The major psychoactive ingredient contained in the marihuana plant is delta-9-tetrahydrocannabinol (THC). THC content in cannabis plants varies not only among the different parts of a single plant (flowers, leaves, stems, seeds, etc.), but also at different stages of development of the same part of a single plant. The geographic location in which the plant is grown and the time of day at which the plant is harvested also affect THC content.

The variability of THC content in natural plant material tends to render the marihuana plant, resin, leaves, and seeds difficult substances for precise scientific investigation, and scientific and medical evaluations have therefore focused primarily on THC itself, and its immediate synthetic precursor, cannabidiol.

Nonetheless, marihuana itself is currently under investigation in the United States as an agent useful in, among other purposes, the control of nausea and vomiting from cancer chemotherapy, in the reduction of the vision-destroying increase in intraocular pressure which occurs in open-angle glaucoma, and in the reduction of muscular spasticity in certain neurologic diseases (Ref. 1).

Cannabis, cannabis resin, cannabis extracts, and tinctures of cannabis are controlled in Schedule I of the 1961 Single Convention on Narcotic Drugs (Single Convention), to which the United

States is a party. Schedule I is the most restrictive schedule in the Single Convention with mandated regulatory controls. Schedule I also includes heroin, morphine, and cocaine. Its major controls are import/export permits, quotas, prescriptions, and prevention of drug stockpiling and accumulations. In addition, cannabis and cannabis resin are controlled concurrently in Schedule IV of the Single Convention. Schedule IV is best described as a "Super Schedule I" because it highlights the need for additional controls to be placed on certain drugs scheduled concurrently in Single Convention Schedule I. Heroin is the prototype for drugs in this schedule. The drugs in Schedule IV of the Single Convention are considered particularly dangerous and lack demonstrated therapeutic value. Although Schedule IV drugs are not subject to specific additional controls under the Single Convention, the treaty calls upon individual countries to use discretion in imposing whatever additional controls are necessary to protect the public health, including, if appropriate, a prohibition on production and trade. The Single Convention requires the United States to impose certain domestic controls on the marihuana plant materials listed above. The United States carries out these responsibilities under the Controlled Substances Act (CSA) (21 U.S.C. 801 et seq.).

In 1970 Congress enacted the CSA, establishing control schedules I through V (21 U.S.C. 812(b) (1) through (5)). Congress placed marihuana in schedule I of the CSA, the classification providing for the most stringent domestic controls. See 21 U.S.C. 812. The findings required for schedule I drugs or substances are: high potential for abuse; no currently accepted medical use in treatment in the United States; and lack of accepted safety for use under medical supervision. The major schedule I controls are: limitation of dispensing to research use only; the requirement of separate recordkeeping; and limitation of the amounts produced during a given calendar year, i.e., quotas.

The CSA contains procedures by which changes in scheduling can be effected (21 U.S.C. 811(a)) including "on petition of any interested person". In May 1972, the National Organization for the Reform of Marijuana Laws (NORML) petitioned the Bureau of Narcotics and Dangerous Drugs (now the Drug Enforcement Administration, DEA) under section 201(a) of the CSA (21 U.S.C. 811(a)) to remove marihuana and its components from control under the CSA or to move marihuana and its components to a less restrictive schedule. DEA denied NORML's requests (37 FR 18097; September 1, 1972). NORML appealed the denial to the United States Court of Appeals for the District of Columbia Circuit, and, in *NORML* v. *Ingersoll*, 497 F.2d 654 (D.C. Cir. 1974), the court ordered DEA to hold hearings and reconsider the NORML petition on the basis of evidence introduced at the hearings. Following these hearings, DEA again denied the NORML petition and ruled that the substances at issue would remain in CSA schedule I (40 FR 44164; September 25, 1975). NORML appealed the second denial and the court remanded the petition to DEA with instructions to refer it to the Secretary of DHHS for medical and scientific findings and recommendations for rescheduling. *NORML* v. *DEA*, 559 F.2d 745, 750 (D.C. Cir. 1977). The court directed the Secretary of DHHS to make evaluations and recommendations for each of the following cannabis materials: "cannabis" and "cannabis resin" (minimum control—CSA II); cannabis leaves (minimum control—CSA V); cannabis seeds capable of germination (minimum control—CSA V); synthetic tetrahydrocannabinol (THC) (no minimum control under CSA). The "minimum controls" schedules are the least restrictive domestic schedules consistent with the treaty obligations under the Single Convention on Narcotic Drugs, 1961, as interpreted by the court. THC was not listed by the court as having a minimum domestic schedule because THC is not controlled under the Single Convention. (THC is subject to control under the Psychotropic Convention, however, and thus is subject to control under the CSA.)

In addition, the court directed DEA to comply with the rulemaking procedures in 21 U.S.C. 811 (a) and (b) after it received the Secretary's evaluation and recommendation.

In June 1977, DEA referred the NORML petition to the Secretary of the Department of Health, Education, and Welfare (now DHHS). FDA's Controlled Substances Advisory Committee (CSAC) considered the NORML petition in November 1977 and March 1978. The CSAC (now the Drug Abuse Advisory Committee (DAAC)) recommended that the marihuana plant materials remain in CSA scheule I and that THC and cannabidiol be rescheduled to CSA schedule II. by letter dated June 4, 1979, the Secretary recommended that all these substances remain in schedule I. The advisory committee's rationale for recommending placing THC and cannabidiol in Schedule II was that it would facilitate research on the substances. The Secretary concluded, however, that facilitation of research was not relevant to any of the scheduling criteria established by the statute and, therefore, was not an appropriate basis for a scheduling recommendation.

In the **Federal Register** of June 20, 1979 (44 FR 36123), DEA denied NORML's petition and denied a request for hearing on the ground that there was lack of substantial evidence to support lesser control of the substances that are the subject of NORML's petition.

NORML petitioned the Court of Appeals for review of DEA's final order denying the petition. On October 16, 1980, the court ordered that the case be remanded to DEA and that DEA refer all the substances at issue to DHHS for scientific and medical findings and recommendations on scheduling. The court directed that the DHHS review take into acount new evidence concerning medical use of the substances at issue. *NORML* v. *DEA and HEW*, No. 79–1660 (D.C. Cir., October 16, 1980). On April 22, 1981, DEA referred the NORML petition to DHHS for review. DHHS Has adopted the following procedures in making the evaluations and scheduling recommendations for cannabis-containing substances (a separate procedure applies to THC, see 47 FR 10080, March 9, 1982):

1. Review by FDA of evidence concerning the uses of those substances, including comment from other appropriate units in DHHS.

2. Publication of the proposed scientific and medical evaluations and scheduling recommendations in this **Federal Register** notice for public comment.

3. The holding of a legislative-type hearing under 21 CFR Part 15 on the proposed findings and recommendations (see details below in Part IV).

4. Consideration of the comments received as a result of the **Federal Register** notice and consideration of the pertinent information generated by the hearing in preparing FDA's findings and recommendations for the Assistant Secretary for Health.

5. Review of the evaluations and recommendations by the Assistant Secretary for Health and transmittal to DEA.

II. Scheduling Recommendation

FDA proposes to recommend to the Assistant Secretary for Health that the marihuana plant materials that are the subject of the NORML petition remain in schedule I.

FDA notes that the ultimate determination of the scheduling status of the marihuana plant materials under the CSA will be influenced not only by the results of these proceedings but also by U.S. treaty obligations under the Single Convention as interpreted by the court in *NORML* v. *DEA*. In *NORML* v. *DEA*, the court found that the Single Convention prescribes different controls for various parts of the marihuana or cannabis plant. Thus, the court concluded that the minimum domestic controls under the CSA for those materials required by the Single Convention were also different. 559 F.2d 735, 757 (D.C. Cir. 1977). The court, in its directive to the Secretary of DHHS to make evaluations and recommendations on the cannabis materials subject of the NORML petition, delineated the minimum domestic control schedule required by the Single Convention for each of the substances at issue (see above). FDA's proposed conclusions are, however, based solely on its medical and scientific review of available data, not on its interpretation of this country's treaty obligations. FDA has carefully considered, from a medical and scientific standpoint, each of the five CSA schedules as well as no control and tentatively concludes that the marihuana substances at issue meet the findings only for CSA schedule I.

Marihuana Materials To Be Considered

Under the CSA (21 U.S.C. 802(15)):

The term "marihuana" means all parts of the plant Cannabis Sativa L., whether growing or not; the seeds thereof; the resin extracted from any part of such plant; and every compound, manufacture, salt, derivative, mixture, or preparation of such plant, its seeds or resin. Such term does not include the mature stalks of such plant, fiber produced from such stalks, oil or cake made from the seeds of such plant, any other compound, manufacture, salt, derivative, mixture, or preparation of such mature stalks (except the resin extracted therefrom), fiber, oil, or cake, or the sterilized seed of such plant which is incapable of germination.

As previously noted, this ducument will address three separate categories of marihuana products: (1) cannabis and cannabis resin, (2) cannabis leaves, and (3) cannabis seeds capable of germination.

Cannabis is the entire plant material including the seeds, the resin, the leaves, the stems, the stalk, and all extracts obtained from the plant. Cannabis resin, which is generally referred to as hashish, is a concentrated extract from the plant. The composition of the cannabis plant, and of cannabis extract, has been investigated and reported in the Journal of Natural Products (Ref. 2). This reference reports a total of 421 known chemicals with new ones constantly being discovered and reported. Among the known compounds reported are 61 cannabinoids (chemical compounds perhaps unique to cannabis). In the following discussion, cannabis and cannabis resin will be referred to in most places collectively as "cannabis".

Cannabis leaves contain the active substance THC and are the primary ingredients for making cannabis cigarettes. An analysis of the THC content of cannabis plant parts published in the Journal of Pharmaceutical Sciences (Ref. 3) showed the male flowers contained 1.6 percent THC, the bracts, or female flower, 3.7 percent, the small female leaves, 1.4 percent, leaves from the male plant, 1.0 percent, stems from the male plant, 0.89 percent THC, and seeds from the female plant, 0.01 percent. THC content varies significantly in leaves from various cannabis plants and from leaves within the same plant. The National Institute on Drug Abuse has reported results from an analysis of various samples of cannabis obtained in 1976. The THC content of leaves from five separate samples varied from 2.51 percent THC to 4.68 percent.

The third category of marihuana material that must be analyzed is cannabis seeds capable of germination. As discussed above, the seeds themselves have a very low percentage of THC content and are not known to have any potential for misuse except in being used to grow marihuana plants.

In making a scheduling recommendation, the Department must consider the eight factors listed at 21 U.S.C. 811(c). FDA's analysis of these eight factors with respect to each of the marihuana plant materials that are the subject of the NORML petition follows:

1. *Its actual or relative potential for abuse (21 U.S.C. 811(c)(1)).* The legislative history of the CSA, or Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (see House Report 91–1444, Part I (Ref. 4)), defines potential for abuse as including the following elements:

(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;

(2) There is significant diversion of the drug or drugs containing such a substance from legitimate drug channels;

(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

(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.

These elements will be discussed for each of the materials at issue.

a. *Cannabis and cannabis resin.* 1. FDA proposes to fin that individuals take cannabis in sufficient amounts to create a hazard to their health or to the safety of other individuals, or of the community. The extent of this use is discussed under Factors 4 and 5. The hazards to health are discussed under Factors 2, 3, and 6.

2. FDA proposes to find that there is not now a significant diversion of cannabis from legitimate drug channels. Cannabis is currently available through legitimate channels for reserach purposes only. The lack of significant diversion may result from the availability of illicit cannabis of equal or greater potency. If the illicit availability were not so widespread, there would presumably be additional pressure for diversion from legitimate channels.

3. FDA proposes to find that a significant number of persons take cannabis on their own initiative rather than on the basis of medical advice. When compared with the amount illicit cannabis available for persons to take on their own initiative, the amount of drug distributed in the course of medical research (the only currently authorized taking of cannabis under medical supervision) is insignificant. Approximately 10,000 to 15,000 times as much illicit cannabis as legitimate cannabis is available for distribution. Of the total amount of cannabis available for legitimate use, only approximately 5 to 10 percent was actually distributed for research in 1980 and the remainder remained under security in storage. It can be concluded that the overwhelming majority of individuals using cannabis do so on their own initiative, not on the basis of medical advice from a practitioner licensed to administer the

drug in the course of professional practice. An indication of the numbers of individuals taking the drug illicitly is given under Factors 4 and 5 concerning the current pattern and scope of abuse.

4. The fourth element in potential for abuse defined in the legislative history and discussed above does not apply to cannabis.

Considering the four elements discussed above, FDA proposes to conclude that because of the large amount of materials which is illicitly available and the number of individuals taking the drugs on their own initiative that cannabis and cannabis resin have a high potential for abuse.

b. *Cannabis leaves.* The four elements described above can be applied to cannabis leaves in two ways. First, cannabis leaves can be considered in the way they are now available in illicit use, i.e., in conjunction with other parts of the marihuana plant in the mixture that has been referred to above as "cannabis". Alternatively, one could view cannabis leaves as a separate product, containing only the leaves, although this product is not currently widely known or available in this country. The first approach seems more reasonable and is adopted in this proposal. FDA's discussion of cannabis (above) applies equally well to cannabis leaves; FDA therefore proposes to conclude that cannabis leaves have a high potential for abuse.

Alternatively, if "cannabis leaves" are considered to be a separate product, the fourth element identified from the legislative history is applicable. Cannabis leaves are, because of their content of THC, so related in their action to "cannabis," described above, that it is reasonable to assume that there may be significant diversions from legitimate channels (assuming that those diversions became easier than obtaining cannabis from other illicit sources), that there may be significant use contrary to or without medical advice, and the product would have a substantial capability of creating hazards to the health of the user. These conclusions are reached on the basis of the agency's experience with and knowledge of cannabis itself. Under this alternative analysis, FDA again proposes to find that cannabis leaves have a high potential for abuse.

c. *Cannabis seeds capable of germination.* Cannabis seeds capable of germination may be planted and cultivated to produce the cannabis plant. According to one source, the amount of illicit marihuana being grown or produced and harvested in the United States has an estimated value of more than $1 billion per year and is continuing to increase (Ref. 5, Washington Post, November 15, 1981 (F–13)).

When the four elements from the legislative history are applied to cannabis seeds, they would not identify the seeds themselves as having an actual or relative potential for abuse. Thus, there is no evidence that individuals are taking cannabis seeds in an amount sufficient to create a hazard to their health or the safety of others. There is not a significant diversion of cannabis seeds from legitimate drug channels, though it is reasonable to assume that if diversion became easy, it would occur because the seed could be used to grow marihuana. Individuals do not appear to take marihuana seeds on their own initiative. Marihuana seeds do not have an action so related to drugs already listed as having a potential for abuse as to require their identification as drugs subject to abuse.

Yet, Congress in articulating the bases for conclusions concerning the actual or relative potential for abuse of a product did not expect FDA to close its eyes to reality. Cannabis seeds capable of germination can obviously be used to produce cannabis, cannabis resin, and cannabis leaves, all of which plainly present a potential for abuse. For that reason FDA proposes to find that cannabis seeds capable of germination present a significant actual or relative potential for abuse as those terms are used in 21 U.S.C. 811(c)(1).

2. *Scientific evidence of its pharmacological effect if known (21 U.S.C. 812(c)(2)).* House Report 91–1444 (Ref. 4) states "The state of knowledge with respect to the effect of uses of a specific drug is, of course, a major consideration, e.g., it is vital to know whether or not a drug has an hallucinogenic effect if it is to be controlled because of that effect. The best available knowledge of the pharmacological properties of a drug should be considered."

House Report 91–1444 (Ref. 4) states that this factor and factor 3 ("The state of current scientific knowledge regarding the drug or other substance" (21 U.S.C. 811(c)(3))) are closely related. This document distinguishes between factors 2 and 3 in the following manner: The discussion of factor 2 uncritically summarizes the relevant, available scientific evidence. In contrast, the discussion of factor 3 presents the agency's evaluation of what may be reasonably and fairly concluded on the basis of the evidence discussed under factor 2.

a. *Cannabis and cannabis resin.* The voluminous literature on marihuana (over 8,000 references) precludes, for any practical purpose, a complete and systematic review by agency staff of the original references concerning the pharmacological effects of cannabis and its derivatives. The agency, in evaluating the evidence, has reviewed major original articles as well as authoritative secondary sources. Major reviews in the following list are easily available sources of the evidence described in this section.

Institute of Medicine Report, 1982 (Ref. 6).

NIDA Research Monograph, 1980 (Ref. 7).

Addiction Research Foundation, 1981 (Ref. 8).

Journal of Clinical Pharmacology, August-September 1981 (Ref. 9).

"Marihuana," ed R. Mechoulam, Academic Press, 1973 (Ref. 10).

"Pharmacology of Marihuana," ed. Braude and Szara, Raven Press, 1976 (Ref. 11).

Evidence on the effects considered to be related to the use of cannabis is presented in two separate sections: Central Nervous System and Other Major Body or Organ Systems.

Central Nervous System

A. *Cognitive and subjective effects.* Cannabis and its derivatives have been reported to cause disorders in each of the following areas: (1) experience of self, (2) perception and the interpretation of the meaning of perceptions (apperception), (3) thought, (4) feelings and effects, (5) will or volition, (6) control of instinctual behavior or drives, (7) memory, and (8) the higher intellectual functions, which include cognition, reason, and judgment (Ref. 6).

1. *Disordered experience of the self.* Cannabis use can be associated with alterations in the experience of the self in bizarre but well-characterized ways.

For example, depersonalization (the sense that one is not one's normal, natural self) and distortions of body image (the sense that one's body is distorted or different) have been commonly reported in association with the use of cannabis. In the more severe clinical syndromes associated with cannabis use, disturbances in the experience of self of psychotic proportion have been described (e.g., the heart vibrating the entire body, limbs growing longer, the head enlarging). Cannabis use is said to cause distortions in the subjective experience of time and in one's sense of relatedness to the environment (derealization).

2. *Disordered perception and apperception.* Perception and apperception are part of the complex

process by which an individual interacts with the environment, obtains (via the senses) data about the environment, and comes to understand the processed sensory data in a normal, meaningful way. Cannabis use has been associated with varied types of psychopathology affecting perception and apperception.

Sensory distortions are commonly reported with cannabis use and can involve changes in the intensity or quality of perceptions as well as their form (i.e., size, shape, proportions). For example, visual images may seem unusually intense, or three-dimensional objects may appear flat. Sensory stimuli may be misperceived (i.e., illusions) and frank hallucinations (i.e., perceptions without a corresponding environmental stimulus) may occur. These phenomena may be quite frightening or disturbing to the person who experiences them and may be associated with a paranoid experience (see discussion below).

3. *Disturbances of thought.* Two types of disturbances of thought may be associated with the use of cannabis: (1) a formal thought disorder and (2) disorders of thought content. A formal thought disorder consists of several related phenomena involving impairments in a person's ability to control the sequence, organization, and rate of thoughts. A formal thought disorder often appears to the observer as an inability of a person to communicate in a meaningful way. Speech may seem interrupted in an irregular and unpredictable manner by abrupt silences or by illogical, garbled, nonsensical, or unintelligible utterances.

The disorders of thought content consist for the most part of delusions (fixed, illogical, idiosyncratically held beliefs from which the individual cannot be persuaded by appeals to logic or reason) or delusion-like beliefs. Delusions may be classified as to their specific content or type (i.e., grandiose, paranoid, etc.). Among the various types of delusions, those of paranoid character are probably most important. Because a person suffering a paranoid delusion may act upon it as though it were factual, inappropriate aggressive behavior may sometimes be expressed by such persons. Less-organized paranoid beliefs merge imperceptibly with feelings or moods and are described in the next section on feeling and affects.

4. *Feeling and affects.* Feeling and affects (the conscious, subjective aspects of an emotion) subsume a wide variety of moods and states, both pleasing and dysphoric.

Euphoria, or a state of elevated mood, is often reported as a result of cannabis use. This feeling state, variously described as a "high" or as mellow contentment, is thought to contribute to the widespread illicit use of cannabis.

Dysphoric mood states also occur, however. Paranoia, the feeling of being and object of ridicule or persecution, is sometimes reported—especially in persons who may be considered to have less stable personality organizations (i.e., persons more prone to exhibit psychopathology under adverse circumstances). Paranoid experiences and behavior are also reported to be associated with the acute organic brain syndromes (i.e., delirium) attributed to cannabis intoxication. Paranoia may be more organized and take the form of a delusion-like idea or a full-blown delusional system (see discussion above).

Unrealistic fright or fear, sometimes occurring in discrete episodes of overwhelming terror (panics), has been reported to occur in a relatively large proportion (i.e., one-third) of cannabis users (Ref. 6). Lesser degrees of anxiety or dysphoria may occur quite frequently in a large proportion of users. Indeed, intolerance to the dysphoric mood effects of cannabis is said to impair its usefulness as a potential therapeutic agent in many groups (i.e., the elderly).

5. *Disturbances of will or volition.* The "amotivational syndrome" is reported to be a consequence of chronic cannabis use. Apparently, some especially heavy, usually daily, users of cannabis demonstrate a loss of ambition and interest in the more commonly held life goals. Work or school performance deteriorates and the affected person shows features of what might be considered a personality disorder (i.e., apathy, ineffectiveness, inability to plan for the long-term, etc.). Convincing proof that cannabis use is the cause rather than the result of these personality changes is lacking, however, as the evidence is based upon casual clinical observations (case reports).

6. *Disturbances in the control of instinctual urges or drives.* The acutely intoxicated person may, by virtue of organic central nervous system depression or delirium exercise poor judgment and control. The potential for hostile behavior may be increased, especially when the person experiences paranoid feelings in the state of altered consciousness of intoxication caused by cannabis. Aggression is also alleged to occur idiosyncratically, independent of intoxication, in some cannabis users.

7. *Disorders of memory and attention.* Cannabis may alter the ability of a person to attend to a task, to concentrate, to learn new information, to retain that information, or to recall at a later time that information acquired while under the influence of cannabis. Ability to recall information acquired in the intoxicated state may be improved by re-intoxication (an example of state-dependent learning).

8. *Distrubances of higher intellectual functions.* These functions include those of reason, intellect, and judgment. The "amotivational syndrome" can be categorized as an example of this class of pathology, but it has been discussed above as a disorder of volition.

B. *Impairment of motor and psychomotor performance.* General motor coordination may be affected when cannabis is taken in amounts equivalent to that used in social settings. The degree of impairment is dose-related. Reaction time, which is a measure of attentiveness as well as motor agility, may also be compromised. Tracking, the ability to follow a moving target, is impaired at low doses of cannabis intake. Tracking skill is correlated with driving and flying ability (Ref. 6).

Other Major Body or Organ Systems

1. *Cardiovascular.* Acute cannabis use is associated with an acceleration of the heart rate; however, there may be some tolerance to this effect after chronic exposure. In addition, cannabis has effects (these vary with body position, dose, and chronicity of use) on cardiac output, blood pressure, and peripheral vascular resistance (Ref. 6).

2. *Pulmonary.* The effect of cannabis on the pulmonary system is difficult to distinguish from the effects of smoking itself. Cannabis, in small doses, has an acute bronchodilator effect; but this action may, with time, be overshadowed by the irritant properties of smoke which can cause bronchoconstriction. Indeed, chronic smoking of cannabis may cause respiratory system pathology, similar to that produced by tobacco cigarette smoking (Ref. 6).

3. *Reproductive system.* In men, chronic cannabis use may lead to reduced sperm counts and motility; however, the relationship of these changes to male fertility is not known (Ref. 6). In women, there is some reason to believe that cannabis use might contribute to "subfertility," but the evidence to support this belief is indirect (Ref. 6).

4. *Genetic information.* The evidence for a mutagenic effect of delta-9-THC must be distinguished from the mutagenic effect of cannabis when smoked. There is evidence of mutagenicity for the drug when it is smoked. There are also reports of chromosomal breaks occurring in cell

samples obtained from persons using cannabis (Ref. 6).

5. *Immune system.* Cannabis use may be associated with impairment of the function of the immune system (Ref. 6).

b. *Cannabis leaves.* As noted above, cannabis leaves are a constituent of the marihuana product that is normally used both illicitly and in research. Thus, the discussion above is directly applicable to cannabis leaves when viewed in the context in which they have been used. Because cannabis leaves are not known to have been used separated from other parts of the marihuana plant, there is no body of scientific evidence on the pharmachlogical effect of a product containing only cannabis leaves. Because cannabis leaves contain a percentage THC content that is roughly equivalent to the percentage of THC in the cannabis discussed above, however, it is a reasonable scientific conclusion that the effects discussed in the previous section are also those of cannabis leaves alone.

c. *Cannabis seeds capable of germination.* FDA is not aware of scientific evidence of any pharmacological effect of cannabis seeds capable of germination in and of themselves. In fact, because the THC content of the seeds is relatively low, it would not be expected that the seeds by themselves would produce the effects discussed above. On the other hand, as previously noted, the seeds would predictably be used to grow marihuana plants and by that route produce the pharmacological effects discussed in subsection (a) of this discussion.

3. *The state of current scientific knowledge regarding the drug or other substance (21 U.S.C. 811(c)(3)).* as noted previously, this discussion presents FDA's evaluation of the evidence discussed under factor 2 above.

a. *Cannabis and cannabis resin.* In weighing the scientific evidence on the effects of cannabis use, the agency has concluded that much of what is said and written about the plant and its derivatives is unsupported testimony and argument. Such evidence cannot be used to estimate rates of risk for specific effects or establish cause and effect relationships. It is not known what proportion of a representative sample of normal persons would experience many of the effects described in the preceding section. The relationship of the observed effects of cannabis to the quantity of drug consumed and to the duration of its use is not always evident. Moreover, the mere association of a drug with a phenomenon does not demonstrate that the drug caused the phenomenon. The putative drug effect may be merely coincidentally associated with drug use.

In light of these many qualifications about the nature of the available scientific evidence, it is important to explain how the agency distinguished reliable from unreliable information and reached its conclusions about the "state of current scientific knowledge regarding" cannabis.

First, members of the agency's staff who are expert in issues of illicit drug use and the requirements for scheduling recommendations relied upon their own experience and knowledge of cannabis and experience in reviewing other scheduled drugs to reach their conclusions.

Second, the expertise of the agency's expert staff and other appropriate agency officials has been supplemented with expertise from specific experts on cannabis who are or where either special government employees or members of the agency's Drug Abuse Advisory Committee.

Finally, the agency has relied upon the scientific literature. Recent published evidence reviewed by the agency includes the report by the Institute of Medicine (IOM), National Academy of Sciences, on *Marihuana and Health* (National Academy Press, Washington, 1982) (Ref. 6). The IOM report is not only recent and comprehensive but the IOM committee that wrote the report appears to be an impartial and disinterested group of scientists whose goal was an accurate statement of our current knowledge about the relationship of cannabis use to the public health.

FDA's conclusion about the state of current scientific knowledge regarding cannabis follows; they are organized by body or organ system in a manner that parallels the presentation of the evidence under factor 2.

Central Nervous System

Although the agency has no means to estimate the exact proportion of cannabis users that will be affected, there is little reason to doubt that cannabis has potent effects on psychological and neurological behaviors of people. Available evidence shows that cannabis use can alter perception (cause illusions and hallucinations) and mood (cause anxiety, dysphoria, paranoia, etc.), and can cause panic and reactions of psychotic degree. Cannabis use can impair motor and psychomotor performance, and can alter the level of consciousness, impulse control, and, perhaps, judgment. The acute effects of cannabis range from mild, subjectively pleasing changes in affective state to frank, organic delirium. The acute behavioral effects are linked to cannabis use in a causal way. In contrast, evidence on the long-term adverse consequences is less persuasive. In particular, it is not clear whether the well-characterized "amotivation" syndrome associated with chronic, heavy marihuana use is a manifestation of the personal character or psychopathology of some marihuana users or an expression of drug effect.

Body Systems Other Than the Central Nervous System

Cannabis has effects on the heart, lungs, and endocrine systems. The magnitude and significance of these effects is not known, but each must be considered a possible potential risk to the public health.

In summary, the effects of major social and medical significance associated with cannabis use and important to a scheduling recommendation are largely related to the central nervous system but include the cardiovascular and pulmonary systems. Cannabis does not appear to have major effects of known significance on other organ systems. It is important to emphasize, however, that the available evidence often does not address the critical questions.

The agency agrees with the general conclusion of the IOM (Ref. 6) that, "[t]he scientific evidence published to date indicates that marihuana has a broad range of psychological and biological effects, some of which, at least under certain conditions, are harmful to human health. Unfortunately, the available information does not tell us how serious this risk may be" (p. 5).

b. *Cannabis leaves.* The conclusion in the previous discussion concerning cannabis and cannabis resin applies to cannabis leaves for the reasons and to the extent stated in this document's discussion of Factor 2 as it applies to cannabis leaves. Current scientific knowledge concerning cannabis leaves not in conjunction with other parts of the marihuana plant is totally undeveloped because the leaves are not used separately.

c. *Cannabis seeds capable of germination.* Although current scientific knowledge concerning the pharmacological effects of cannabis seeds is undeveloped, because the THC content of the seeds is relatively very low, it can be fairly concluded that the seeds themselves will not have the pharmacological effects associated with other parts of the marihuana plant. As previously noted, however, the pharmacological effects of cannabis, discussed above, may be said to be associated with the seeds in that the

seeds will likely be used to grow the plant.

4. *Its history and current pattern of abuse (21 U.S.C. 811(c)(4)).* In the legislative history of the CSA, Congress commented on Factor 4 as follows: "To determine whether or not a drug should be controlled, it is important to know the pattern of abuse of that substance, including the social, economic, and ecological characteristics of the segments of the population involved in such abuse."

The following information demonstrates a history and current pattern of widespread illicit use of cannabis in the United States, as measured by wide use and illegal importation and distribution.

a. *Cannabis and cannabis resin.* Cannabis use goes back to the beginning of recorded history. For example, cannabis preparations have been used for thousands of years in Asia. Cannabis spread West to Europe and by the time Europeans reached the New World, they were using the cannabis plant as a source of cloth and as an intoxicant. Marihuana or cannabis use began to grow in popularity in the United States during the 1920's. By 1927, 46 States and the District of Columbia had passed laws against marihuana and in the same year, the Federal government enacted the Marihuana Tax Act. This Act made registration and taxation of marihuana buyers and sellers mandatory, and imposed criminal penalties. The Act effectively banned the possession and use of cannabis preparations. Subsequently in 1961, it was controlled under the Single Convention on Narcotic Drugs. In the United States, it was subsequently controlled under Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970.

There have been a number of studies on the pattern of use and abuse of cannabis related to the pattern of use of other drugs of abuse. These studies show that cannabis is used concurrently with alcohol or other drugs of abuse (e.g., Ref. 13).

Results from a 1979 survey on drug use reported by the National Institute on Drug Abuse (Ref. 14) were as follows: in 1979, 8 percent of 12 and 13 year-olds reported some experience with cannabis, and by ages 14 and 15, the percentage who had used cannabis increased to 32 percent. More than half (51 percent) of 16 and 17 year-olds had used cannabis. In the overall 12 to 17 year-old group, 31 percent had "ever experienced" marihuana use, more than double the figure (14 percent) which was reported in 1972. The peak use was in the age group from 18 to 25 years; 68 percent in 1979 compared with 48 percent in 1972.

With respect to current use of cannabis, defined as use within the month preceding the survey, 16.7 percent of the 12 to 17 year-old group in the 1979 survey currently used cannabis, while 35 percent of the 18 to 25 year-old group were currently using cannabis. In the 1979 survey, in the age group 26 years and over, 19.6 percent reported ever having used cannabis, while 6 percent reported current use. Corresponding figures for 1972 were 7.4 percent for having experienced cannabis use and 2.5 percent currently using cannabis. Current users age 12 to 17 in 1972 represented 7 percent of that age group, while in 1979 that same group (now members of the 18 to 25 year-old group) had a current use rate of 35 percent. Thus approximately 28 percent of the individuals who were current users between the ages of 18 and 25 in 1979 (the differences between 7 percent and 35 percent) began using after the age of 17.

A similar study, using different age parameters and focusing on the year 1977, provides confirmatory data. According to the NIDA Research Monograph, No. 35, May 1981 (Ref. 15), in 1977 there were 9,632,000 (56.8 percent) out of 16,958,000 young adults age 18 to 21 years, and 9,261,000 (60.3 percent) out of 15,358,000 young adults age 22 to 25 years who reported ever having used marihuana. These rates represent increases of 4 percent and 13 percent over the 1974 rates for 18 to 21 years and 22 to 25 years, respectively. The survey indicates there were 3,233,000 regular users of marihuana out of 13,415,000 (24.1 percent) age 18 to 25 years in 1977.

The special problem of drug abuse among women was reported in 1980 (Ref. 16). Results were obtained from a sample of 14,428 women clients in treatment centers. The paper addressed differences in use of heroin, marihuana amphetamines, barbiturates, and sedatives according to age, race, and education. Marihuana was the second most commonly abused drug among these women.

A special U.S. population that has been surveyed is the military. "Highlights from the Worldwide Survey of Nonmedical Drug Use and Alcohol Use Among Military Personnel, 1980" (Ref. 17). For the total military, 27 percent reported using any drug within the past 30 days, and 26 percent reported using marihuana or hashish within the past 30 days. Twenty-six percent reported using marihuana, or hashish, during the past 30 days. Thirty-six percent reported using any drug during the past 12 months, while 35 percent reported using marihuana or hashish during the past 12 months. Further, for the total military, 19 percent of the population reported using marihuana or hashish at least once a week during the past 30 days. The next closest drug group used frequently by the military was amphetamines or other stimulants, at the rate of 3 percent at least once a week during the past 30 days. Cannabis, i.e., marihuana or hashish, is thus by far the most widely abused drug in the military.

The National Institute on Drug Abuse (NIDA) also has reported on demographic trends in drug abuse, 1980–1995 (Ref. 15). In this report, NIDA uses information from previous surveys, up to the 1977 survey, to predict illicit drug use for the next 10 to 15 years. NIDA concluded that illicit drug use is decreasing among all age groups.

b. *Cannabis leaves.* The discussion above of the history and current pattern of abuse of cannabis and cannabis resin applies to cannabis leaves as commonly used. FDA is unaware of any significant history of use of cannabis leaves separated from all other parts of the marihuana plant.

c. *Cannabis seeds capable of germination.* The discussion above on the history and current pattern of abuse of cannabis and cannabis resin applies to cannabis seeds capable of germination because cannabis may be produced by use of such seeds. FDA is unaware of any history or current pattern of abuse of the seeds other than their use to grow cannabis.

5. *The scope, duration, and significance of abuse (21 U.S.C. 811(c)(5)).* In House Report 91–1444, Congress stated that:

In evaluating existing abuse, not only must the Attorney General know the pattern of abuse, but he must also know whether the abuse is widespread. He must also know whether it is a passing fad, or whether it is a significant chronic abuse problem like heroin addiction. In reaching his decision, the Attorney General should consider the economics of regulation and enforcement attendant to such a decision. In addition, he should be aware of the social significance and impact of such a decision upon those people, especially the young, that would be affected by it.

a. *Cannabis and cannabis resin.* The discussion in the previous section of percentages of marihuana users demonstrates that the cannabis abuse is of wide scope, involving, among others, the young and members of the military, is of considerable significance, and has continued for over a decade. Further

evidence on cannabis abuse is provided by information concerning the total amount of cannabis available in this country from illicit sources.

According to the Drug Enforcement Administration (DEA), about 10,000 to 15,000 metric tons of cannabis (marihuana) were smuggled into the United States in 1978, a 4 percent increase over the 12,000 metric tons smuggled in 1977 (Ref. 20). The value of the marihuana in 1978 was estimated by DEA to be $15 to 23 billion (approximately $19,000,000,000 in 1977) (id).

For 1979, DEA has estimated the total cannabis supply to be between 10,000 and 13,600 metric tons. Seventy-five percent of the total cannabis in 1979 was from Columbia, 11 percent from Mexico, 7 percent from Jamaica, and 7 percent from domestic U.S. sources. For the year 1980, the current estimate is 10,600 to 15,500 metric tons. Columbia supplies 75 percent, Mexico 9 percent, Jamaica 10 percent, and domestic U.S. sources account for 6 percent. The total amount would convert to 23,320,000 to 34,100,000 pounds of cannabis available in the United States in 1980. This amount compares with the estimated 24,000,000 pounds available in 1977. The amount of cannabis grown for scientific and medical investigations in the United States in 1979 was 986 kilos or 2,100 pounds and approximately 2,000 kilos or 4,400 pounds for the year 1980.

These statistics show that the scope of the illicit cannabis traffic is significant, and has been significant for a least 5 years. Also, the extent of the illicit use of cannabis, particularly among the young and the young adults, is widespread throughout the United States. Further, these statistics show that the drain of funds into illicit channels as a result of cannabis use is significant.

b. *Canabis leaves.* The discussions above regarding the scope, duration, and significance of abuse for cannabis and cannabis resin apply to cannabis leaves when used in conjunction with other parts of the marihuana plant. FDA is unaware of any use of cannabis leaves separated from all other parts of the marihuana plant and the agency, thus, has no information about scope, duration, and significance of abuse of leaves separated from other parts of the plant.

c. *Cannabis seeds capable of germination.* There are no data concerning the extent of illicit traffic in cannabis seeds capable of germination. As discussed previously, there are no data available on abuse of the seeds per se, as opposed to the plants that may be grown from the seeds.

6. *What, if any, risk there is to the public heatlh (21 U.S.C. 811(c)(6).* With respect to this factor, House Report 91–1444 states: "If a drug creates no danger to the public health, it would be inappropriate to control the drug under this bill."

a. *Cannabis and cannabis resin.* Under factors 2 and 3 above, the scientific evidence of the pharmacological effects and the state of current scientific knowledge regarding cannabis are discussed in detail. The agency agrees with the general conclusions of the IOM (Ref. 6) that, "[t]he scientific evidence published to date indicates that marijuana has a broad range of psychological and biological effects, some of which, at least under certain conditions, are harmful to human health. Unfortunately, the available information does not tell us how serious the risk may be" (p. 5).

The adverse consequences associated with marihuana use include both acute and chronic effects. The acute health hazards are most important and include, among others, impairments in almost all aspects of central nervous system function, and decrements in psychomotor performance skills necessary for driving or flying. Certain cardiovascular effects (e.g., those that can lead to increased heart rate and associated circulatory changes) may be harmful, especially to those with pre-existing heart disease. The acute health hazards often result in medical problems requiring immediate medical attention at hospital emergency rooms.

The chronic hazards of marihuana use are less well established. One probable risk of importance is the one associated with the common route of cannabis administration, smoking. Smoking of tobacco cigarettes is a well-documented health hazard, and it is reasonable to assume that smoking of cannabis cigarettes is hazardous as well.

Much of the most recent evidence about the effects of marihuana use in humans is reported in the Addiction Research Foundation Report, 1981 (Ref. 8) prepared by internationally recognized scientists in the field of drug abuse and effects of marihuana and the Institute of Medicine Report, 1982 (Ref. 6), previously discussed. The National Institute on Drug Abuse also provided much of the most recent information relative to the epidemiology of effects of cannabis on the public use. The risk to the public health from acute and chronic cannabis use is evaluated on the basis of the effects included in these reports. Also, as is discussed in Part III below, cannabis or marihuana has no currently accepted medical use in treatment in the United States. Thus, in weighing the risks against the benefits of marihuana use, FDA proposes to conclude that the scale is tipped heavily towards the risks. Clinical investigations designed to determine whether marihuana has medical utility and whether marihuana may be used safety under medical supervision are still ongoing.

In estimating the number of individuals who use cannabis and, thus, are at risk of suffering the reported adverse health consequences, the Federal government uses data from several sources including certain surveys, including the Drug Abuse Warning Network (DAWN), the National Household Survey on Drug Abuse (Household Survey), and the High School Senior Survey (High School Survey). DAWN represents an ongoing reporting system, while the Household Survey and the High School Survey are periodic data collection efforts. Each survey contributes valuable information to the overall drug abuse picture.

The reports of death from medical examiners collected by DAWN for the calendar year 1980 placed marihuana at the lower end of the spectrum of frequency among the 100 drugs or substances reported. During the same period, however, marihuana was listed at the top end of the spectrum of frequency among the 100 drugs or substances reported as the reason for an emergency room visit during this period (Ref. 21). Marihuana was, for example, mentioned more than twice as often as amphetamines. Thus, it would appear that the adverse effects from marihuana use rarely result in a fatal outcome but are serious enough to be one of the major drug causes for seeking emergency room treatment.

In the High School Survey, high school seniors reported that they believe the regular use of marihuana has caused them to experience significant problems. For example, 28 percent reported they think less clearly, while 11 percent reported they felt less stable emotionally. Young people are believed to be especially at risk from the use of marihuana because of their ongoing physical and emotional maturation. It is possible that young, regular marihuana users may not be able to develop appropriate "life skills" on schedule, and that failing to do so it may be difficult, if not impossible, for them to make up these developmental differences later in life (Ref. 12).

As discussed earlier, although certain adverse effects have been reported from cannabis use, the exact percentage of cannabis users who are experiencing these adverse effects is unknown. FDA tentatively concludes that the risk to the

public health from marihuana use is particularly serious because the number of marihuana users is so large. Whatever the precise risk, widespread use of cannabis will obviously produce a greater incidence of harm than relatively little use of cannabis. Moreover, although in some cases the relationship of cannabis use to reported adverse effects is not certain, particularly the emotional and "amotivational" effects, the consequences of these effects, if real, are so great that, in the absence of good evidence against the reported association, the risk to the public health must be considered great. FDA's proposed conclusion that cannabis does create a significant risk to public health is thus based on its known adverse effects and adverse effects that are suggested but not yet proved to be related to marihuana use, both in a setting of relatively widespread use.

Based on the 1979 Household Survey, teenagers in the United States use more marihuana than teenagers anywhere else in the world (Ref. 22). Although a recent trend shows that marihuana use and use of other drugs has declined, it is too early to tell whether this decrease will continue or is merely a pause in the rise. Despite this recent trend, the overall prevalence of use of marihuana has remained at approximately 60 percent of high school seniors for the years 1978, 1979, and 1980 (Ref. 6). Currently, it is estimated that 22 million or about 10 percent of the total U.S. population now use marihuana (Ref. 22). In 1960, less than 7 percent of young adults age 18 to 25 had used marihuana. In 1979, more than 60 percent of young adults had used marihuana (Ref. 22).

FDA, thus, proposes to conclude that cannabis may produce significant adverse health effects to persons who use marihuana. And, because approximately 22 million Americans are reported to be current users of marihuana, FDA proposes to conclude that there is a significant risk to the public health from marihuana or cannabis use.

b. *Cannabis leaves.* The risk to the public health associated with use of cannabis leaves in the state in which they are normally found, i.e., in conjunction with others parts of the marihuana plant, is significant for the reasons stated in subsection (a) above. There is virtually no reported experience with a product containing cannabis leaves separated from all other parts of the marihuana plant. Because the leaves themselves have significant THC content, however, it is reasonable to conclude that a use of a leaf-only product would present the same risk as use of cannabis itself.

c. *Cannabis seeds capable germination.* The risk associated with cannabis seeds derives only from the probability that such seeds would be used to grow marihuana, which would in turn produce the risks described above.

7. *Its psychic or physiological dependence liability (21 U.S.C. 811(c)(7)).* In House Report 91–1444, Congress states that: "There must be an assessment of the extent to which a drug is physically addictive or psychologically habit-forming, if such information is known."

a. *Cannabis and cannabis resin.* (1) *Psychological (psychic) dependence liability.* In the Federal Register of March 9, 1982 (47 FR 10083), FDA proposed to conclude that some individuals should be considered sufficiently strong drug-seeking in their behavior to be considered severely psychologically dependent on cannabis. The basis for this conclusion is our belief that repeated seeking of an illicit drug with an established potential to cause injury constitutes prima facie evidence of psychological dependence. Also, it should be noted that a report of the American Medical Association's (AMA) Council on Scientific Affairs, as adopted by the AMA House of delegates, concluded that marihuana is hazardous to health and that there was a growing prospect of appreciable number of marihuana users incurring physiological and psychological impairment (Ref. 23). Since the March 9, 1982 Federal Register publication, FDA has completed a review of two recent and significant reports on marihuana and health (Institute of Medicine Study and Addiction Research Study) (Refs. 6 and 8). These reports include nothing that changes FDA's earlier proposed conclusions. Thus, FDA proposes to conclude that marihuana use can result in severe psychological dependence.

(2) *Physical (physiological) dependence liability.* The agency defines physiological dependence as the appearance of a characteristic syndrome, consisting of physical signs and symptoms, that appears upon cessation of drug use. Only one investigator has reported withdrawal signs and symptoms after frequent large doses of THC (Ref. 11). Other investigators have failed to observe a withdrawal syndrome. However, it is important to emphasize that drugs now well known to cause physiologic dependence (such as barbiturates, benzodiazepines, amphetamines, and some mixed opioid agonist/antagonist analgesics) were for many years assumed to be free of any such liability. It was only after many years of medical use, under conditions of close scrutiny, that the serious physiological dependence caused by these drugs was recognized. Thus, although the agency is unable to conclude at this time, on the basis of the evidence available, that cannabis produces physiologic dependence, the experience with known dependence-producing drugs (described above) must be considered.

b. *Cannabis leaves.* For the reasons discussed above, cannabis leaves present a psychological dependence liability. This conclusion necessarily follows from the evidence concerning cannabis, whether the leaves are considered as components of marihuana as generally used or as a separate product that, because of its THC content, would have the same effects as cannabis. Like cannabis, cannabis leaves cannot now be considered to have a physiological dependence liability.

c. *Cannabis seeds capable of germination.* As previously noted, the seeds do not themselves present a dependence liability, but, because they may be used to grow marihuana, have a liability associated with that fact.

8. *Whether the substance is an immediate precursor of a substance already controlled under this title (21 U.S.C. 811(c)(8).* House Report 91–1444 states that: "The bill allows inclusion of immediate precusors on this basis alone into the appropriate schedule and thus safeguards against possibilities of clandestine manufacture."

a. *Cannabis and cannabis resin.* Cannabis and cannabis resin are not precursors of any substance already controlled. Cannabis and cannabis resin are substances which are themselves already controlled in Schedule I of the Controlled Substances Act.

b. *Cannabis leaves.* Cannabis leaves are not an immediate precursor to a substance already controlled under this title. Because they are viewed as a component of cannabis, they are already controlled in schedue I.

c. *Cannabis seeds capable of germination.* Cannabis seeds capable of germination are not an immediate chemical precursor to a substance already controlled under this title. They are a "precursor" of cannabis in the sense that cannabis may be grown from the seeds. Because they are a component of cannabis, they are already controlled in schedule I.

III. Criteria For Scheduling

The eight factors described above are used to determine into which of the five

CSA schedules, if any, a given drug or substance should be placed. Each of the five CSA schedules (I to V) has three criteria (A to C) to aid in this determination. To assign a substance to a schedule, the Attorney General must find that the substance meets the statutory criteria for that schedule. See 21 U.S.C. 811(a).

Criterion A for all five schedules is a series of descriptions of abuse potential, declining from high to low abuse potential. Schedules I and II are identical in this regard, both requiring a finding of "high" potential for abuse. Schedules III through V require findings of lower, though still some, abuse potential.

Criterion B for all five schedules deals with whether the drug, or other substance, has a currently accepted medical use. Schedule I drugs must be found to have "no currently accepted medical use in treatment in the United States" while schedules II through V all require a "currently accepted medical use * * *." In addition, criterion B for schedule II allows an alternative finding: "currently accepted medical use with severe restrictions."

Criterion C is different for schedule I than for the other schedules. For schedule I, the criterion requires a finding of "lack of accepted safety for use of the drug or other substance under medical supervision." For schedules II through V, this criterion consists of a sliding scale of the drug's dependence-producing capacity, either physical or psychological. Schedule II drugs require a finding of the highest dependence-producing capacity while schedule V drugs require the lowest.

In the Federal Register of June 20, 1979 (44 FR 36127), DHHS stated that it believed, from a medical/scientific standpoint, that the marihuana (or cannabis) plant materials "could be placed in either schedule I or schedule II" but recommended continued control in schedule I. A factor in the determination that both schedules I and II were appropriate from a medical scientific standpoint included the statements that: "Conceivably, the current investigational use of some of the substances could be classified as 'a currently accepted medical use with severe restrictions' within the meaning of the second criterion for schedule II. That is a plausible interpretation of that criterion but its appropriateness is not free from doubt." (It should be noted that these statements were made in the context of the 1979 proceedings which applied to THC as well as the marihuana (or cannabis) plant materials at issue here.)

Although certain developments have occurred with respect to these substances in the intervening years (i.e., Federally approved research continues, legislation in some States provides for various degrees and kinds of research controls, and FDA has approved, on the recommendation of its oncologic drugs advisory committee, THC distribution under the National Cancer Institute's "Group C" system), these developments do not change the fact that, as explained below, in FDA's opinion the marihuana plant materials, as opposed to THC, meet all three criteria only for schedule I. Accordingly, FDA proposes that they remain in schedule I.

A. *Criterion A*—On the sliding scale of abuse potential, FDA proposes to conclude that cannabis, cannabis resin, cannabis leaves, and cannabis seeds capable of germination (because they are planted, cultivated, grown, and harvested to produce the plant) have a high potential for abuse and thus meet this criterion for schedules I and II (the criterion is identical for these two schedules).

As plant constituents, these cannabis substances have been shown to have a high potential for abuse (see discussion in factor 1 above). Thus, although licit plant materials have not been abused because they have been subject to stringent controls as an investigational drug under the Federal Food, Drug, and Cosmetic Act and a schedule I substance under the CSA, illicit plant materials are widely abused. These substances have marked psychotropic effects and, if more freely available, their abuse would very likely increase as major drugs of abuse (see discussions in factors 4 and 5). If the stringent CSA controls are removed from these substances, it can be anticipated that there would be attempted thefts, that attempts would be made to divert the drug from legitimate channels, and that any drug so diverted would command premium prices in the illicit market.

The tentative conclusion that these substances have a high potential for abuse (thus meeting criterion A for schedules I and II) logically precludes them from meeting criterion A for schedules III through V, for drugs in each of these three schedules have a progressively lower abuse potential than schedule I and II drugs.

B. *Criterion B*—This criterion involves the "accepted medical use" of the drug and has three different variations among the five schedules, as follows:

1. *Schedule I:* "The drug or other substance has no currently accepted medical use in treatment in the United States."

2. *Schedule II:* "The drug or other substances has a currently accepted medical use in treatment in the United States *or* a currently accepted medical use with severe restrictions." (Emphasis added.)

3. *Schedules III through V:* "The drug or other substances has a currently accepted medical use in treatment in the United States."

FDA interprets the term "accepted medical use" to mean lawfully marketed under the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 301, et seq. The agency stated this interpretation previously in the Federal Register document dealing with THC (47 FR 10084). NORML, in a subsequent action brought in the United States Court of Appeals for the District of Columbia, challenged that interpretation as conflicting with a statement made by the court in a footnote in *NORML* v. *DEA, supra,* 559 F.2d at 750, n.65. In the footnote, the court noted that the interrelationship between the Federal Food, Drug, and Cosmetic Act, in particular its "new drug" approval provision, and the Controlled Substances Act was far from clear. The court stated that it was appropriate for NORML to apply for rescheduling of marihuana under the Controlled Substances Act before obtaining approval of a new drug application under the Federal Food, Drug, and Cosmetic Act. *Id.*

A drug may be marketed lawfully under the Federal Food, Drug, and Cosmetic Act after approval of a new drug application (NDA) for that drug. There are, theoretically, other ways in which a drug could be marketed legally. The drug could satisfy either the requirements for exemption from the definition of "new drug" in 21 U.S.C. 321(p) or the requirements for a "grandfather clause" from the new drug approval provision, see, 21 U.S.C. 321(p)(1) and Pub. L. 87–781, sec. 107(c)(4). It is obvious, however, that the marihuana substances at issue here would not qualify either for exemption from the "new drug" definition or for the "grandfather clause" exceptions to premarket clearance.

A drug may also, theoretically, be legally marketed without violating the Federal Food, Drug, and Cosmetic Act if it is manufactured, processed, and used entirely within a single State without any connection at all with interstate commerce. (See, however, Article 23 and 28 of the Single Convention on Narcotic Drugs regarding restrictions imposed by treaty on manufacture of marihuana.) The agency has considered whether there is any basis to conclude that the

substances at issue in this document have obtained "accepted medical use" by virtue of totally intrastate production and use and has found no basis for a conclusion that these products have obtained acceptance of their medical use by that means.

Thus, there is no reason to conclude that the marihuana substances at issue here would qualify for "accepted medical use" in the absence of the approval by FDA of an NDA.

The mechanism set up by Congress for lawful marketing of a new drug requires submission of an NDA to FDA and FDA approval of that application before marketing. Before FDA can approve an NDA, however, the drug sponsor must submit data from an extensive battery of experimental testing on both animals and humans to establish the drug's safety and effectiveness for its proposed uses. In addition, the sponsor must submit data on manufacturing controls demonstrating that standards of identity, strength, quality, and purity will be met. Finally, the sponsor must submit labeling which adequately reflects the proper conditions for use. See 21 U.S.C. 355(d) and 21 CFR 314.1. Only after FDA has evaluated this information can the agency make a decision on whether the NDA should be approved and the drug marketed.

Thus, the lack of an approved NDA for a drug substance leads FDA to find that that substance lacks an "accepted medical use in treatment" for two reasons. First, if use of the drug is unlawful whenever interstate commerce is involved, medical use of the drug cannot be classified as accepted. Second, in the absence of the data necessary for approval of an NDA, the agency has no basis for concluding that medical use of the drug in treatment can be considered acceptable by medical standards.

Because "currently accepted medical use * * * " (schedules III through V and schedule II, first clause) means lawfully marketed under the act, "no currently accepted medical use * * * " must mean not lawfully marketed. The substances at issue fit into the later category because they are new drugs within the meaning of the act and there is not an approved NDA for the drugs. Thus, they cannot be legally marketed without an approved NDA. The lack of data from any sources demonstrating that use of these substances is medically acceptable, i.e., that sufficient data exists to qualify the substances for NDA approval, confirms the finding that these substances do not meet this criterion for schedules III through V. Therefore, these substances meet criterion B for schedule I.

A plausible argument exists, however, that these substances also meet the second clause of criterion B for schedule II because they have "a currently accepted medical use with severe restrictions." Although this clause is not defined in either the statute or the legislative history, the agency believes that only certain investigational drugs in the later stages of the investigational process may fall within this statutory language.

Investigational drugs progress from experimentation in a very limited, closely supervised setting involving only a few individuals to use in a broader investigational protocol using hundreds of patients. Under FDA's regulations, reports of these clinical studies are periodically sent to FDA so that the agency can monitor properly the ongoing research and progression to broader clinical trials. See 21 CFR Part 312.

The placement of THC in National Cancer Institute's "Group C" distribution scheme is an example of clinical research progression that qualifies as a "currently accepted medical use with severe restrictions." See 47 FR 10080, March 9, 1982. Clinical research on the marihuana (cannabis) materials at issue, however, has not progressed to the point that FDA believes that they have a currently accepted medical use with severe restrictions. In typical drug development, following studies in animals, studies in humans are conducted in phases or stages to provide necessary information. The information gathered at each phase must be evaluated and determinations made based on the evaluation before a subsequent phase may begin. Early phase studies usually involving small numbers of patients are necessary to provide initial evidence as to safety, pharamacological effects, and dose-related side effects, principally so that later studies can be carefully designed. Subsequent phases of studies are necessary to provide evidence of clinical safety and effectiveness, i.e., knowledge of effective dose and side effects and indications of therapeutic potential in humans. Later phases of studies are conducted to confirm and extend the findings indicated by earlier phase studies. In later phases a drug is used the way it would be administered when marketed. By the time these later studies are completed, the drug or substance usually has been studied in several hundred to several thousand patients. Generally by this time sufficient data have been generated to that FDA can make a dertermination regarding whether the drug is safe and effective under the statutory definitions. See 21 U.S.C. 355(d).

THC is a drug in the late phases of investigation as described above while the investigational studies on the marihuana plant materials are properly classified as in the earlier phases of study. Moreover, before a drug substances may be used in the practice of medicine it must have a composition of active ingredients that has been established and accepted as standard (for example, conjugated estrogens and powdered digitalis). Such standardized identity, purity, potency, and quality are specified either in a new drug application or in official compendium, e.g., U.S. Pharmacopeia or National Formulary. There is no standard cannabis substance.

Legislation in more than 20 States authorizes the use of marihuana and/or THC for medical research, primarily to combat nausea and vomiting associated with cancer chemotherapy and in the treatment of glaucoma. Such uses, however, should not be confused with the "accepted medical use" standard. These uses are all investigational uses. At least 11 States FDA-approved protocols for such investigations. The American Medical Association's Council on Scientific Affairs, in its report entitled "Marihuana in the '80s" (Ref. 23), makes the following statement: "For those [s]tates with enabling legislation that has not as yet been implemented, it is recommended that appropriate regulations and guidelines be established to insure that bonafide research is carried out, and that medical use beyond the context of clinical investigation is not permitted." This statement clearly is in accord with FDA's view that cannabis materials, as investigational research substances, are without accepted medical use in therapy or treatment by physicians practicing medicine in the United States.

Such State legislation, often referred to in their titles as "Therapeutic Research Acts," should not be confused with State laws which "decriminalize" the possession or transfer of certain marihuana materials for personal use, including recreational uses. These latter State laws involve reductions in criminal penalties and do not address medical research with these substances. Consequently, FDA tentatively concludes that although an argument that the second clause of criterion B for schedule II might be bet by certain marihuana substances under investigational use, the marihuana

substances at issue here do not meet criterion B for schedule II.

C. *Criterion C*—FDA proposes that the substances at issue meet criterion C for schedule I because there is "a lack of acccepted safety for use of the drug or other substance under medical supervision." FDA believes that "accepted safety," like "accepted medical use," has not been shown for a drug product that has not qualified for lawful marketing under the act. Accordingly, because these substances are not lawfully marketed, there is a "lack of accepted safety * * *."

As noted above, the Federal Food, Drug, and Cosmetic Act provides that FDA approve an NDA upon scientific evidence that the drug has been shown to be safe and effective for its proposed uses. See 21 U.S.C. 355(d). Because no drug is ever completely safe in the absolute sense, FDA considers "safe" to mean (in the context of a human drug) that the therapeutic benefits to be derived from the drug outweigh its known and potential risks under the conditions of use in the labeling. For this reason, FDA requires, before approval of an NDA, that extensive clinical and preclinical testing be conducted to establish the safety of the drug. Indeed, FDA must deny approval of an NDA if inadequate information about the drug's adverse reactions is presented. See 21 U.S.C. 355(d)(1).

Another factor considered by FDA in assessing the drug's safety is the proposed labeling, which is approved at the time of approval for marketing. A drug might be considered safe for some proposed uses but not others. Only those proposed uses where the benefit/risk ratio is favorable will be included in the indications section of the drug's labeling. Physicians depend on detailed labeling for information on when and how a drug should be used, and any claim in the labeling must be supported by clinical studies. False or misleading proposed labeling also precludes FDA approval of an NDA. 21 U.S.C. 355(d)(6).

Clearly, the further along a drug is in the investigational process, the more information about safety and effectiveness there will be. But it is only upon approval for marketing, when there has been an institutional decision based on scientific judgment by the regulatory agency charged with the responsibility of evaluating the safety and efficacy of new drugs, that a drug becomes "accepted" as safe under medical supervision.

The safety and efficacy of the cannabis materials at issue have not yet been fully studied. Indeed, these materials are currently distributed to a limited number of physicians and several States as investigational new drugs only, and a considerable amount of clinical research is still needed before an NDA could be submitted. Only when full information is received and reviewed by FDA can a responsible, scientific judgment be made that marihuana materials have "accepted safety for use * * * under medical supervision". Accordingly, under the present facts, FDA proposes that the cannabis substances at issue meet criterion C for schedule I.

Criterion C for schedule II provides that "[a]buse of the drug or other substance *may* lead to severe psychological *or* physical dependence" (emphasis added). FDA proposes that abuse of the substances at issue may lead to severe psychological dependence in some individuals (see discussion in factor 7). Whether this psychological dependence might be better characterized as "high" (schedule III criterion) rather than "severe" (schedule II criterion) is a matter of scientific judgment. However, FDA tentatively concludes, based on the information before it, that the psychological dependence-producing ability of these substances lies at the top end of the spectrum and is most appropriately characterized as "severe," thereby meeting the criterion for schedule II.

In terms of possible physical dependence, FDA believes the available information before it, at this time, is insufficent to determine with certainty whether physical dependence occurs.

D. *Summary chart.* FDA's proposed recommendations on scheduling criteria for cannabis, cannabis resin, cannabis leaves, and cannabis seeds capable of germination may be summarized in the following chart:

Note.—The criterion varies according to the schedule.)

	Criterion A	Criterion B	Criterion C
Schedule I	Met	Met	Met.
Schedule II	Met	Not met	Met.
Schedule III	Not met	Not met	Possibly met.
Schedule IV	Not met	Not met	Not met.
Schedule V	Not met	Not met	Not met.

E. *Conclusion.* FDA proposes to recommend that, based on the scientific and medical evaluation, each of the cannabis materials at issue meet all three criteria for schedule I. FDA proposes to recommend that each of the cannabis materials at issue remain in schedule I.

IV. Public Hearing

Under 21 CFR Part 15, the Commissioner of Food and Drugs may, as a matter of discretion, permit persons to present information and views at a public hearing on any matter pending before FDA. The Commissioner has concluded that it is in the public interest to hold such a public hearing for the purpose of obtaining information and views on the material in Parts II and III above concerning the appropriate scheduling status under the CSA of cannabis, cannabis resin, cannabis leaves, and cannabis seeds capable of germination.

The public hearing will be be held on September 16, 1982, from 9 a.m. to 4 p.m. in Conference Rms. D and E, Parklawn Bldg., 5600 Fishers Lane, Rockville, MD 20857.

Every effort will be made to accommodate each person who wants to participate in the public hearing. However, each person who wants to ensure his or her participation in the hearing is encouraged by close of business on August 27, 1982, to: (a) submit the text of the presentation so that the presiding officer and any other persons who may serve on a panel conducting the hearing may formulate useful questions to be posed at the hearing (a comprehensive outline may be submitted as an alternative to the text); and (b) file a written notice of participation containing the name, address, phone number, affiliation, if any, of the participant, topic of presentation, and approximate amount of time requested for the presentation. Oral notice of participation may be made by telephone as an alternative to the written notice.

The text or comprehensive outline and the written or oral notice of participation may be made to: Frederick J. Abramek, Bureau of Drugs (HFD–120), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–443–3800.

Shortly after August 27, 1982, the amount of time allotted to each person and the approximate time that oral presentation is scheduled to begin will be determined. A hearing schedule showing the persons making oral presentations and the time allotted to each person will be filed with the Dockets Management Branch (address above) and mailed or telephoned to each participant before the hearing. If the number of persons formally requesting time for presentation exceeds the number that can be accommodated during the day session, the hearing will be carried over past the scheduled time and, if necessary, to the following day. An attempt will be made to hear, at the conslusion of the hearing, any person who is late. Other interested persons attending the hearing who did not

request an opportunity to make an oral presentation will be given an opportunity to make an oral presentation at the conclusion of the hearing, in the discretion of the presiding officer, to the extent that time permits. The hearing will be informal in nature and the rules of evidence do not apply.

References

The following information has been placed in the Dockets Management Branch (address above) and may be seen by interested persons from 9 a.m. to 4 p.m., Monday through Friday.

1. Marihuana and Health, 8th Annual Report, 1980.
2. *Journal of Natural Products*, 42(2) March-April 1980.
3. *Journal of Pharmaceutical Sciences*, 60:1264, 1971.
4. House Report 91-1444 (Part I), Comprehensive Drug Abuse Prevention and Control Act of 1970.
5. Washington Post, November 15, 1981, (F-13).
6. Institute of Medicine Report, pp. 25, 27, 29, 38, 41, and 43.
7. NIDA, Research Monograph Series No. 31, "Marihuana Research Findings, 1980."
8. Addiction Research Foundation, 1981.
9. *Journal of Clinical Pharmacology*, 21 (8 and 9, Supplement), August-September 1981.
10. "Marihuana," ed. Raphael Mechoulam, Academic Press, 1972.
11. "Pharmacology of Marihuana," ed. Braude and Szara, Raven Press, 1976.
12. Statement of William Pollin, M.D., Director, National Institute on Drug Abuse, before the Committee on Foreign Affairs, House of Representatives, April 20, 1982.
13. *American Journal of Drug and Alcohol Abuse*, 6(4), pp. 447-462, 1979.
14. NIDA, "Excerpts from the National Survey on Drug Abuse—1979," U.S. Printing Office, 1980, O-311-246/6014.
15. NIDA, Research Monograph Series No. 35, "Demographic Trends and Drug Abuse 1980-1995."
16. *International Journal of the Addictions*, 15(3), pp. 304-321, 1980.
17. Burt Associates, Inc., "Highlights from the Worldwide Survey of Nonmedical Drug Use and Alcohol Use Among Military Personnel, 1980," Contract No. NIDA 903-79-C-0667, Bethesda, MD.
18. Bulletin on Narcotics, XXXII, No. 4, pp. 29-45, 1980.
19. Bulletin on Narcotics, XXXIII, No. 1, pp. 9-19, 1981.
20. Drug Enforcement Administration, *Drug Enforcement*, March 1980.
21. Project DAWN Annual Report—1980, Drug Enforcement Administration and National Institute on Drug Abuse.
22. "Health Consequences of Marijuana Use," Government Printing Office 869-675, 1980.
23. AMA Council on Scientific Affairs, "Marijuana in the '80s," Adopted by the House of Delegates, December 1980.

Interested persons may, on or before October 1, 1982, submit to the Dockets Management Branch (address above), written comments regarding this notice. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: June 7, 1982.

Arthur Hull Hayes, Jr.,

Commissioner of Food and Drugs.

[FR Doc. 82-17331 Filed 6-28-82; 8:45 am]
BILLING CODE 4160-01-M

Advisory Committees; Meeting

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: This notice announces a forthcoming meeting of public advisory committees of the Food and Drug Administration (FDA). This notice also sets forth a summary of the procedures governing committee meetings and methods by which interested persons may participate in open public hearings conducted by the committees and is issued under section 10(a)(1) and (2) of the Federal Advisory Committee Act (Pub. L. 92-463, 86 Stat. 770-776 (5 U.S.C. App. I)), and FDA regulations (21 CFR Part 14) relating to advisory committees. The following advisory committee meeting is announced:

Circulatory System Devices Panel

Date, time, and place. July 23, 8:30 a.m., Rm. 403-425A, 200 Independence Ave. SW., Washington, D.C.

Type of meeting and executive secretary. Open public hearing, 8:30 a.m. to 9:30 a.m.; open committee discussion, 9:30 a.m. to 10:30 a.m.; closed committee deliberations, 10:30 a.m. to 3:45 p.m.; open committee discussion 3:45 p.m. to 4:00 p.m.; Glenn A. Rahmoeller, Bureau of Medical Devices (HFK-450), Food and Drug Administration, 8757 Georgia Ave., Silver Spring, MD 20910, 301-427-7559.

General function of the committee. The committee reviews and evaluates available data on the safety and effectiveness of medical devices currently in use and makes recommendations for their regulation.

Agenda—Open public hearing. Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee. Those desiring to make formal presentations should notify the contact person before July 14, 1982, and submit a brief statement of the general nature of the evidence or arguments they wish to present, the names and addresses of proposed participants, and an indication of the approximate time required to make their comments.

Open committee discussion. The committee will discuss several premarket applications (PMA's) for pacemakers and may also review one or more PMA's for other cardiovascular devices.

Closed committee deliberations. The committee may discuss trade secret or confidential commercial information relevant to one or more PMA's for pacemakers or other cardiovascular devices. This portion of the meeting will be closed to permit discussion of this information (5 U.S.C. 552b(c)(4)).

Each public advisory committee meeting listed above may have as many as four separable portions: (1) An open public hearing, (2) an open committee discussion, (3) a closed presentation of data, and (4) a closed committee deliberation. Every advisory committee meeting shall have an open public hearing portion. Whether or not it also includes any of the other three portions will depend upon the specific meeting involved. The dates and times reserved for the separate portions of each committee meeting are listed above.

The open public hearing portion of each meeting shall be at least 1 hour long unless public participation does not last that long. It is emphasized, however, that the 1 hour time limit for an open public hearing represents a minimum rather than a maximum time for public participation, and an open public hearing may last for whatever longer period the committee chairman determines will facilitate the committee's work.

Meetings of advisory committees shall be conducted, insofar as is practical, in accordance with the agenda published in this Federal Register notice. Changes in the agenda will be announced at the beginning of the open portion of a meeting.

Any interested person who wishes to be assured of the right to make an oral presentation at the open public hearing portion of a meeting shall inform the contact person listed above, either orally or in writing, prior to the meeting. Any person attending the hearing who does not in advance of the meeting request an opportunity to speak will be allowed to make an oral presentation at the hearing's conclusion, if time permits, at the chairman's discretion.

Persons interested in specific agenda items to be discussed in open session may ascertain from the contact person the approximate time of discussion.

A list of committee members and summary minutes of meetings may be

Counsel, Federal Energy Regulatory Commission, 825 North Capitol Street, NE., Washington, DC 20426, (202) 357–8530.

SUPPLEMENTARY INFORMATION:

On January 25, 1988, the Commission issued a Notice of OMB control number in Order No. 484, establishing a list for utilities to use in classifying certain property at nuclear power plants as "retirement units" for accounting purposes. (53 FR 2593, Jan. 29, 1988). This notice corrects the title shown on the prior notice. At 53 FR 2593, second column (page 1 of the Commission's order), the title is revised to read: "List of Property for Use in Accounting for the Addition and Retirement of Reactor Plant Equipment."

Lois D. Cashell,

Acting Secretary.

[FR Doc. 88–3685 Filed 2–19–88; 8:45 am]

BILLING CODE 6717-01-M

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. 84–48]

Schedules of Controlled Substances; Scheduling of 3,4-Methylenedioxymethamphetamine (MDMA) Into Schedule I of the Controlled Substances Act; Remand

AGENCY: Drug Enforcement Administration.

ACTION: Final rule.

SUMMARY: This is a final rule placing the drug 3,4-methylenedioxymethamphetamine (MDMA) into Schedule I of the Controlled Substances Act (CSA) following a remand from the United States Court of Appeals for the First Circuit. This rule will classify MDMA as a Schedule I hallucinogenic controlled substance and is the culmination of a formal rulemaking on the record conducted before an Administrative Law Judge of the Drug Enforcement Administration (DEA). The original final rule placing MDMA in Schedule I was published on October 14, 1986, with an effective date of November 13, 1986. (51 FR 36552). On review by the United States Court of Appeals for the First Circuit the rule was vacated and remanded to the Administrator for further findings. Following a review of the record in this matter, the Administrator concludes that MDMA should be classified as a Schedule I controlled substance. This rule will impose the criminal and regulatory controls of Schedule I on the manufacture, distribution and possession of MDMA.

EFFECTIVE DATE: The effective date of this order is March 23, 1988.

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

SUPPLEMENTARY INFORMATION: On October 14, 1986, the Administrator of DEA, following rulemaking on the record which included a hearing before an Administrative Law Judge, issued a final rule placing MDMA into Schedule I under the Controlled Substances Act. (52 FR 36552) The effective date of this rule was November 13, 1986. In this final rule, the Administrator made findings required by the statute, 21 U.S.C. 812(a), and concluded that MDMA met the criteria for placement of substances into Schedule I. The Administrator found that MDMA: (1) Had no currently accepted medical use in treatment in the United States; (2) lacked accepted safety for use under medical supervision; and (3) had a high potential for abuse.

On September 19, 1987, the United States Court of Appeals for the First Circuit issued its opinion on the Petition for Review of the Order of the Drug Enforcement Administration. See, *Grinspoon v. Drug Enforcement Administration*, 828 F.2d 881. The mandate was issued on December 22, 1987. The Court found that the Administrator applied an incorrect standard in determining the meaning of the phrases "currently accepted medical use in treatment in the United States" and "lack of accepted safety for use under medical supervision." Specifically the Court stated that—

> The Administrator erroneously applied an interpretation of the "accepted medical use in treatment in the United States" and "accepted safety for use . . . under medical supervision" criteria of section 812(b)(1) that directly conflicts with congressional intent. We therefore vacate the Administrator's determination that MDMA should be placed in Schedule I of the CSA and remand the rule for further consideration by the DEA. On remand, the Administrator will not be permitted to treat the absence of FDA interstate marketing approval as conclusive evidence that MDMA has no currently accepted medical use and lacks accepted safety for use under medical supervision. 828 F.2d 881, 891.

The Court did not provide any further parameters for the Administrator in reconsidering his decision, stating that it would not infringe on the Administrator's statutory authority to develop such a standard.

The Administrator concludes that further hearings are not necessary in this matter since the record below is extraordinarily complete and since all the parties had the opportunity to provide evidence and brief all the relevant issues, which included:

What consititutes "currently accepted medical use in treatment in the United States" within the purview of 21 U.S.C. 812(b)?

What constitutes "accepted safety for use . . . under medical supervision" within the purview of 21 U.S.C. 812(b)?

Does MDMA have a "currently accepted medical use in treatment in the United States" within the purview of 21 U.S.C. 812(b)?

Is there a lack of "accepted safety for use [of MDMA] under medical supervision" within the purview of 21 U.S.C. 812(b)?

The Administrator further concludes that since all parties have had ample opportunity to be heard on these issues, there is no necessity to publish his conclusions as a proposed rule, but rather as a final rule.

Findings

The Administrator adopts the following findings regarding "accepted medical use in treatment in the United States" and "accepted safety for use under medical supervision" which were published as part of the original final rule found at 51 FR 36552 (October 14, 1986); 1, 2, 3, 4, 5, 6, 7, 8, 11, 12, 13, 14, 15, 16, 44, 45, 46, 47. These findings are incorporated into this final rule as though they were set out fully herein. The Administrator further finds, based upon the record in the proceedings conducted before the Administrative Law Judge:

A. The published scientific and medical literature and the information from the files of the Food and Drug Administration do not establish or support claims of therapeutic use of MDMA, as an adjunct to psychotherapy, in treatment in the United States.

B. There are insufficient and inadequate studies and reports characterizing MDMA from a chemical, toxicological and pharmacological perspective to justify use of MDMA in humans.

C. There were no published accounts of MDMA's pharmacology or toxicology until 1973, when an animal study conducted by the U.S. Army Chemical Corps was released. It showed that the acute lethal doses of MDMA and MDA were similar.

D. Three reports published by Alexander Shulgin and others beginning in 1976 mention the effects of MDMA in humans. These studies describe MDMA's psychopharmacological profile in relation to other psychoactive drugs such as marijuana, psilocybin and MDA. Minimal descriptions of test procedures were included, and the studies included no data to indicate a potential therapeutic utility of MDMA as an adjunct to psychotherapy in humans.

E. The therapeutic use of MDMA is not mentioned in any medical, psychiatric or psychotherapy textbooks, pharmacopeia or clinical pharmacology textbooks.

F. An unpublished study entitled "MDMA: A New Psychotropic and its Effects in Humans" was prepared by Dr. George Greer. Dr. Greer is a psychiatrist in New Mexico with a private practice and little or no background as a researcher. His report describes the administering of MDMA to 29 individuals for a variety of reasons ranging from curiosity and fun to a desire to change consciousness and behavior patterns. Only nine of the individuals had diagnosable psychiatric disorders. Dr. Greer reported that all the individuals experienced "positive" effects and relatively few side effects.

The conclusions were based upon the subjective observations of Dr. Greer and a nurse, as well as conclusions of the subjects. Dr. Greer described the study as anecdotal and not a study designed to determine the efficacy of MDMA. Experts in psychiatry, psychotherapy and pharmacology concluded that Dr. Greer's study did not provide a reasonable basis for regarding MDMA as efficacious for enhancing therapeutic benefits of psychotherapy, and lacked scientific merit. They agreed that the study was not scientifically sound and produced only anecdotal results. The study contained no controls; it was not a blind or double blind study and thus significant bias was introduced; there were no criteria to measure improvement or change; there was no defined therapeutic procedure; and the investigator lacked standing as a scientist and researcher.

G. An unpublished study entitled, "MDMA Pilot Study—Physiological, Psychological and Sociological Study," by Dr. Joseph J. Downing examined the effects of MDMA in 21 healthy individuals with no diagnosable psychiatric disorders. Dr. Downing is not a researcher and has little or no experience in designing and conducting toxicological or clinical studies. All the subjects had previously used MDMA and a variety of other psychoactive drugs. The individuals brought their own alleged MDMA to the study and determined the dose to be taken. The subjects concluded that they had "benefitted" from the use of MDMA. Dr. Downing concluded that "there is insufficient evidence to judge accurately either harm or benefit." Scientific experts who reviewed Dr. Downing's work concluded that his study suffers from the same problems as Dr. Greer's and that it has little or no scientific merit. An FDA pharmacologist, experienced in evaluating the safety and efficacy of drugs, concluded that the study presents no data or evidence to support a claim that MDMA is effective as a therapeutic agent.

H. Four psychiatrists presented evidence that they had used MDMA in their practices. Several other psychiatrists testified that use of MDMA by these individuals was consistent with accepted medical practice in their community. Each physician also described MDMA only in terms of therapeutic potential. All agreed that no scientific studies were done on which to conclude that MDMA has therapeutic utility. Most of these physicians had used MDMA themselves. The number of physicians who have used MDMA in their practices is very small in relation to the physician population.

I. The World Health Organization (WHO) Expert Committee on Drug Dependence reviewed MDMA for possible scheduling under the 1971 Convention on Psychotropic Substances in April 1985. The Expert Committee included internationally recognized experts in the field of psychiatry, clinical pharmacology and other medical professions. The Committee found that MDMA had no defined therapeutic use. The Committee further noted that the anecdotal data regarding MDMA's clinical utility were intriguing but that the studies lacked appropriate methodological design to ascertain the reliability of the observations and results. The Expert Committee recommended that MDMA be placed into Schedule I of the Convention because there was insufficient evidence to indicate that the substance has therapeutic usefulness. The United States is a party to the 1971 Convention on Psychotropic Substances.

J. Published scientific literature does not support the safety of MDMA for use in humans. It strongly suggests that MDMA may not be safe for human use.

K. Unpublished studies by Drs. Greer and Downing indicate that all individuals who took MDMA under their supervision experienced unpleasant side effects ranging from nausea and vomiting to ataxia, anxiety attacks, hallucinations and short-term memory loss. Dr. Greer's and Dr. Downing's studies suffer from severe methodological and other problems which lead experts to conclude that they contain no scientific evidence to assess the safety of MDMA. Dr. Downing concluded that there is insufficient evidence to accurately judge MDMA's safety.

L. The substance administered by Dr. Greer in his study, as well as that administered by the other psychiatrists, was made by them under the supervision of a medicinal chemist and was not manufactured or tested under controlled conditions.

M. The substances ingested by the subjects in Dr. Downing's study were provided by the subjects themselves, and were of unknown origin, composition and purity.

Discussion

In order for a drug or other substance to be placed into Schedule I, a finding is required that the substance has "no currently accepted medical use in treatment in the United States." The other four Schedules require a finding that the drug or other substance has a "currently accepted medical use in treatment in the United States." The United States Court of Appeals for the First Circuit has indicated that "currently accepted medical use in treatment in the United States," does not mean that a drug or other substance is lawfully marketed in the United States pursuant to the Federal Food, Drug and Cosmetic Act of 1938. While the Court clearly stated that whether a substance is lawfully marketed in the United States may be a factor to be considered in making a determination of accepted medical use, it may not be the sole factor upon which the Administrator relies in making that determination.

The characteristics of a drug or other substance with an accepted medical use in treatment include scientifically determined and accepted knowledge of its chemistry; the toxicology and pharmacology of the substance in animals; establishment of its effectiveness in humans through scientifically designed clinical trials; general availability of the substance and information regarding the substance and its use; recognition of its clinical use in generally accepted pharmacopeia, medical references, journals or textbooks; specific indications for the treatment of recognized disorders; recognition of the use of the substance by organizations or associations of physicians; and recognition and use of the substance by a substantial segment

of the medical practitioners in the United States. The drug MDMA has not been approved for marketing in the United States by the Food and Drug Administration. The chemistry, toxicology and pharmacology of MDMA have not been sufficiently studied in animals to provide a scientific basis for experimentation or clinical use in humans. The published literature contains no references to the clinical use of MDMA nor animal studies to indicate such a clinical use. Recognized texts, reference books and pharmacopeia contain no references to the therapeutic use of MDMA. The two unpublished studies supporting the therapeutic use of MDMA which were presented during the hearings, do not contain any data which can be assessed by scientific review to draw a conclusion that MDMA has a therapeutic use. Indeed, the psychiatrists who conducted the studies admit that the information which they obtained was anecdotal, and that the studies were not scientifically controlled.

Evidence in the record indicates that at least four psychiatrists have administered MDMA in their practice to approximately 200 subjects. These physicians were not conducting scientific studies with MDMA, they were administering the drug as if it was an approved product which had been scientifically tested. The evidence they presented was merely anecdotal accounts of observations of patients.

While many witnesses in this proceeding, including those presented by the agency, indicated that MDMA may have a potential therapeutic use, such a potential use is not sufficient to establish accepted medical use. A panel of international experts reached the same conclusion, namely that there was insufficient evidence to indicate that the substance had therapeutic usefulness.

The evidence in the record in this proceeding does not support a finding that MDMA has a "currently accepted medical use in treatment in the United States." MDMA's lack of marketing approval by the Food and Drug Administration, coupled with the absence of reliable scientific data to establish the therapeutic usefulness and absence of widespread acceptance and recognition in the medical community, clearly demonstrates that it has "no currently accepted medical use in treatment in the United States."

The second of the three factors required for placement of a substance in Schedule I is that there is "lack of accepted safety for use of the drug or other substance under medical supervision." The United States Court of Appeals for the First Circuit indicated that "lack of accepted safety for use of the drug or other substance under medical supervison," is not conclusively demonstrated by lack of FDA approval for marketing of a drug or other substance in the United States. The fact that a drug or other substance is not lawfully marketed in the United States may be a factor to be considered in determining whether a substance lacks accepted safety for use under medical supervision, but it is not conclusive.

Before a drug may be tested in humans, the Food and Drug Administration, the agency charged by Congress with determining the safety and efficacy of drugs, requires that it be safe as demonstrated by animal testing. The first requirement in determining the safety of a substance is that the chemistry of the substance must be known and reproducible. The next step is to conduct animal toxicity studies to show that the substance will not produce irreversible harm to organs at proposed human doses. Limited clinical trials may then be initiated but they must be carefully controlled so that adverse effects can be monitored and studies terminated if necessary. Very little of this information has been generated for MDMA. Safety in humans is evaluated as a risk/benefit ratio for a specific use. Any side effects found in human testing are required to be made known to the physician in labeling or package inserts which accompany the drug. MDMA is not available under these conditions.

The claims of safety by the psychiatrists who have administered MDMA are based on gross observations of the few subjects treated as well as self-evaluation by the subjects. These anecdotal observations, while useful in the overall evaluation of a substance, cannot substitute for controlled studies in animals and humans. There have been studies in animals to show that MDMA produces long term serotonergic nerve terminal degeneration. Such effects would not necessarily be observed immediately in individuals who had taken the drug. The long term safety of MDMA has not been established through reproductive or carcinogenic studies. Since MDMA has not been shown to be effective for treating a specific condition, it is impossible to make a risk/benefit analysis of the drug. Two psychiatrists who testified on behalf of the agency in the proceedings indicated that they would not administer MDMA to humans until and unless further studies had been conducted to establish its safety and lack of neurotoxicity.

Although a few psychiatrists claim that there has been relatively little reported major harm to individuals who have used MDMA, this does not establish that MDMA is safe for use under medical supervision. Scientists and prudent physicians have concluded that administration of MDMA to humans must not occur until further animal studies are conducted to adequately assess its potential toxicity in humans Based upon the lack of MDMA's established safety by animal and human testing, the lack of an FDA finding that MDMA is safe and may be safely administered to humans, its neurotoxicity in animals, and scientific and medical opinions that further testing is necessary prior to human use, the Administrator concludes that MDMA lacks accepted safety for use under medical supervision.

MDMA has no accepted medical use in treatment in the United States and lacks accepted safety for use under medical supervision. The Administrator previously found that MDMA had a high potential for abuse, a finding that was upheld on review by the United States Court of Appeals for the First Circuit. The Administrator therefore concludes that MDMA should be placed into Schedule I of the Controlled Substances Act.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Narcotics, Prescription drugs.

Under the authority vested in the Attorney General by section 201(a) of the Controlled Substances Act (21 U.S.C. 811(a)) and delegated to the Administrator of the Drug Enforcement Administration by regulations of the Department of Justice, 28 CFR 0.100(b), the Administrator hereby orders that Part 1308, Title 21, Code of Federal Regulations, be amended as follows:

PART 1308—SCHEDULES OF CONTROLLED SUBSTANCES

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

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

2. Section 1308.11 is amended by redesignating the existing paragraphs (d)(7) through (d)(24) as (d)(8) through (d)(25) and adding a new paragraph (d)(7) as follows:

§ 1308.11 Schedule I.

* * * * *

(d) * * *

(7) 3,4-methylenedioxymethamphetamine (MDMA)..... 7405

* * * * *

Dated: February 18, 1988.
John C. Lawn,
Administrator.
[FR Doc. 88-3801 Filed 2-19-88; 8:45 am]
BILLING CODE 4410-09-M

DEPARTMENT OF THE INTERIOR

Office of Surface Mining Reclamation and Enforcement

30 CFR Part 902

Approval of Amendment to Alaska Permanent Regulatory Program

AGENCY: Office of Surface Mining Reclamation and Enforcement (OSMRE), Interior.

ACTION: Final rule.

SUMMARY: OSMRE is announcing the approval of a proposed amendment to the Alaska permanent regulatory program [hereinafter referred to as the Alaska program] received by OSMRE pursuant to the Surface Mining Control and Reclamation Act of 1977 (SMCRA). This amendment consists of modification to eight articles of the Alaska regulations addressing the following areas: Environmental Resource Information; Reclamation and Operation Plan; Performance Standards; Inspection and Enforcement; Conflict of Interest; Training, Examination and Certification of Blasters; Abandoned Mines; and General Provisions. The Federal rules at 30 CFR Part 902 codifying decisions concerning the Alaska program are being amended to implement this action. This final rule is being made effective immediately to expedite the State program amendment process and to encourage States to bring their programs into conformance with the Federal standards without undue delay. Consistency of State and Federal standards is required by SMCRA.

EFFECTIVE DATE: February 22, 1988.

FOR FURTHER INFORMATION CONTACT: Mr. Jerry R. Ennis, Director, Casper Field Office, Office of Surface Mining Reclamation and Enforcement, 100 East "B" Street, Room 2128, Casper, Wyoming 82601-1918; Telephone: (307) 261-5776.

SUPPLEMENTARY INFORMATION:

I. Background on the Alaska Program

On May 2, 1983, the Secretary of the Interior approved the Alaska program. Information pertinent to the general background, revisions and amendments to the Alaska program submission, as well as the Secretary's findings and the disposition of comments, can be found in the March 23, 1983 **Federal Register** (48 FR 12274-12289). Subsequent actions concerning the Alaska program and amendments to the program are identified at 30 CFR 902.16.

II. Discussion of Proposed Amendment

On March 2, 1987, by letter dated February 24, 1987, OSMRE received a proposed amendment from the State of Alaska. By notice published in the May 12, 1987 **Federal Register**, the Assistant Director, Western Field Operations, announced receipt of this proposed amendment and requested public comment on its adequacy (52 FR 17772). The comment period closed June 11, 1987. Since no one requested a public hearing, none was held.

The amendment revised eight articles of Title 11, Chapter 90 of the Alaska Administrative Code (AAC) as described below:

Article 4—Environmental Resource Information Requirements

Subsection (b) of 11 AAC 90.065 is amended by adding language that allows registered professional land surveyors to prepare and/or certify certain maps, planviews and cross-sections.

Article 5—Reclamation and Operation Plan

Subsection (d) of 11 AAC 90.077 is amended by adding language that allows registered professional land surveyors to prepare and/or certify certain maps, planviews and cross-sections.

Article 11—Performance Standards

Paragraph (a)(3) of 11 AAC 90.331 is amended by adding language that requires sedimentation ponds to provide sediment storage volume and detention time sufficient to meet applicable Federal effluent limitations and water quality standards as well as State standards.

Subsection (f) of 11 AAC 90.461 is amended by replacing an incorrect reference to subsection (d) with the correct reference to subsection (e).

Article 12—Inspection and Enforcement

Section 90.601 is amended by making minor editorial revisions to subsections (d), (e) and (f) and by adding a new paragraph (g), which addresses inspection frequency requirements for those operations that have temporarily ceased operation or have met the Phase II (revegetation) bond release requirements of Alaska Statutes (AS) 27.21.170 (c)(2) and (d).

Section 90.625 is amended by deleting all existing provisions and replacing them with language establishing a specific formula for computing penalty assessments. Subsection (a) of 11 AAC 90.627 is amended by adding language that grants the operator an opportunity to request an informal meeting with the State to discuss the facts surrounding the alleged violation. Subsection (b) of this section has also been revised to extend the time within which the Commissioner must render a decision and propose a penalty from 20 days to 30 days.

Article 14—Conflict of Interest

Section 90.751 is amended by replacing the reference to a specific form, OSM Form 705-1, with a more general reference to the "required OSM form."

Article 15—Training, Examination and Certification of Blasters

The February 24, 1987 amendment package includes a completely new Article 15, which contains requirements concerning the training, examination and certification of blasters, as required by 30 CFR 850.12(a) and 902.16(a)(1). As discussed in the May 12, 1987 **Federal Register** (52 FR 17772), Alaska had previously submitted a blaster certification program amendment on May 28, 1985 (50 FR 34863, August 28, 1985), which, on November 19, 1986, it supplemented with a cooperative agreement between the Department of Natural Resources (DNR) and the University of Alaska (52 FR 4630, February 13, 1987).

The February 24, 1987 submission contained regulations replacing those originally submitted on May 28, 1985. At the time of the February 24, 1987 submission, OSMRE had not yet completed processing of the original blaster certification amendment. Therefore, the Director is combining the March 28, 1985 amendment and all related modifications with the February 24, 1987 amendment and is addressing both in this notice.

Article 16—Abandoned Mines

To accommodate the addition of the blaster training, examination and certification regulations at Article 15, the State has redesignated the previous contents of Article 15 as Article 16. The article, which concerns the abandoned mine land reclamation program, is otherwise unchanged.

Article 17—General Provisions

The contents of this article, previously known as Article 16, have been redesignated as Article 17, but, except for minor revisions to 11 AAC 90.907 (d) and (g), remain otherwise unchanged.

101 West Lombard Street, Baltimore, MD 21201, and at the Region III office of the Environmental Protection Agency, 841 Chestnut Building, Philadelphia, Pennsylvania 19107. Copies of the consent decree may also be examined at the Environmental Enforcement Section, Land and Natural Resources Division, Department of Justice, Room 1647, Ninth Street and Pennsylvania Avenue, NW., Washington, DC 20530. A copy of the Consent Decree may be obtained in person or by mail from the Environmental Enforcement Section, Land and Natural Resources Division, Department of Justice. In requesting a copy please enclose a check in the amount of $1.90 (10 cents per page reproduction cost) payable to the Treasurer of the United States.

Richard B. Stewart,
Assistant Attorney General, Land and Natural Resources Division.
[FR Doc. 89-30267 Filed 12-28-89; 8:45 am]
BILLING CODE 4410-01-M

Antitrust Division

Proposed Termination of Final Judgments

Notice is hereby given that defendants Union Camp Corporation and Bemis Company, Inc. have filed with the United States District Court for the Eastern District of Virginia separate motions to terminate the final judgments in *United States* v. *Union Camp Corporation and Bemis Company, Inc.*, Civil No. 5005-A; and that the Department of Justice ("Department"), in a stipulation also filed with the Court, has consented to termination of the judgments as to both Union and Bemis, but has reserved the right to withdraw its consent pending receipt of public comments. The complaint in this case (filed on November 4, 1968) alleged that defendants conspired to restrain and monopolize interstate trade and commerce in the manufacture and sale of mesh window paper bags (used principally for packaging potatoes) by asserting patent claims they knew to be invalid and by agreeing (with each other and with Union's licensees) to refuse patent licenses to certain applicants. The complaint also alleged that Union attempted to monopolize such manufacture and sale by improperly controlling entry therein and that Bemis did so by improperly using a patent it obtained by fraud and thus knew to be invalid.

The judgments (entered against defendant Union on February 24, 1969, and against defendant Bemis on July 1, 1969) require, among other things, that until the end of 1996 Union attach a copy of its judgment to any claim of infringement of certain patents, and that Bemis (a) distribute to certain of its personnel copies of its judgment plus instructions for compliance therewith, and (b) impose on certain Bemis personnel a duty to report to management any facts such personnel learn which would invalidate or prevent issuance of any Bemis patent. The judgments also enjoin Union from (a) asserting the validity of certain patents which it believes should not have been issued or should be declared invalid, and (b) consulting or agreeing with current or prospective licenses over whether to grant further licenses under certain patents; and enjoin Bemis from (a) filing or further prosecuting any patent application, or enforcing or threatening to enforce any patent, whenever it learns of facts which would prevent the issuance of or would invalidate the patent, and (b) consulting or agreeing with its licensors or licensees over whether to grant additional patent licenses.

The Department has filed with the Court a memorandum setting forth the reasons why the Department believes that termination of the judgments would serve the public interest. Copies of the complaint and final judgments, defendants' motion papers, the stipulation containing the Government's consent, the Department's memorandum, and all further papers filed with the Court in connection with these motions will be available for inspection at Room 3233, Antitrust Division, Department of Justice, 10th Street and Pennsylvania Avenue NW., Washington, DC 20530 (telephone 202/633-2481), and at the Office of the Clerk of the United States District Court for the Eastern District of Virginia, 200 South Washington Street, Alexandria, Virginia 22314. Copies of any of these materials may be obtained from the Antitrust Division upon request and payment of the copying fee set by Department of Justice regulations.

Interested persons may submit comments regarding the proposed termination of the decrees to the Department. Such comments must be received within the sixty (60) day period established by court order, and will be filed with the Court. Comments should be addressed to Robert E. Bloch, Chief, Professions and Intellectual Property Section, Antitrust Division, Department of Justice, Washington, DC 20530 (telephone: 202/724-7425).

Joseph H. Widmar,
Director of Operations, Antitrust Division.
[FR Doc. 89-30268 Filed 12-28-89; 8:45 am]
BILLING CODE 4410-01-M

Drug Enforcement Administration

[Docket No. 86-22]

Marijuana Scheduling Petition; Denial of Petition

This is a final order of the Administrator of the Drug Enforcement Administration (DEA) denying the petition of the National Organization for Reform of Marijuana Laws (NORML) to reschedule the plant material marijuana from Schedule I to Schedule II of the Controlled Substances Act. This order follows a rulemaking on the record as prescribed by the Controlled Substances Act, 21 U.S.C. 801, *et seq.*, and the Administrative Procedures Act, 5 U.S.C. 551, *et seq.* There are seven parties in the rulemaking proceeding. Four parties, NORML, the Alliance for Cannabis Therapeutics (ACT), the Cannabis Corporation of America (CCA), and Carl Eric Olsen, comprised the pro-marijuana parties, those advocating the rescheduling of marijuana from Schedule I to Schedule II. The three remaining parties, who advocated that marijuana remain in Schedule I, were DEA, the National Federation of Parents for a Drug-Free Youth, and the International Association of Chiefs of Police (IACP).

The two issues involved in a determination of whether marijuana should be rescheduled from Schedule I to Schedule II are whether marijuana plant material has a currently accepted medical use in treatment in the United States, or a currently accepted medical use with severe restrictions; and whether there is a lack of accepted safety for use of marijuana plant material under medical supervision. After a thorough review of the record in this matter, the Administrator rejects the recommendation of the administrative law judge to reschedule marijuana into Schedule II and finds that the evidence in the record mandates a finding that the marijuana plant material remain in Schedule I of the Controlled Substances Act.

The pro-marijuana parties advocate the placement of marijuana plant material into Schedule II for medical use in the treatment of a wide variety of ailments, including nausea and vomiting associated with chemotherapy, glaucoma, spasticity in amputees and

those with multiple sclerosis, epilepsy, poor appetite, addiction to drugs and alcohol, pain, and asthma. The evidence presented by the pro-marijuana parties includes outdated and limited scientific studies; chronicles of individuals, their families and friends who have used marijuana; opinions from over a dozen psychiatrists and physicians; court opinions involving medical necessity as a defense to criminal charges for illegal possession of marijuana; state statutes which made marijuana available for research; newspaper articles; and the opinions of laypersons, including lawyers and associations of lawyers. The Administrator does not find such evidence convincing in light of the lack of reliable, credible, and relevant scientific studies documenting marijuana's medical utility; the opinions of highly respected, credentialed experts that marijuana does not have an accepted medical use; and statements from the American Medical Association, the American Cancer Society, the American Academy of Ophthalmology, the National Multiple Sclerosis Society, and the Federal Food and Drug Administration that marijuana has not been demonstrated as suitable for use as a medicine. Each of these areas will be discussed separately.

The record contains many research studies which have been published in scientific journals and many unpublished studies conducted by individual states. In order to evaluate the validity of any research study many factors must be considered. Certain scientific practices have been generally accepted by the scientific community which are designed to increase the validity of experimental studies. Studies or research projects which do not follow these accepted scientific practices have very limited, if any, credibility. A review of such studies must first examine the degree to which researchers control, or hold constant, all the variables which could affect the results, except the variable being studied. For example, if you wish to evaluate the effectiveness of marijuana on a group of glaucoma patients, you must control any other medication which the patient is taking. Otherwise, it is impossible to conclude that the results are attributable to the marijuana.

The second factor, or aspect of the design of a research project which must be evaluated, is the placebo effect. This is the tendency of research subjects to act and respond in a manner they believe is expected of them. To eliminate this factor, research subjects are usually "blinded," or not informed, of what drug they are receiving. Results of non-blind studies are questionable since they could be attributable, in large part, to psychological reactions of subjects rather than any real effects from the experimental drug. The next factor which must be minimized or eliminated for a research study to be valid is the expectation of the researcher. This is especially true where the effect being measured is subjective and not objective. For example, if the researcher is evaluating if the patient is nauseated, that is very subjective. If the researcher knows which patients are receiving the experimental drug, his perception of the results could be significantly altered.

Other factors to be considered when evaluating the validity of research include the number of subjects in the study, how the subjects are selected for the study, the length of the study, or how many times the experimental drug is administered, and the measurement of results in quantifiable, objective terms. The fewer the subjects in a research study, the less valid the results. If the sample of subjects is not statistically significant, the chances of the same results being duplicated in other individuals is reduced. Subjects for a research study should be randomly selected and representative of the population that is targeted to use the drug. Testing of marijuana in cancer patients for relief of nausea and vomiting should not be limited to those who have previously used marijuana recreationally and request its use in the study. The length of a study is particularly significant when the drug is to be used to treat a chronic condition such as glaucoma or spasticity. Studies based upon acute or one-time administration of the drug must be viewed with caution when the goal is treatment of a chronic condition. The effectiveness of the drug for long-time administration and the existence of side effects resulting from chronic use will not be revealed in acute studies.

In addition to factors related to the design and execution of a research study, there are two other factors which must be reviewed in evaluation of a research study. Research results are always considered tentative or preliminary until they have been replicated or confirmed by another researcher. The research study must be reported in sufficient detail to permit others to repeat it. Finally, publication of a study in a scientific journal, especially a journal which subjects an article to review prior to publication, adds validity to a study. Journal publication subjects a study to review and scrutiny by the scientific community and opens the door to replication of the studies. Unpublished studies are inherently suspect.

While research studies with the limitations mentioned above may provide useful and preliminary data which will be valuable in designing further studies, research studies with substantial limitations are not sufficient to support a determination that a drug has an accepted medical use. Both the published and unpublished research studies submitted by the pro-marijuana parties in this proceeding to support marijuana's medical use suffer from many deficiencies. They are, in essence, preliminary studies. None of these studies has risen to the level of demonstrating that marijuana has an accepted medical use for treatment of any medical condition. The three medical conditions for which the majority of evidence in the record was presented are: (1) Nausea and vomiting associated with chemotherapy, (2) glaucoma, and (3) spasticity associated with amputation or multiple sclerosis. Evidence presented in each area will be discussed separately.

Nausea and Vomiting

Five studies were presented by the pro-marijuana parties to support the medical use of marijuana as an antiemetic. The first study by Sallan, et al., *Antiemetic Effect of Delta-9-Tetrahydrocannabinol in Patients Receiving Cancer Chemotherapy*, 293 New England Journal of Medicine, 795–797(1975), utilized synthetic tetrahydrocannabinol (THC) and not the plant material marijuana. Although delta-9-THC is an active ingredient in the marijuana plant material, marijuana contains over 400 other chemicals. At least 61 of these chemicals are cannabinoids. All these chemicals could have some effect on the human body. Since THC is only one of many active ingredients in marijuana, THC studies are of very limited value in evaluating the therapeutic utility of marijuana. The route of administration, smoking versus oral injection, is a significant difference between use of marijuana and THC. Therefore, the results of the Sallan study are of little or no benefit in evaluating the medical utility of marijuana for treatment of nausea and vomiting associated with chemotherapy.

The second study compared a combination of pure THC and marijuana to placebo cigarettes. This study by Chang, et al., *Delta-9-Tetrahydrocannabinol as an Antiemetic in Cancer Patients Receiving High-Dose Methotrexate*, 91 Annals of Internal Medicine, 819–824 (1979), was

randomized, double-blind, and placebo controlled. The study concluded, "that a combination of oral and smoked THC is a highly effective antiemetic compared to placebo * * *" This study was limited to 15 subjects, some of whom received both marijuana and THC at the same time. The validity of the results of this study is severely limited by its small size and administration of the mixture of the two drugs, THC and marijuana. The study is not helpful in determining the therapeutic utility of marijuana alone in treating nausea and vomiting.

The third study conducted by Dr. Thomas J. Ungerleider, a psychiatrist, involved the administration of marijuana to 16 bone marrow transplant patients suffering from severe nausea and vomiting from radiation therapy. The results of this study are of little value due to the limited number of patients, the subjective nature of the data, and the fact that the results of the study were never published. The conclusion that there was less nausea and vomiting with use of marijuana was based upon the subjects' and researcher's subjective determination. There were no objective measurements, such as number of incidents or frequency of vomiting. During cross-examination, Dr. Ungerleider indicated that the results of the study were not published because there was not enough hard data.

The fourth study compared marijuana to THC as an antiemetic. Levitt, et al,. *Randomized Double Blind Comparison of Delta-9-Tetrahydrocannabinol (THC) and Marijuana As Chemotherapy Antiemetics.* (Meeting Abstract), 3 Proc. Annu. Meet. Am. Soc. Clin. Oncol. 91 (1984). It concluded that THC is superior to marijuana in controlling nausea and vomiting. A specific formulation of synthetic THC has been approved for marketing and is available as a prescription drug for treatment of nausea and vomiting associated with cancer chemotherapy.

The fifth study presented by the pro-marijuana parties is actually a group of programs, collectively labeled "Controlled Substances Therapeutic Research Programs," conducted by six states in the 1970's and 1980's. These programs involved the use of both marijuana cigarettes and synthetic THC capsules. The programs were given Investigational New Drug (IND) approval by the Food and Drug Administration (FDA) and the marijuana and THC were supplied by the Federal Government. The protocols of these programs were very loosely constructed. There were no controls. That is, there were no individuals who did not take the experimental drugs to compare with those who did. The studies were not blind or double-blind. Every research subject knew what drug they were receiving and, in many cases, were permitted to request either marijuana or THC. The studies were not randomized. In most instances, the results were measured by the subject's subjective evaluation of the drug's effectiveness. This is even more of a problem where the drug in question is a psychotropic or mind-altering substance like marijuana, which by its very nature makes some individuals feel "high," and may distort their perception of physical symptoms. There were no objectively measured results. The results were not published in scientific journals and, in some cases, data were lost or not recorded. The number of individuals who actually smoked marijuana in these studies was relatively small. These state studies were born of compassion and frustration. They abandoned traditional scientific methods in favor of dispensing marijuana to as many individuals as possible on the chance that it might help them. Though well-intentioned, these studies have little scientific value.

The research studies presented by the pro-marijuana parties in this proceeding do not support a conclusion that marijuana has a therapeutic use for treatment of nausea and vomiting associated with chemotherapy.

The pro-marijuana parties presented many testimonials from cancer patients, their families, and friends about the use of marijuana to alleviate nausea and vomiting associated with chemotherapy. These stories of individuals who treat themselves with a mind-altering drug, such as marijuana, must be viewed with great skepticism. There is no scientific merit to any of these accounts. In many cases the individuals were taking a variety of other medications and were using anything which might help treat the cancer as well as the nausea. They were using marijuana purchased on the street, and were unaware of the strength of the drug. They were not using the drug under medical supervision. Many of these individuals had been recreational users of marijuana prior to becoming ill. These individuals' desire for the drug to relieve their symptoms, as well as a desire to rationalize their marijuana use, removes any scientific value from their accounts of marijuana use. There is no doubt that these individuals and their loved-ones believed that marijuana was beneficial. The accounts of these individuals' suffering and illnesses are very moving and tragic; they are not, however, reliable scientific evidence, nor do they provide a basis to conclude that marijuana has an accepted medical use as an antiemetic.

There were many physicians and other medical experts who testified in this proceeding. In reviewing the weight to be given to an expert's opinion, the facts relied upon to reach that opinion and the credentials and experience of the expert must be carefully examined. The experts presented by the pro-marijuana parties were unable to provide a strong scientific or factual basis to support their opinions. In addition, many of the experts presented by the pro-marijuana parties did not have any expertise in the area of research in the specific medical area being addressed. The pro-marijuana parties presented the testimony of five psychiatrists to support the use of marijuana as an antiemetic. None of these individuals is an oncologist, nor have they treated cancer patients. Three of the psychiatrists, Drs. Grinspoon, Ungerleider and Zinberg are current or former board members of NORML or ACT. All these physicians indicated that they relied on scientific studies which they had read, their experience with cancer patients, or stories from others, to reach their conclusions. When questioned on cross-examination as to which studies they relied upon, most were unable to list one study. A review of the available literature has already demonstrated the unreliability of the studies that exist. The testimonials upon which these psychiatrists relied are also scientifically suspect. The opinions of these psychiatrists are, therefore, of little value in determining whether marijuana is therapeutically useful as an antiemetic.

Two pharmacologists, Drs. Morgan and Jobe, presented testimony on behalf of the pro-marijuana parties. Dr. Morgan is a professor at the City College of New York. He does not treat patients, nor is he an oncologist. His opinions are based upon a review of scientific studies and stories told to him by others. He has ties to NORML and is in favor of legalizing marijuana. Dr. Jobe is a pharmacologist and psychiatrist. He testified that his knowledge of marijuana's effects as a drug are based upon a review of the literature and stories from individuals undergoing chemotherapy. On cross-examination, Dr. Jobe indicated that this anecdotal information came from approximately four or five individuals. He also indicated that his knowledge of the scientific studies conducted with marijuana was not current. The opinions of Drs. Morgan and Jobe are of little value in determining whether marijuana has a medical use.

Two general practitioners, Drs. Weil and Kaufman, also provided testimony on behalf of the pro-marijuana parties. Neither are oncologists, nor do they treat cancer patients. Dr. Weil is a wellness counselor at a health spa, and Dr. Kaufman is an officer of a company that audits hospital quality control programs. Dr. Weil has written a number of books on drugs and admitted that he has personally used every mind-altering, illicit drug he has written about. Dr. Kaufman stopped practicing medicine in 1974, and was unable to provide any information on cross-examination regarding the basis for his opinion that marijuana has an accepted medical use. Neither Dr. Weil nor Dr. Kaufman has a credible basis for their opinions regarding marijuana, and, therefore, their testimony will be disregarded.

Four oncologists presented testimony on behalf of the pro-marijuana parties. They were Drs. Goldberg, Silverberg, Bickers, and Stephens. Dr. Goldberg is a board certified oncologist, but practices primarily internal medicine. She only administers chemotherapy to one or two patients a year. In her career, she has administered chemotherapy to no more than ten patients whom she believed to be using marijuana. On cross-examination, she could not recall any studies regarding marijuana. Dr. Goldberg was a member and financial contributor to NORML. Dr. Silverberg has practiced oncology for 20 years. He is a Professor of Clinical Oncology at the University of California at San Francisco, but is not a board certified oncologist. In his testimony, Dr. Silverberg indicated that there was voluminous medical research regarding marijuana's effectiveness in treating nausea and vomiting. On cross-examination, Dr. Silverberg could not identify any studies, and was forced to admit that he had been incorrect and that there were, in fact, very few studies conducted using marijuana as an antiemetic. Although Dr. Silverberg has advised patients to use marijuana to control nausea and vomiting associated with chemotherapy, he has never been involved in any research nor has he documented any of his observations. Dr. Bickers is an oncologist in New Orleans and is a Professor of Medicine at the Louisiana University School of Medicine. Although Dr. Bickers claims that young patients have better control over nausea and vomiting after using marijuana, he has never documented this claim. Dr. Bickers was unable to identify any scientific information which he relied upon in reaching his conclusion regarding marijuana. Dr. Stephens, an oncologist, Professor of Medicine and Director of Clinical Oncology at the University of Kansas, characterized marijuana as a "highly effective, and in some cases, critical drug in the reduction of chemotherapeutically-induced emesis." During cross-examination, Dr. Stephens stated that he was unaware of any scientific studies which had been done with marijuana, and that he had never done research or treated patients with marijuana. He indicated that he received his information about the patient's use of marijuana from the nursing staff or the patient's family. None of these oncologists based their opinions about marijuana on scientific studies or their own research. Most did not base their opinions on their direct observations, but on the opinions of others. In light of lack of scientific basis for these opinions, they will be given little regard.

The agency presented the testimony of nationally recognized experts in oncology. Dr. Ettinger, a Professor of Oncology at Johns Hopkins School of Medicine, is the author of over 100 published articles on cancer treatment. Dr. Ettinger testified:

> There is no indication that marijuana is effective in treating nausea and vomiting resulting from radiation treatment or other causes. No legitimate studies have been conducted which make such conclusions.

He continued by stating that:

> Although extensive research has been conducted using * * * (THC) * * * as antiemetic treatment for cancer chemotherapy patients, very little research has actually been conducted using marijuana * * * for the same purpose. Most of the information concerning marijuana's effectiveness is anecdotal or comes from uncontrolled studies.

Dr. Gralla, a Professor of Medicine at Cornell University Medical College, and an Associate Attending Physician at Sloan-Kettering Memorial Cancer Center, is an oncologist who has spent his entire professional career devoted to cancer research and treatment. Dr. Gralla has conducted extensive research with antiemetic drugs and testified that there are currently many new medicines that control nausea and vomiting associated with chemotherapy more effectively than marijuana. He also stated that most physicians and oncologists have little interest in marijuana because of its negative side effects and other problems associated with its use. In conclusion, Dr. Gralla stated that he and his fellow cancer specialists at Sloan-Kettering do not accept marijuana as being medically useful to treat nausea and vomiting associated with chemotherapy.

Dr. Laszlo, currently Vice President of Research for the American Cancer Society, is an expert who has devoted the majority of his over 30 years in medicine to the treatment of cancer. During his career, he spent eleven years as the Director of Clinical Programs at the Duke University Comprehensive Cancer Center. Dr. Laszlo has authored numerous scientific articles about cancer research and treatment and has written a book titled, *Antiemetics and Cancer Chemotherapy*. In his testimony for this proceeding, Dr. Laszlo stated that he does not advocate the use of marijuana as an antiemetic, in part, because there has not been sufficient testing of marijuana to show that it is a safe and effective drug. He also indicated that because there are other available, highly effective antiemetics, a physician does not need to resort to a crude drug such as marijuana. Dr. Laszlo concluded that marijuana does not have a currently accepted medical use in the United States for treatment of nausea and vomiting resulting from cancer chemotherapy.

The American Cancer Society provided DEA with its policy statements regarding medical use of marijuana. The administrative law judge refused to admit this document into evidence in this proceeding, relegating it to the "public comment" section of the record. The Administrator, however, considers this document to be extremely relevant and, indeed, of substantial importance in this matter. The American Cancer Society has, and continues to, support research with substances which may provide relief to cancer patients, including marijuana. It states, however, that the results of clinical investigations are insufficient to warrant the decontrol of marijuana for medical use. The American Medical Association has expressed a similar opinion.

The Food and Drug Administration has provided DEA with a scientific and medical evaluation of marijuana, as well as testimony from one of its leading pharmacologists. Evaluating marijuana against its criteria for safety and effectiveness, FDA has concluded that there is inadequate scientific evidence to support a finding that marijuana is safe and effective for treating nausea and vomiting experienced by patients undergoing chemotherapy.

The pro-marijuana parties presented cases in which courts did not convict individuals of a crime associated with possession and use of marijuana based upon a legal defense of "medical necessity." These cases have no relevance to this proceeding which relates to marijuana's possible medical

use. The courts found only that these individuals, who were seriously ill and believed that marijuana would help them, did not have criminal intent in possessing or using marijuana. The judges and juries in these proceedings were not deciding medical and scientific facts, but legal issues. These decisions do not provide scientific evidence that marijuana has a medical use.

The pro-marijuana parties also presented evidence that 34 states passed laws permitting marijuana's use for medical purposes in those states. These laws provided that marijuana should be available for medical research. The term "research" is essential to a reading of these statutes. These laws made marijuana available for research and, in some states, set up research programs to study marijuana's safety and effectiveness as a medicine. These statutes are read for what they are, encouraging research involving marijuana. They are not an endorsement by state legislatures that marijuana has an accepted medical use in treatment.

The numerous testimonials and opinions of lay persons which were presented in this proceeding by the pro-marijuana parties are not useful in determining whether marijuana has a medical use. While experiences of individuals with medical conditions who use marijuana may provide a basis for research, they cannot be substituted for reliable scientific evidence. For the many reasons stated in the previous discussion of scientific evidence, these statements can be given little weight. Similarly, endorsements by such organizations as the National Association of Attorneys General, that marijuana has a medical use as an antiemetic, are of little persuasive value when compared with statements from the American Cancer Society and the American Medical Association.

Glaucoma

The pro-marijuana parties presented several studies to support their contention that marijuana has a medical use for treatment of glaucoma. In order for a drug to be effective in treating glaucoma it must lower the pressure within the eye for prolonged periods of time and actually preserve sight or visual fields. The studies relied upon by the pro-marijuana parties do not scientifically support a finding that marijuana has a medical use for treatment of glaucoma. Five of the studies presented by the pro-marijuana parties are pure THC studies. As previously noted, THC is only one constituent among hundreds found in marijuana. Therefore, the consequences of an individual ingesting pure THC as compared to smoking marijuana are vastly different. A few of the studies presented do document that heavy doses of marijuana over a short time period reduce eye pressure in most individuals. However, there are no studies which document that marijuana can sustain reduced eye pressure for extended time periods. The acute, or short-term, studies also show various side effects from marijuana use, including lowered blood pressure, rapid heart beat, and heart palpitations. In a 1979 study conducted by Drs. Merritt, Crawford, Alexander, Anduze, and Gelbart, the conclusions included a statement: "It is because of the frequency and severity with which untoward events occurred that marijuana inhalation is not an ideal therapeutic modality for glaucoma patients."

The pro-marijuana parties presented testimonials of individuals who suffer from glaucoma and believe their condition has benefited from the use of marijuana. Most of these individuals used marijuana recreationally prior to discovery of their illness. Chief among the individuals presenting statements was Robert Randall. Mr. Randall is president of ACT, and has been on NORML's Board of Directors since 1976. He has been a strong advocate for medical use of marijuana. Mr. Randall also has glaucoma. Mr. Randall began smoking marijuana as a college student in 1968, long before he was diagnosed in 1972 as having glaucoma. At that time Mr. Randall was treated with standard glaucoma medications. In the mid 1970's Mr. Randall was involved in a preliminary research study conducted by Dr. Robert Hepler. Dr. Hepler conducted some of the first published short-term marijuana studies relating to glaucoma. Dr. Hepler told Mr. Randall that he believed that marijuana in combination with other standard glaucoma medications would be helpful in reducing his eye pressure. In 1975, Mr. Randall was arrested for growing and possessing marijuana. His defense was medical necessity. Subsequently, he began receiving marijuana under an Investigational New Drug (IND) protocol sponsored by his physician. He also continued to receive standard glaucoma medications. Since 1978, Mr. Randall has been treated by Dr. North. Mr. Randall receives marijuana from the Federal Government and continues to take standard glaucoma medications. Two physicians who treated Mr. Randall, including Dr. North, testified that Mr. Randall's eye pressure appears to have been controlled and his vision kept stable for the last several years.

Mr. Randall smokes approximately 8 to 10 marijuana cigarettes a day. Since Mr. Randall continues to take other glaucoma medications, his controlled eye pressure cannot be attributable solely to marijuana use. In fact, Dr. North testified that Mr. Randall needs the standard medications as well as marijuana, and that the marijuana itself is not totally effective in decreasing Mr. Randall's eye pressure. Mr. Randall's experience with marijuana, although utilized under a physician's directions, is not scientific evidence that marijuana has an accepted medical use in treatment of glaucoma. Dr. Merritt, one of Mr. Randall's physicians, responded to the question of why he did not publish the results of Mr. Randall's treatment by saying, "A single isolated incident of one person smoking marijuana is not evidence for other ophthalmologists who may want to use the drug."

Dr. Hepler, the physician who conducted preliminary studies with marijuana and initially advised Mr. Randall to use marijuana with his other medications, now states that there is insufficient scientific evidence to conclude that marijuana is effective in treating glaucoma. The pro-marijuana parties rely primarily on the opinions of two of Mr. Randall's physicians, Drs. North and Merritt, in supporting their contention that marijuana has a medical use in treatment of glaucoma. Dr. North indicated that his conclusion that marijuana has a medical use in treatment of glaucoma is based solely on his observations of Mr. Randall. Dr. Merritt is a board certified ophthalmologist and researcher who has authored many articles on the use of marijuana and cannabinoids to reduce eye pressure. Dr. Merritt based his opinion that marijuana has a medical use in treatment of glaucoma on published scientific studies, treatment of Mr. Randall, and treatment of other glaucoma patients. As previously stated, all the available studies concern high doses of marijuana taken over short periods of time. Even Dr. Merritt admitted that there are no studies to show that marijuana repeatedly lowers eye pressure over long time periods. The maintenance of lowered eye pressure is crucial in treating individuals with glaucoma. On cross-examination, Dr. Merritt was unable to provide either the specific number of individual patients he had observed or any scientific data relating to those patients. Although Dr. Merritt is a well-known ophthalmologist, the basis for his opinion that marijuana has a medical use in the treatment of glaucoma is not scientifically sound.

The agency presented several experts who testified that there is insufficient scientific evidence to support a conclusion that marijuana has a medical use in treatment of glaucoma. In addition to Dr. Hepler, they include Dr. George Spaeth, Professor of Ophthalmology, Director of the Glaucoma Service at Will's Eye Hospital in Philadelphia and President of the American Glaucoma Society; and Dr. Keith Green, Professor of Ophthalmology, pharmacologist and researcher who has conducted research with both marijuana and THC. Perhaps the most persuasive evidence concerning the use of marijuana in treating glaucoma is the opinion of the American Academy of Ophthalmology, an organization representing 12,000 physician members and 6,000 other medical professionals who specialize in the treatment of ophthalmology. The Academy has concluded that insufficient data exists to demonstrate the safety and efficacy of using smoked marijuana in the treatment of glaucoma. FDA has also determined that there is insufficient evidence to conclude that marijuana has a medical use in treatment of glaucoma.

Spasticity

In support of their contention that marijuana has a medical use in treatment of spasticity in amputees and those with multiple sclerosis, the pro-marijuana parties presented three studies involving THC, testimonials of individuals with spasticity who use marijuana, medical opinions, and state court decisions on the medical necessity defense. The three studies presented by the pro-marijuana parties were very small studies. All three totalled 17 patients, and used THC, not marijuana, to treat spasticity. There are no studies using marijuana to treat spasticity. These studies do not provide a scientific basis to conclude that marijuana has a medical use in treating spasticity.

Dr. Denis Petro, a board certified neurologist, testified on behalf of the pro-marijuana parties that he believes that marijuana has a currently accepted medical use in treating spasticity. He testified that his opinion is based on the THC studies, experiences and observations of patients, and historical accounts of marijuana use. Dr. Petro knew of no studies in which marijuana was used to treat spasticity. He testified that his information from patients consisted of them telling him how the street marijuana these patients used at home affected their spasticity. He did not conduct any clinical studies or make objective measurements. Dr. Petro's opinion is not based upon any reliable scientific evidence. The same psychiatrists and general practitioners who reported marijuana had a medical use in treating nausea and vomiting and glaucoma also stated that marijuana had a medical use in treating spasticity. None of these physicians based their opinions on reliable scientific evidence.

The agency presented the testimony of national experts in the area of multiple sclerosis and spasticity. Dr. Kenneth Johnson is the Chairman of the Department of Neurology at the University of Maryland School of Medicine and manages the Maryland Center for Multiple Sclerosis (MS). He is the author of over 100 scientific and medical articles on MS. Dr. Johnson has spent most of his medical career researching MS and has diagnosed and treated more than 6,000 patients with the disease. He testified that he is unaware of any legitimate research involving marijuana to treat symptoms of MS. He further stated that, "[t]o conclude that marijuana is therapeutically effective without conducting vigorous testing would be professionally irresponsible." Dr. Donald Silberberg, Chairman of the Department of Neurology at the University of Pennsylvania School of Medicine and Chief of Neurology Service at the Hospital of Pennsylvania, has been actively researching and treating MS for most of his career. He has written over 130 medical articles on MS. He concluded that not only is there no legitimate medical or scientific evidence to support a conclusion that marijuana is effective in treating MS or spasticity, but that long-term treatment of MS patients with marijuana could be worse than the original disease. Dr. Silberberg placed no value on the reports of patients who claimed relief of their symptoms with marijuana because of the sporadic and episodic nature of MS attacks.

The National Multiple Sclerosis Society has concluded that marijuana is not an accepted medical treatment for spasticity. Dr. Stephen Reingold, Assistant Vice President for Research of the National Multiple Sclerosis Society, indicated in his testimony that because there are no well-designed, well-controlled research studies using marijuana to treat spasticity, the society does not endorse or advocate the use of marijuana for such a purpose.

The evidence presented by the pro-marijuana parties regarding use of marijuana to treat various other ailments such as pain, decreased appetite, alcohol and drug addiction, epilepsy, atopic neurodermatitis, scleroderma and asthma was limited to testimony of individuals who had used marijuana for those conditions and the testimony of the psychiatrists or general practice physicians mentioned earlier. There is not a shred of credible scientific evidence to support any of their claims.

With regard to marijuana's safety for use under medical supervision, the Administrator must again rely on the scientific evidence. While the pro-marijuana parties argue that no one has died from marijuana use, and the individuals who use it have testified that they have not experienced adverse effects, there is little or no scientific evidence to support their claims. For example, while Robert Randall claims marijuana smoking has had no adverse effect on his health or respiratory system, he has not had a physical examination or pulmonary function test in over ten years.

In order to be effective, a drug's therapeutic benefits must be balanced against, and outweigh, its negative or adverse effects. This has not been established with marijuana. As the previously discussed evidence has demonstrated, there is as yet no reliable scientific evidence to support marijuana's therapeutic benefit. It is, therefore, impossible to balance the benefit against the negative effects. The negative effects of marijuana use are well-documented in the record. Marijuana smoking, the route of administration advocated by many witnesses presented by the pro-marijuana parties, causes many well-known and scientifically documented side effects. These include decreased blood pressure, rapid heart rate, drowsiness, euphoria, disphoria and impairment of motor function, not to mention various negative effects on the respiratory and pulmonary systems. Therefore, the only conclusion is that marijuana is not safe for use under medical supervision, because its safety has not been established by reliable scientific evidence.

In summary, the Administrator finds that there is insufficient, and in many instances no, reliable, credible, scientific evidence, supported by properly conducted scientific research, to support a conclusion that marijuana has a medical use to treat any ailment or disease. In addition, there is a lack of scientific evidence to support a conclusion that marijuana is safe for use under medical supervision. This agency, and the Government as a whole, would be doing the public a disservice by concluding that this complex psychoactive drug with serious adverse effects has a medical use based upon

anecdotal and unreliable evidence. The evidence presented by the pro-marijuana parties in this proceeding consisted of a few published scientific studies involving marijuana and THC, testimony of general practice physicians and psychiatrists, and testimony of individuals who have used marijuana for various medical conditions. The majority of these individuals did not use marijuana under medical supervision and used "street" marijuana. In contrast, recognized, credentialed specialists in the fields of oncology, glaucoma and multiple sclerosis, and organizations involved in medical research in these areas, have concluded that marijuana does not have an accepted medical use in treatment in the United States. The Administrator would be abdicating his responsibility to the public if he concluded that marijuana has a medical use and is safe for use under medical supervision.

The preceding discussion is based upon the Administrator's review of the entire record in this matter. This record contains volumes of documents and testimony. The procedural history of this scheduling has extended for many years. The procedural history and the findings of fact and conclusions of law upon which the Administrator's decision is based are set forth below.

Procedure

This rulemaking proceeding was originally initiated by a petition filed by NORML on May 18, 1972, with the Bureau of Narcotics and Dangerous Drugs (BNDD). This petition requested that marijuana be removed from the Controlled Substances Act, or in the alternative, be moved to Schedule V of the Act. After a series of proceedings, including hearings before BNDD and DEA and remands by the United States Court of Appeals for the District of Columbia Circuit, the matter was again the subject of a DEA hearing. This hearing followed a 1980 remand by the United States Court of Appeals for the District of Columbia Circuit, *NORML* v. *DEA and HEW*, No. 79-1660 (D.C. Cir. Oct. 16, 1980), in which the Court ordered DEA to refer all matters to the Department of Health and Human Services (HHS) for a scientific and medical evaluation and recommendation for scheduling. The matter was forwarded to HHS by DEA, and the Food and Drug Administration (FDA) published "Proposed Recommendations to the Drug Enforcement Administration Regarding the Scheduling Status of Marijuana and Its Components and Notice of Public Hearing," in the **Federal Register**. 47 FR 28141 (1982). On September 16, 1982, FDA conducted a legislative-type hearing at which it received written and oral testimony. On May 13, 1983, the Assistant Secretary for Health forwarded his department's scientific and medical findings and scheduling recommendation regarding marijuana plant material to the Administrator of DEA. In this document the Assistant Secretary recommended that marijuana plant material continue to be controlled in Schedule I. On July 2, 1987, the Assistant Secretary for Health submitted a letter to the DEA Deputy Administrator in which he stated that it continued to be the position of the Department of Health and Human Services that marijuana continue to be controlled in Schedule I based upon its lack of accepted medical use in treatment in the United States.

This current proceeding was initiated by publication of a notice of hearing in the **Federal Register** on June 24, 1986, which advised any individual interested in participating in the proceedings to file a written notice of such intent. Seven organizations or individuals participated in the proceeding. Four prehearing conferences were held in late 1986 and 1987. Direct and rebuttal testimony were filed in written affidavit form. Fourteen days of hearings, for the purpose of cross-examination of witnesses, were held in three cities. All parties were permitted to file proposed findings of fact, conclusions of law and argument with Administrative Law Judge Francis L. Young. The pro-marijuana parties, as petitioners, filed their proposed findings on April 15, 1988. The Government filed its proposed findings on May 16, 1988. The pro-marijuana parties then filed rebuttal on June 3, 1988. The administrative law judge issued his opinion and recommended ruling, findings of fact, conclusions of law and decision on September 6, 1988. Exceptions to the administrative law judge's recommended decision were filed by NORML, ACT, and the Government. By letter dated December 9, 1988, the administrative law judge forwarded the entire record to the Administrator of DEA.

The Administrator has carefully reviewed the entire record in this matter and hereby issues this final order as prescribed by 21 CFR 1316.67. The Administrator does not accept the recommendation of the administrative law judge that marijuana has an accepted medical use in treatment of some medical conditions, that marijuana has accepted safety for use under medical supervision, and that marijuana should be rescheduled into Schedule II of the Controlled Substances Act. The Administrator finds that marijuana must remain in Schedule I of the Controlled Substances Act because it has no accepted medical use in treatment of any condition in the United States and it is not safe for use under medical supervision. The Administrator has reviewed the proposed findings of fact submitted by all parties and those formulated by the administrative law judge. The Administrator adopts the findings of fact submitted by the Government as his own and in their entirety. They are as follows:

Findings of Fact

1. The cannabis plant (*Cannabis sativa L.*) is an annual weed which belongs to the plant family Cannabaceae. This family has only one genus, the genus *Cannabis* which consists of one highly variable species, *sativa*. Many varieties of this species are known to exist.

2. Over 400 different chemicals have been identified in the extracts of the plant *Cannabis sativa*. They belong to 18 chemical classes of organic compounds. There are at least 61 different cannabinoids. The proportions and concentrations of these cannabinoids, including THC, differ from plant to plant depending on growing conditions, age of the plant, and factors surrounding harvest. THC levels found in cannabis may vary from less than 0.2% in some plants to greater than 10% in high quality plants.

3. Cannabis or marijuana cannot be defined chemically, nor can it be easily standardized. No totally reliable classification system based on a single chemical analysis exists. Twenty-one (21) cannabinoids have been clinically evaluated. Most of this testing centered on the psychotropic effects of the compounds, and only eight or nine of the cannabinoids have been tested for therapeutic utility. These studies have only been cursory except for the testing of synthetic THC. Cannabigerol (CBG) cannabinoids show antibacterial activity against gram positive bacteria, and have been shown to effect basic cell metabolism. Cannabinol (CBN) type compounds have exhibited anticonvulsant, anti-inflammatory, immunological, and behavioral effects. CBN has also exhibited possible potentiation of THC effects in man. Cannabidiol (CBD) has exhibited anticonvulsant activity.

4. As well as significant variations in naturally occurring active substances in natural cannabis, there are variations in the active substances based on conditions under which the plant material has been maintained or stored.

THC is labile to air oxidation forming cannabinol (CBN). Cannabidiol (CBD), in the presence of oxygen and light and upon heating, is converted to cannabielsoic acids.

5. It is not known how smoking or burning marijuana plant material affects the chemical composition of cannabinoids and their products. A large number of pyrolytic products is produced by burning that have not been identified for most of the constituents in *Cannabis*. Smoking as a dosage form to deliver marijuana to the human body is unsuitable for medical treatment due to: (1) Lack of standardization of the marijuana, (2) lack of knowledge of the amounts of each constituent available, (3) lack of knowledge of the activity of the chemicals while burning, (4) amount of product ingested being dependent on the individual's smoking technique, and (5) possible carcinogenic effect of smoking. There are no drugs which are delivered by smoking which are medically used in the United States.

6. *Cannabis sativa L.* was one of the first plants to be used by man for fiber, food, medicine, and in social and religious rituals. There were approximately 20 traditional medicinal uses of cannabis preparations in the 19th century. These included those recognized in 19th century medicine as well as folkloric use. These uses were based upon tradition and experience rather than scientific proof. Early literature is replete with reports of the inconsistent or contradictory effects of marijuana preparations. The cannabis used for medical purposes in the United States and in Western medicine from the mid-19th to the early 20th century was cannabis extract which was orally administered as tinctures and pills. By 1938, marijuana preparations were seldom used in medical practice, and the American Medical Association stated that, "Cannabis at the present time is slightly used for medicinal purposes * * * " In 1941, marijuana passed out of the *National Formulary* and *The United States Pharmacopeia.*

7. Historically, man used natural plants to treat various ailments. With the advent of science, man began to use plant extracts to determine their effects. These extracts were crude drugs. Fifty years ago *The United States Pharmacopeia* listed many crude drugs. In recent times, scientists discovered that crude extracts owed their activity to chemical compounds and began isolating the chemical compounds from the plants and their extracts. Current technology emphasizes the development of synthetics of natural drugs by using the natural drugs as models.

8. Currently, there are only four plants used in their natural states for medical purposes in the United States. Three others are utilized in crude extract form. These include ipecac and opium extracts, which must meet standards for potency and purity established in *The United States Pharmacopeia* before they can be used for medical purposes. In contrast to variations in cannabinoid content evident in cannabis, naturally occurring opium derivatives remain quantitatively stable and the potency can be chemically standardized.

9. Modern drug research is based on the use of well-defined preparations of pure compounds which, when administered to patients, allow reproducible results. The problems associated with using natural substances as drugs include the inability to regulate the doses of active constituents, and the interaction of the active constituents with other potentially active compounds in the natural substance. The presence of active constituents in most natural drugs may vary based on genetic factors, country of origin and growing conditions. As a result, most natural drugs cannot meet established quality control standards in the United States. Before a drug substance may be used in the practice of medicine, it must have a composition of active ingredients that has been established and accepted as standard. Such standardization, which includes identity, purity, potency, and quality, is specified in either a New Drug Application (NDA) or an official compendium such as *The United States Pharmacopeia* or *National Formulary.*

10. There is no difference in the pharmacological effect between the THC isolated from cannabis and the synthetically produced THC which is now marketed in the United States.

11. In the late 1960's, the Department of Health, Education and Welfare (DHEW) initiated a process to facilitate research with marijuana and THC. The FDA reviewed Investigational New Drug (IND) applications for marijuana and THC, assisted researchers and physicians in preparing IND protocols, and sent out information packets and model protocols.

12. The IND procedure is the process by which drugs are introduced into man and their safety and effectiveness is evaluated over a period of years. The stated objectives of the FDA in regulating the clinical testing of new drugs are to "protect the rights and safety of human subjects of such testing while, at the same time, facilitating the development and marketing of beneficial drug therapies." The Food, Drug, and Cosmetic Act emphasizes the need to carry out scientifically valid studies as well as the need to control the investigational drug supply and obtain informed consent of the subject or patient. The drug used in the study must be able to be traced to the patient, and the investigator must submit annual reports to FDA and report adverse reactions.

13. The protocols for the INDs with marijuana, especially the state protocols and the protocols for individual patients did not describe controlled studies. Controlled studies are necessary as the basis of a New Drug Application (NDA). No NDA for marijuana has been submitted to FDA for approval. Thus, marijuana remains an investigational drug subject to IND requirements. Due to the lack of an approved NDA, marijuana is not available by prescription in the United States.

14. As of January 6, 1987, there were 30 active INDs for marijuana; 82 INDs for marijuana have been discontinued.

15. The National Institute on Drug Abuse (NIDA) has shipped a total of 160,700 marijuana cigarettes for human studies from 1976 to 1986. Fifty-nine thousand (59,000) cigarettes were shipped to eight sponsors for human use outside state-sponsored programs. More than half of those, 30,900 cigarettes, were shipped to one sponsor during that period.

16. Thirty-four states have passed legislation concerning the use of cannabis (marijuana) and THC by physicians. Of these states, at least 24 define this use of marijuana and THC as research. Of these 34 states, only 17 states (New Mexico, Illinois, Louisiana, Washington, Florida, Michigan, Oregon, Colorado, California, Nevada, Ohio, West Virginia, Georgia, Arizona, New York, Vermont and Tennessee) had approved INDs for marijuana or marijuana/THC as of March 1, 1984. Ten state-sponsored programs received marijuana cigarettes from the NIDA during the period 1978 to 1986. During this period 101,700 cigarettes were distributed to those states; California received 38,700 cigarettes, the most of any state. New Mexico received 8,700 cigarettes in the period from 1978 to 1986. In 1986, four state programs received a total of 1,860 cigarettes. In March 1982, a National Conference on the Therapeutic Application of Cannabinoids was held. The report of that conference indicates that "state programs in general had a small volume of participation and a high loss of data." The report also concluded that the designs of the state programs varied widely.

17. The California Research Advisory Panel, a California government agency, sponsored the California Cannabis Therapeutic Research Program. After six years of operation, from 1979 to 1986, the Research Advisory Panel found that only 101 patients received 210 treatments with marijuana cigarettes. Slightly more than one-third of the patients received a second treatment of marijuana cigarettes. Approximately 20 percent of the patients stopped using the cigarettes either because the cigarettes were ineffective, or the side effects were too severe.

18. Approximately 250 individuals received marijuana and/or THC capsules under the New Mexico Controlled Substances Therapeutic Research Program from February 1979 to June 1986 for control of nausea and vomiting associated with cancer chemotherapy. For admission to the program, patients must have experienced nausea and vomiting in previous chemotherapy. An average of four to six individuals a month participated in the program. Approximately 20 New Mexico physicians participated in the state-wide program. There was no randomization in the study; the patients themselves chose to use either marijuana or THC. They were also free to switch from one drug to the other once they began treatment. Under the program, 16 individuals switched from one drug to the other; 13 switched from cigarettes to capsules, the others from capsules to cigarettes. Of the patients selected for evaluation, 94 used THC capsules and 75 used marijuana cigarettes. There was no objective measurement of success or failure. The patients evaluated themselves based upon the degree of nausea and vomiting in previous chemotherapy sessions as compared with the degree of nausea and vomiting when marijuana or THC was used.

19. One hundred-five patients enrolled in the State of Georgia marijuana and THC research study which was designed to evaluate the efficacy and toxicity of marijuana and THC as an antiemetic in cancer patients undergoing chemotherapy treatment. Emory University enrolled 85 patients in their marijuana and THC research study. Thirty-eight patients from the State of Georgia study, and 81 patients from the Emory University study were evaluated. Of the 119 patients evaluated in the combined studies, 44 smoked marijuana; the other 75 used THC capsules. The success rate for use of THC capsules was 76 percent, and the success rate for smoking marijuana was 68.2 percent. Success was measured by patient self-assessment or satisfaction. The primary reason for marijuana's failure as a treatment was the patients' intolerance of the cigarettes, or its failure to improve nausea and vomiting.

20. Of the 165 individuals evaluated in the Michigan Therapeutic Research Project for the years 1980–1982, 63 received only marijuana. Another 31 received marijuana after receiving Toracan (a phenothiazine in the same family as Compazine) during the same trial. The purpose of the trial (Trial A) was to evaluate the efficacy of marijuana to control nausea and vomiting induced by cancer chemotherapeutic agents. Thirty-four (34) of the patients discontinued the study because they did not like smoking marijuana. Twenty-one (21) patients reported the adverse effect of sleepiness/fatigue, 13 reported sore throat, 7 reported headache, and 4 reported being light-headed after smoking marijuana. Of 93 individuals who smoked marijuana at the first patient session, 14 reported no nausea, 31 reported mild nausea, 22 reported moderate nausea, and 19 reported severe nausea. Of the 93 patients who smoked marijuana in the initial session, 63 percent reported they felt "high," and 58 percent reported no increased appetite stimulation.

21. The State of New York Controlled Substances Therapeutic Research Program Report for 1982 indicates that by the end of July 1982, 840 marijuana cigarettes had been distributed to 45 patients under the New York program. These 45 patients had 99 treatment episodes. The treatment of 18 patients was evaluated, and 15 found that they benefited from smoked marijuana in some manner. For the period from November 1981 to May 1986, 199 patients received marijuana cigarettes under the New York program. During that period, 6,044 marijuana cigarettes were distributed. Of the 199 patients who received marijuana, only 90 were evaluated. The evaluations were based solely on patient self-assessments of nausea and vomiting, appetite, physical status, mood, "high" feeling, and a record of the amount of drug taken. The program was also plagued by lack of compliance with reporting procedures. The results of the evaluations indicated that large percentages of the individuals who received chemotherapeutic agents which are known to produce moderate to severe emesis failed to respond to the smoked marijuana. The New York Summary Report concluded that while preliminary results of the "Inhalation Marijuana Research Project" were encouraging, further analysis, more data, and more research are needed.

22. The July 1983 Report of the State of Tennessee program to evaluate marijuana and THC in treatment of nausea and/or vomiting associated with cancer therapy indicates that 43 patients have been enrolled in the program. Of these, 27 were evaluated. The patients enrolled in the program self-evaluated their nausea and vomiting, appetite and food intake, physical state, mood, high, and dosages of the drugs they received. Twenty-one (21) of the 27 patients used marijuana cigarettes. Nineteen (19) of the 21 evaluated the cigarettes as successful, success being defined as partially, moderately or very effective. The major reason for failure of marijuana cigarettes was smoking intolerance.

23. Nausea and vomiting (emesis) are common side effects of cancer chemotherapy. Vomiting is controlled by two distinct areas in the brain, the vomiting center and the chemoreceptor trigger zone (CTZ). Various cancer chemotherapeutic agents can trigger the vomiting center and the CTZ, thus causing nausea and vomiting. The incidence of emesis resulting from cancer chemotherapy often depends upon the type of agent used for the chemotherapy treatment. Chemotherapeutic agents most often associated with emesis also induce emesis of the greatest severity. Cisplatin causes the highest incidence of emesis, whereas methotrexate causes only a moderate incidence of emesis. Other factors not specifically related to chemotherapy can also influence a patient's emesis, such as emotional status, alcohol consumption, age, and past chemotherapy experience.

24. Prior to 1980, little research was conducted regarding antiemetics used to treat nausea and vomiting related to cancer chemotherapy. At that time, the most commonly used antiemetic was Compazine (prochlorperazine). Compazine was largely ineffective in treating emesis caused by most cancer chemotherapy regimens. Since 1980, research with new antiemetics has proliferated. As a result of this additional research, several new and highly effective antiemetics and their combinations are now available including: metoclopramide, thiethylperazine malate, haloperidol, dexamethasone, diphenhydramine, droperidol, fluphenazine hydrochloride, perphenazine, lorazepam, dronabinol (synthetic THC) in sesame oil in a soft gelatin capsule, and nabilone (a synthetic substance chemically and pharmacologically similar to THC).

25. To properly evaluate the effectiveness of a new antiemetic drug, researchers must perform carefully conducted randomized, double-blind testing of the drug against either a placebo or an established antiemetic, using a statistically significant patient population. Several factors are important when planning or evaluating an antiemetic study; these include: (a) Standardization of the emetic stimulus, (b) accuracy in data collection, with the use of objective parameters, such as the number of emetic episodes and the volume and duration of emesis, (c) standardization of patient population, with an indication of whether or not patients had previously received chemotherapy, and (d) proper selection of route of administration, and drug schedule and dosage, based upon proper trials with the agent. In addition, it is important to determine quantitatively the efficacy of antiemetic agents used singularly, so that results can be compared and further trials, including combination studies, can be planned appropriately.

26. For a new antiemetic drug to be considered effective, it must be as effective or more effective in controlling emesis than the currently-available antiemetics.

27. Relatively few scientific or medical studies have been conducted to evaluate marijuana's effectiveness as an antiemetic. Information concerning marijuana's antiemetic properties is primarily anecdotal. The research that has been conducted with marijuana has been primarily in the form of loose, uncontrolled studies which provide little valuable information as to the drug's effectiveness. Most research with marijuana has been conducted under state protocols. The state sponsored research conducted thus far has not employed carefully controlled double-blind, randomized testing of marijuana, nor has it involved large patient populations. As a result, little reliable information can be gleaned from these types of studies.

28. Based upon the lack of quality testing, marijuana's antiemetic activity is not as established as that of THC or other available antiemetics. There are no double-blind randomized studies which have concluded that marijuana is as effective or more effective than synthetic THC, or any of the other currently available antiemetics. In fact, in 1984, the only controlled, randomized, double-blind, crossover study comparing the antiemetic effectiveness of smoked marijuana to orally ingested synthetic THC involved 20 patients and concluded that orally ingested THC was superior to smoked marijuana.

29. Although THC is usually a constituent present in marijuana, since marijuana also contains at least 60 other active cannabinoids in varying quantities, the results of antiemetic trials using THC cannot be extrapolated in evaluating marijuana's antiemetic properties. For example, cannabidiol, a constituent present in marijuana, can potentiate some effects of THC, while suppressing other effects, including the antiemetic effect.

30. No formal, well-controlled studies have been conducted which compare marijuana's effectiveness as an antiemetic against any of the currently available antiemetics such as metoclopramide, haloperidol, dexamethasone, prochlorperazine, nabilone, lorazepam, or any of the highly effective combinations of available antiemetics.

31. The only studies which have been conducted using marijuana as an antiemetic include the following: (1) The state programs (discussed previously); (2) the study mentioned above which compared smoked marijuana to oral synthetic THC and concluded that THC was more effective; (3) a "compassionate" study conducted by Thomas J. Ungerleider involving 16 bone marrow transplant patients. In that study, the efficacy of the drug was measured only by subjective testing techniques; and (4) a study conducted by Alfred E. Chang which involved 15 patients receiving methotrexate chemotherapy.

32. The purpose of the Chang study was to compare the antiemetic effectiveness of THC to a placebo. Initially in the study, patients randomly received either an oral THC capsule or placebo capsule prior to chemotherapy. Neither the patients nor the researchers were aware of which drug they received. Three separate chemotherapy trials were conducted during the study. Only if the patient vomited during a trial would he or she receive a marijuana cigarette for the remaining doses of that chemotherapy trial. All patients who received marijuana cigarettes were experienced smokers. The study does not indicate how many patients resorted to smoking marijuana during each trial. Since six patients did not vomit at all on the THC, they did not receive marijuana cigarettes. The purpose of the study was not to compare the effectiveness of oral THC to marijuana but, rather, to compare THC's effectiveness against a placebo. Dr. Chang concluded that the combination of oral THC and smoked marijuana is a highly effective antiemetic in patients receiving methotrexate chemotherapy. Although Dr. Chang found that smoked marijuana was more reliable than oral THC in achieving therapeutic blood levels, he also found that it had drawbacks in patient acceptability; patients complained of its adverse taste, which induced nausea and vomiting in some instances. He also surmised that patients who are nonsmokers may not be willing and/or able to smoke marijuana. Based upon these drawbacks, Dr. Chang concluded that "an alternative parenteral drug route needs to be established if THC [or marijuana] is to have wide clinical acceptability." In addition, he determined that additional studies relating to drug tolerance, effectiveness against nausea and vomiting produced by other chemotherapy regimens, and comparisons with conventional antiemetics needed to be conducted.

33. A study conducted by Stephen E. Sallan, M.D., which is cited by both NORML and ACT, involved a double-blind, randomized evaluation of the antiemetic effect of synthetic THC capsules in 16 patients receiving chemotherapy (although 22 patients participated in the study, only 16 received oral THC). There is no indication as to what types of chemotherapeutic agents were administered to the patients during the study. Dr. Sallan concluded that THC had antiemetic effects. In addition, he made some "preliminary observations" comparing the antiemetic effect of smoked marijuana and oral THC capsules, based upon some patients' illicit use of marijuana which was neither qualitatively nor quantitatively controlled. He found that "[f] or most patients, both smoked and oral routes had identical effects." This study was not a scientific comparative study of smoked marijuana and oral THC, but rather a formal comparison between oral synthetic THC and placebo.

34. Even in its limited use, marijuana has not been shown to be very effective in reducing nausea and vomiting when used with chemotherapeutic agents which produce severe emesis.

35. In contrast to marijuana, synthetic oral THC (dronabinol), nabilone, metoclopramide, and other currently available antiemetics have been tested extensively through well-designed, controlled double-blind studies for both safety and efficacy. For example, more than 1,300 patients were tested with synthetic THC before it was made available as a Schedule II drug. Marijuana, on the other hand, has only been tested in 20 patients in a formal

comparative study, and roughly less than 500 patients in loosely controlled state studies.

36. Neither marijuana nor oral THC has been demonstrated to be an effective antiemetic for patients receiving radiation therapy. In a THC study conducted at UCLA, Dr. Ungerleider concluded that oral THC was only slightly more effective than Compazine in controlling emesis caused by radiation therapy. No studies evaluating marijuana's effectiveness in this area were introduced during this proceeding.

37. Since the advent of the new, highly effective antiemetics, few cancer chemotherapy patients discontinue treatment as a result of nausea and vomiting.

38. Although the newer antiemetics and their combinations have been shown to be highly effective in treating emesis, even in conjunction with chemotherapy treatments known to produce severe nausea and vomiting in most patients, a small number of patients are refractory to all antiemetic treatment. There is no scientific or medical reason to believe that patients who do not respond well to currently-available antiemetics would respond any better after smoking marijuana. The only method to determine marijuana's effectiveness for that purpose would be to conduct controlled double-blind trials with the drug in that group of patients.

39. There is no scientific or medical support for the hypothesis that marijuana or any of the cannabinoids are effective in treating emesis in children receiving chemotherapy. Again, only controlled trials comparing marijuana to other available antiemetics could support that contention. No such trials have been conducted as of this time.

40. Smoking as a route of administration for antiemetics has not been demonstrated to be more advantageous than intravenous or oral administration. The claimed advantage of self-titration through smoking is only a hypothesis and has not been scientifically proven. In fact, oral administration of antiemetics is highly effective if effective antiemetics are given. Intravenous administration also is highly effective, especially since most chemotherapy agents are intravenously administered as well.

41. Currently available antiemetics are also highly effective in outpatient care. Most patients can receive the newer antiemetics on an outpatient basis. There is no scientific or medical reason to conclude that marijuana is better-suited than currently available antiemetics in the treatment of emesis of outpatients. Carefully conducted clinical trials would be needed to demonstrate otherwise.

42. In addition to not being as effective or more effective than currently-available antiemetics, the use of smoked marijuana in the treatment of emesis in cancer patients has significant drawbacks. As a psychoactive substance, marijuana causes anxiety and panic in inexperienced users. Marijuana smoking also caused nausea and vomiting in some patients, and left an unpleasant residual taste. Because tachycardia and orthostatic hypotension are negative side effects of marijuana smoking, it should not be administered to patients with heart problems such as arteriosclerotic heart disease and angina. Marijuana smoking can also lead to pulmonary problems including bronchitis and emphysema. Marijuana is a crude plant material which contains pathogenic bacteria that could prove harmful to immuno-compromised patients with various cancers or leukemias. The cannabinoids present in marijuana can further suppress the immune functions of individuals whose immune systems are already severely compromised by chemotherapeutic agents. Also, few patients can tolerate marijuana smoking. In fact, in the state programs employing marijuana, significant numbers of patients either switched from smoking to oral THC capsules or withdrew from research because they could not tolerate smoking marijuana. In Dr. Ungerleider's study involving 16 bone marrow transplant patients, three dropped out of the study because they found marijuana smoking to be undesirable, even though at the time of the study, no other antiemetics were available to them. In addition, because of the lack of standardization of the drug and varying smoking techniques, there is a problem with bioavailability and reproducibility of an administered dose of the drug. If the dose is not constant from treatment to treatment, the patient may go unprotected.

43. The combination of currently available antiemetics produce less side effects than do each of the drugs given individually. These combinations produce less side effects than the cannabinoids, including marijuana. There is no scientific or medical evidence which demonstrates that marijuana produces fewer and less severe side effects than the currently-available antiemetics.

44. Patient satisfaction with the combination antiemetic therapy is greater than that seen with marijuana.

45. Interest in research using marijuana to treat emesis in cancer chemotherapy patients has waned as the availability of new, highly-effective antiemetics has increased.

46. Patient interest in using marijuana to treat emesis caused by chemotherapy has also declined in recent years.

47. The oncological community does not consider marijuana to have currently accepted medical use in the United States for the treatment of emesis caused by cancer chemotherapy. In addition, David Ettinger, M.D., Richard Gralla, M.D., and John Laszlo, M.D., each a highly respected oncologist and antiemetic researcher who has treated numerous patients and conducted extensive research with various cannabinoids and highly effective antiemetics, have concluded that based upon their research and knowledge of the field, marijuana does not have a currently accepted medical use in the United States for the treatment of emesis caused by cancer chemotherapy, nor has it been proven safe for use under medical supervision.

48. The American Cancer Society has concluded that insufficient research has been conducted to advocate that marijuana be used as an antiemetic for chemotherapy patients.

49. In its 1984 report, the National Academy of Sciences did not make any conclusions regarding marijuana's accepted medical use in the treatment of emesis in cancer chemotherapy patients. The only conclusion made in the report was that marijuana's antiemetic properties were less established than those of synthetic THC.

50. The American Medical Association has concluded that marijuana does not have a currently accepted medical use in the United States for the treatment of emesis caused by cancer chemotherapy, nor has it been proven to be safe for use under medical supervision.

51. Glaucoma is a term which describes a group of chronic ocular diseases which cause an increase in intraocular pressure that damages the retina and optic nerve and can lead to an eventual loss of vision. The most common form of glaucoma is primary open-angle glaucoma (POAG). This form of glaucoma is caused by an obstruction in the pathways for fluid exit from the eye while fluid inflow continues unabated. As a result, the pressure within the eye (intraocular pressure) increases beyond a level tolerated by the eye and can cause damage to the retina and optic nerve.

52. Persons suffering from glaucoma have intraocular pressures which are higher than their eyes can tolerate. Traditionally, glaucoma was measured

by a statistical measure of intraocular pressure (a norm), meaning that if an individual's pressure was higher than the average, he was thought to have glaucoma; if the pressure was below the norm, he was thought not to have glaucoma. It is now known that this is not the proper method for diagnosing glaucoma. Ninety-five percent of individuals with statistically-elevated intraocular pressure are never afflicted with glaucoma, while one-third of glaucomatose individuals have intraocular pressures in the statistically normal range.

53. Effective treatment for glaucoma involves the use of pharmaceutical agents or surgical procedures that prevent progressive optic nerve damage. If intraocular pressure can be lowered sufficiently, it can usually alter the course of the glaucoma. But, merely reducing intraocular pressure is not necessarily beneficial to the eye, and pressure reduction does not necessarily prevent glaucomatose optic nerve damage. For a treatment to be effective, it must lower intraocular pressure sufficiently to prevent additional damage to the optic nerve and retina, and also not cause unacceptable damage to the eye or to other parts of the body. In addition, it must be able to sustain the lowered pressure and preserve visual function for the patient's lifetime.

54. When new glaucoma treatments are tested for efficacy, they are evaluated for their ability to sufficiently lower intraocular pressure and to maintain visual fields. To properly measure the treatment's effect on both, it must be used in long-term testing. Timolol, a drug currently used to treat glaucoma, has been tested in this manner. Before it was approved for use in treating glaucoma, timolol was rigorously tested in 300 to 400 persons through controlled, double-masked clinical trials. These studies involved treating patients with the drug for a minimum of three months, with a majority of the studies lasting for six months or more, during which time, the patients' visual fields were measured to determine whether there had been any progression of the disease. In addition, other conventional glaucoma medications have proven their efficacy through years of clinical experience. The miotics, epinephrine compounds and carbonic anhydrase inhibitors have been proven effective in lowering intraocular pressure and preserving visual function.

55. The most efficacious way of delivering any drug to the eye is through a topical drop, rather than by systemic application. Topical application reduces the possibility of systemic adverse effects from a drug since the total amount of the drug being delivered to the body is considerably less.

56. In 1971, Robert S. Hepler, M.D. and Ira R. Frank, M.D. published preliminary results of one of the first experiments which measured the effect of smoked marijuana on intraocular pressures of normal, healthy males. The study involved acute administration of smoked marijuana through an ice-cooled water pipe to eleven youthful men who did not suffer from glaucoma. After the one-time administration of the marijuana, nine subjects experienced decreases in intraocular pressure which ranged from 16 percent to 45 percent, one subject experienced a 4 percent increase in intraocular pressure, and one subject experienced no change following smoking. These results were later published in 1974 as part of a larger study in which Thomas J. Ungerleider, M.D. participated, aimed at measuring pupillary constriction, intraocular pressure, tear production, and conjunctival hyperemia (redness and irritation of the eye). The overall study involved 21 healthy subjects who smoked marijuana in an ice-cooled water pipe. Only the 11 subjects described in the earlier publication were tested for changes in intraocular pressures. In addition to the results of changes in intraocular pressures, the authors also noted that smoking marijuana was associated with minor decreases in pupillary size, decrease in tear production, and conjunctival hyperemia. Central visual acuity, refraction, peripheral visual fields, binocular fusion and color vision were not altered by the single-dose administration of the marijuana. In addition, the authors noted that fatigue and sleepiness occurred several hours following the marijuana-induced "high".

57. There are no published scientific reports or studies which demonstrate marijuana's ability to lower intraocular pressures in long-term chronic testing of glaucomatose research subjects. The only long-term study reported was one conducted by Dr. Hepler at U.C.L.A. The study evaluated responses of 19 normal, non-glaucomatose patients for a period of 94 days. The results of the 94-day study were not available at the time Dr. Hepler's paper was published. The only conclusions made were that in the normal research subjects, intraocular pressure showed a prompt drop as soon as the subjects began to smoke, and that there were no indications of cumulative effects upon the intraocular pressure response.

58. There are few published scientific reports or studies which evaluate marijuana's effect on lowering intraocular pressure in glaucomatose individuals. All of the studies involve acute administration of the drug and each involve relatively small numbers of research subjects. In 1976, Drs. Hepler and Petrus reported the results of their study which involved 12 research subjects who suffered from galucoma. Each subject was seen on four occasions. On one occasion, the subjects were given a placebo in a smokable form; on the other occasions, the subjects were either given oral (synthetic) THC or smoked marijuana. Some of the resarch subjects continued their usual courses of medication during the testing. The published study only reported the results of four of the research subjects. Two subjects failed to achieve a reduction in intraocular pressue. Also, the study did not indicate which of the four subjects, if any, had continued their conventional medication during the study. The study did not differentiate between the effectiveness of marijuana or oral THC. The researchers concluded that "patients with proven glaucoma frequently, although not invariably, demonstrate substantial decrease in intraocular pressure following smoking of marijuana or ingestion of THC." In 1976, Drs. Hepler, Frank and Petrus reported on the results of another small study involving 11 galucomatose individuals who were observed after acute administration of marijuana. Of the 11 patients studied, seven demonstrated drops in intraocular pressure averaging 30 percent. The remaining four did not experience any drop in intraocular pressure.

In 1979, Drs. Merritt and Crawford published results of an acute study of the effects of marijuana and placebo on 16 glaucomatose research subjects. They concluded that "inhaled tetrahydrocannabinol (delta-9-tetrahydrocannabinol) lowers blood pressure and intraocular pressure, commensurately with tachycardia [rapid heart rate], in systemic normotensive and hypertensive glaucoma patients." In 1980, Drs. Merritt, Crawford, Alexander, Anduze, and Gelbart reported the results of a study which observed the effect of acute administration of marijuana and placebo to 18 glaucoma patients. They concluded that acute administration of marijuana lowered both intraocular pressure and blood pressure in a heterogenous glaucoma population. They also noted that eight of the patients suffered from anxiety with tachycardia and palpitations; five

suffered from postural hypotension (reduction in blood pressure upon standing); 18 suffered from sensory alterations including hunger, thirst, euphoria, drowsiness and chills; and nine suffered from conjunctival hyperemia and ptosis (drooping upper eyelid). Based on the side effects, the researchers concluded that "it is because of the frequency and severity with which untoward events occurred that marijuana inhalation is not an ideal therapeutic modality for glaucoma patients." A total of no more than 50 glaucomatose individuals have been administered smoked marijuana in a research setting.

Approximately 40 of these individuals received marijuana during limited acute trials of the drug. The progress of the other individuals, who included Robert Randall and other individuals who used marijuana in conjunction with their conventional glaucoma medications, were never published since they only involved anecdotal observations, providing insufficient data to report which would be useful for other ophthalmologists in treating patients with glaucoma.

59. In 1976, Dr. Mario Perez-Reyes reported the results of his preliminary study of acute intravenous administration of various cannabinoids on intraocular pressure. Twelve normal, nonglaucomatose patients were injected with a variety of cannabinoids which are present in marijuana; the cannabinoids were administered individually so that the effects could be evaluated separately. He concluded that several of the cannabinoids had intraocular pressure lowering qualities, including delta-8-tetrahydrocannabinol, which is less psychoactive than THC. THC appears to be the most effective cannabinoid for acutely reducing intraocular pressure, but is also the most psychoactive. Although marijuana, which consists of various cannabinoids, would have a different effect on eye pressure than one of its single constituents, the literature indicates that the effect would either be the same or less.

60. There are no published scientific or medical reports which evaluate marijuana's ability to preserve the visual function of glaucomatose individuals.

61. None of the IND reports or studies submitted in this processing have compared marijuana's effectiveness in lowering intraocular pressure and preserving visual function to any of the currently accepted glaucoma medications. Although not proven through comparative studies, it is accepted that reductions in intraocular pressure continue for longer periods of time following administration of either timolol, pilocarpine, or phospholine iodide, than following administration of smoked marijuana.

62. No evidence was introduced in this proceeding from states which have scientific protocols for researching marijuana's effect in the treatment of glaucoma. In 1986, the California Research Advisory Committee reported the results of its research protocol in this area which covered only the use of THC. Only one individual received marijuana cigarettes for glaucoma. This was after the Research Advisory Panel mailed information about the program to ophthalmologists throughout the State of California. Rhode Island reported that 28 ophthalmologists in that state were contacted to determine if they had any interest in conducting research with marijuana. None of the ophthalmologists contacted responded affirmatively. Those who responded to the inquiry claimed that the drugs which were currently available sufficiently controlled glaucoma.

63. Acute administration of marijuana has demonstrated unacceptable negative side effects in research subjects participating in glaucoma studies. These side effects include orthostatic hypotension, tachycardia, conjunctival hyperemia, euphoria, dysphoria, drowsiness, depersonalization, difficulty in concentrating and thinking, impairment of motor coordination. Since the drop in intraocular pressure after smoking marijuana noted in acute studies lasts for approximately four to five hours, with the maximal fall occurring about one to two hours after administration, to be considered in treating glaucoma, marijuana would have to be administered six to eight times per day for the duration of disease. Such use constitutes chronic administration of the drug. The negative effects of chronic administration of marijuana have not been adequately tested. Yet, specific unacceptable negative effects can be attributed to chronic administration of marijuana. These include: possible brain damage, sore throat, rhinitis, bronchitis and emphysema; suppression of luteinizing hormone secretion in women (which affects the production of progesterone); abnormalities in DNA synthesis, mitosis and growth; carcinogenicity; and genetic mutations.

64. While marijuana plant material and some cannabinoids have been shown to lower intraocular pressure in acutely-treated normal human volunteers and glaucoma patients, it may lower intraocular pressure without preventing visual impairment in glaucoma patients. As noted above, there has been no documentation that marijuana use preserves the visual function of glaucomatose individuals. Because acute studies have shown that marijuana appears to act by lowering intraocular pressure and blood pressure concomitantly, there is some concern that lowering the blood pressure limits the blood supply to the optic nerve. Since the optic nerve relies on a constant supply of blood to function adequately, there is a concern that by reducing its blood supply by lowering systemic blood pressure, visual function will be further impaired in glaucomatose individuals.

65. Based on the lack of documented evidence showing its utility in lowering introacular pressure in the long-term and maintaining visual function, coupled with the adverse side effects associated with its use, most experts agree that smoked marijuana has not been proven to be a viable drug for the treatment of glaucoma. These medical and scientific experts include: Mario Perez-Reyes, M.D. (a source often cited by NORML and ACT); Robert Hepler, M.D.; Keith Green, Ph.D.; George Spaeth, M.D.; Leo Hollister, M.D.; Reese Jones, M.D.; and Raphael Mechoulam, Ph.D. In addition, in previously published articles, John Merritt, M.D., a witness for ACT, has taken the position that marijuana's use in treating glaucoma is unacceptable because of the frequent and untoward side effects associated with its use. Also, the American Academy of Ophthalmology, an organization which represents more than 12,000 physician members and approximately 6,000 other medical professionals who specialize in the field of ophthalmology, has taken the position that insufficient data exists to demonstrate the safety and efficacy of using smoked marijuana in the treatment of glaucoma. The National Academy of Sciences, another source frequently cited by NORML and ACT, also concluded that smoking marijuana is not suitable for the treatment of glaucoma.

66. Multiple Sclerosis (MS) is the major cause of neurological disability among young and middle-aged adults. It is a life-long disease which attacks the myelin sheath (the coating surrounding the message-carrying nerve fibers in the brain and spinal cord). Once the myelin sheath is destroyed, it is replaced by plaques of hardened tissue known as sclerosis. The plaques can obstruct impulses along the nerve systems which will produce malfunctions in the body parts affected by the damaged nervous system. The symptoms can include one or a combination of the following:

weakness, tingling, numbness, impaired sensation, lack of coordination, disturbances in equilibrium, double vision, loss of vision, involuntary rapid eye movement, slurred speech, tremors, stiffness, spasticity (involuntary and abnormal contractions of muscle or muscle fibers), weakness of limbs, sexual dysfunction, paralysis, and impaired bladder and bowel functions. Spasticity can also result from serious injuries to the spinal cord, not related to MS. The effects of MS are sporadic in most individuals, and the symptoms occur episodically, either triggered by the malfunction of the nerve impulses or by external factors. Because of the variability of symptoms of the disease, MS is difficult to detect and diagnose. There is no known prevention or cure for MS; instead, there are only treatments for the symptoms.

67. There are no published scientific reports or studies which evaluate marijuana's effectiveness in treating spasticity. The only existing information regarding the use of marijuana to treat the effects of MS or spasticity is primarily anecdotal. Anecdotal information is only useful for providing a basis for conducting controlled research with the drug to evaluate its effectiveness. In order to sufficiently verify that a drug is effective for treating MS or spasticity, double-blind, controlled studies must be conducted on large groups of persons.

68. The only studies evaluating the effect of cannabinoids on MS and spasticity employed synthetic THC or cannabidiol. These studies have been uniformly small, and the data presented are insufficient to evaluate the nature and quality of controls used. In 1981, Drs. Denis J. Petro and Carl Ellenberger published the results of a limited acute study using synthetic THC. That study involved the acute administration of oral synthetic THC to nine MS patients. The researchers noted that the spasticity scores of four of the nine patients improved significantly after the administration of the synthetic THC; one patient improved after receiving the placebo; only two of three patients who felt improved actually demonstrated improvement by objective criteria. The EMG index of spasticity (electromyography—a method of measuring reflex responses, neuromuscular function and condition, and extent of nerve lesion) was impractical in five of the nine patients. The researchers concluded that further study should be conducted to determine the effectiveness of THC or one of its derivatives in treating spasticity. In a 1986 abstract, W. C. Hanigan, R. Destree, and X. T. Troung reported the results of a 20-day study in which they administered oral synthetic THC to five spastic patients. They concluded that two patients experienced significant reductions in stretch resistance and reflex activity; and one patient withdrew from the study because of negative emotional side effects. In another abstract, R. Sandyk, P. Consroe, L. Stern and S. R. Snider, evaluated the effects of cannabidiol (a major non-psychoactive cannabinoid of marijuana) on three patients suffering from Huntington's Disease (a progressive central nervous system disease characterized by muscular twitching of the limbs or facial muscles). The first week they noted mild improvement in choreic movements. Further improvement was noted the second week and remained stable for another two weeks. The only side effects observed were cases of transient, mild hypotension.

69. There are no reported scientific or medical studies which have compared the effectiveness of marijuana, or its derivatives, with conventional treatments for MS and spasticity. There is no indication that marijuana would be more effective or safer than currently available treatments. In addition, conventional drugs may reduce spasticity with fewer side effects than marijuana.

70. No long-term clinical studies employing marijuana, or any of its derivatives, have been conducted with respect to treating MS or spasticity.

71. The long-term safety of using marijuana to treat MS and spasticity has yet to be established. Marijuana's long-term effects on memory and intellect, its pulmonary effects, risks in pregnancy, and tolerance to the drug, are unresolved. Since marijuana may have undesirable side effects at doses necessary to reduce spasticity, the use of marijuana for long-term treatment such as is needed to treat MS and spasticity would be worse than the disease itself.

72. None of the state reports submitted in this proceeding indicate that any state research with marijuana was conducted with respect to spasticity. The National Multiple Sclerosis Society does not advocate the use of marijuana to treat spasticity associated with MS. In addition, the International Federation of Multiple Sclerosis Societies does not recommend marijuana's use in treating spasticity. Also, noted neurologists who specialize in treating and conducting spasticity research, including Drs. Silberberg and Johnson, concluded that marijuana has not been proven to have an accepted medical use in the treatment of spasticity, nor has it been proven to be safe under medical supervision. Dr. Denis Petro, a witness for ACT, concluded in his synthetic THC study that "research needs to cover a larger and better controlled sample before any definitive statement would be possible."

73. Epilepsy involves the progressive recruitment of normal brain neurons into rhythmic and then high frequency bursting. With the overwhelming of inhibitory restraints, the pauses between bursts disappear and are replaced by tonic high frequency firing and the seizure appears. A prominent feature of epilepsy is its episodic nature.

74. There are no studies of the effects of crude marijuana on existing epileptic symptoms in man. Only survey and case report data are available. In 1976, Dennis M. Feenely reported the results of his survey among young epileptics in the Journal of the American Medical Association. In that survey, young epileptics were questioned about their illicit use of marijuana, amphetamine, LSD, barbiturate, cocaine and heroin. Most of the subjects reported that marijuana had no effect on their seizures. In addition, one subject reported that his marijuana use reduced the frequency of seizures, while another subject claimed that marijuana caused him to have seizures. Also, published case reports indicate marijuana's conflicting properties of both reducing and causing seizures. Although case reports and surveys of this type are not highly reliable sources of scientific information, they follow the conflicting pattern suggested in animal studies employing synthetic THC.

75. Smoked marijuana has only been tested on experimental epilepsy in one study. That study evaluated marijuana's effect on seizures in five mongrel dogs. After chronic administration of marijuana smoke, two of the five dogs exhibited grand mal convulsions. In a study involving the administration of marijuana smoke to normal rats, "popcorn convulsions" (involuntary vertical jumping) were observed in 50 percent of the animals after 6 to 9 exposures to the drug.

76. Because of its potential to induce convulsant seizures, marijuana should not be used by epileptics.

77. Cannabidiol (CBD) has also been studied for its anticonvulsant effects in animals. CBD is neither psychoactive nor convulsant. Conclusions drawn from animal testing of this drug suggest that CBD shows promise as an anticonvulsant, and that its use should be clinically investigated in human

epilepsy to determine its therapeutic utility.

78. Marijuana has not been proven to be an effective appetite stimulant, or antianorectic drug. Most studies have involved oral THC rather than marijuana. In a doubleblind study employing smoked marijuana, normal patients using marijuana increased their caloric intake more than those using the placebo, but the variability was too great to draw any conclusions. Studies employing THC have failed to demonstrate an appreciable appetite stimulating or antianorectic effect. State reports of cancer chemotherapy patients receiving either synthetic THC or marijuana have failed to support any claims of marijuana's appetite stimulating properties. Several of the currently available antiemetics have appetite-stimulating properties. With patients undergoing cancer chemotherapy, controlling emesis generally eliminates problems with anorexia or appetite loss. Marijuana has not been compared with currently available antiemetics to evaluate its appetite stimulating properties.

79. There is no scientific or medical indication that marijuana is effective in the treatment of either alcoholism or drug addiction. Recent studies now demonstrate that abuse of marijuana and alcohol are frequently combined. In addition, animal studies present no evidence that marijuana is more effective than currently available treatments for opiate withdrawal.

80. Marijuana has not been demonstrated to be an effective analgesic. Studies have demonstrated that marijuana and THC both increase and decrease pain. In addition, there is no indication that marijuana or synthetic THC are as effective or more effective than currently available analgesics.

81. Marijuana has not been shown to be effective in the treatment of asthma and bronchial spasms. Although smoked marijuana and THC were found to have bronchodilating effects following acute and short-term administration, smoke, even if it provides relief, is not desirable for asthmatics. Also, long-term smoking of marijuana reduces bronchodilation and causes significant airway obstruction.

82. Although marijuana has also been suggested for several other medical problems, there is insufficient scientific data to support its use for these purposes. Although marijuana and some of the cannabinoids have sedative or hypnotic effects, their activity is not constant, nor is there any indication that marijuana is even comparable to currently-available antianxiety and insomnia medications. There also is no support for marijuana's use as an antidepressant drug. Nor is there sufficient indication that marijuana, or its constituents, would be a useful medical alternative in the treatment of hypertension, neoplasms (tumors), infections, or migraine headaches.

83. One of the primary methods for determining whether a particular drug is safe for use under medical supervision is to weigh its actual therapeutic benefit against its negative or unintended side effects. A side effect is a pharmacologic activity other than the desired effect. If the measurable therapeutic benefits of the drug outweigh its negative effects, the drug is generally considered safe for use; if the negative effects outweigh the therapeutic benefits, the drug is not considered safe for its intended use.

84. In evaluating the negative side effects of a drug, several factors are taken into consideration. Generally, initial animal studies are conducted to determine the drug's toxicity. An LD-50 is established (the dose which causes death in 50 percent of the animals tested). Factors other than the LD-50 are also considered in determining safety and toxicity. Additional pharmacological data is also needed, including the drug's bioavailability, metabolic pathways and pharmacokinetics. Acute and chronic testing must be conducted; first in animals, then in humans.

85. Most pharmacological research with cannabis or its constituents has actually been conducted with orally ingested THC, rather than smoked marijuana. Although the pharmacologic effects are presumed to be similar, the studies with oral THC do not provide a complete picture of marijuana's effects. Few of the other cannabinoids have been pharmacologically evaluated. The health consequences from smoking marijuana are likely to be quite different than those of orally ingested THC. Yet most of the chronic animal studies have been conducted with oral or intravenous THC.

86. There is a need for more information about the metabolism of the various marijuana constituents and their biologic effects. This requires many more animal studies. Then the pharmacologic information obtained from the animal studies must be tested in clinical studies involving humans. The pharmacologic testing of cannabinoids in animals thus far has shown that while they do not appear to be highly toxic, they exert some alteration in almost every biological system that has been studied.

87. Well-designed studies on the health effects of marijuana are relatively few. This is especially true with respect to chronic studies. Field studies in this area are deficient. Most are too small to detect unusual or rare consequences which could be of great importance. In addition, only modest research has been conducted using healthy male volunteers; very limited studies have been conducted using females, older individuals, or persons in poor health. The studies using marijuana on healthy male volunteers lead to a biased conclusion that the drug is safe without properly evaluating the populations at risk. To eliminate any such bias and to expand our knowledge of the chronic, long-term effects of marijuana use, sophisticated epidemiological studies of large populations, similar to those conducted for alcohol and tobacco use, must be done. It may take years of extensive research before all of marijuana's deleterious effects become apparent.

88. The acute effects of marijuana use are fairly well established. Marijuana smoking usually causes acute changes in the heart and circulation which are characteristic of stress, including rapid heart rate (tachycardia), orthostatic hypotension, and increased blood concentrations of carboxyhemoglobin (hemoglobin combined with carbon monoxide). Therefore, the drug is not indicated for persons who suffer from cardiovascular problems including angina, congestive heart failure, and arteriosclerosis. In addition, acute marijuana use also causes euphoria; dysphoria; anxiety; confusion; psychosis; drowsiness; convulsions; and impairment of motor coordination, tracking ability and sensory and perceptual functions. Based upon these effects, marijuana should not be used by anxious or depressed, or unrecognized psychotic individuals, and epileptics.

89. Many persons who have smoked marijuana in a research setting could not tolerate its harshness and complained of throat soreness and other problems associated with smoking as a route of administration. In addition, many patients cannot, and will not, smoke a substance like marijuana for therapeutic purposes.

90. Even though inadequate studies have been conducted concerning the effects of long-term chronic use of marijuana, certain detrimental effects on respiratory and pulmonary functions are well-established. Marijuana smoke inhibits pulmonary antibacterial defense systems, possibly making marijuana users more susceptible to bacterial infections of the lung. One chronic smoking experiment tested pulmonary functions of healthy volunteer subjects

before and after 47 to 59 days of daily smoking of approximately five cigarettes per day. The study concluded that very heavy smoking for only six to eight weeks caused mild but significant airway obstruction. In addition, a study of heavy hashish (a crude smokable preparation of cannabis resin) users revealed a high incidence of bronchopulmonary consequences, including chronic bronchitis, chronic cough, and mucosal changes of squamous metaplasia (a precancerous change). Chronic smoking can also result in emphysema.

91. Regular and frequent marijuana smoking causes preneoplastic changes in airways similar to those produced by smoking tobacco. Marijuana smoke does not contain nicotine; but like tobacco, it does have an equally complex aerosol of particles in a vapor phase that form a tar mixture. The mixture contains many of the same hydrocarbons contained in tobacco tars which are thought to be associated with cancer causation. Marijuana also contains more tar than tobacco cigarettes. Animal studies using smoked marijuana have documented the growth of precancerous cells after 30 months. Dr. C. Leuchtenberger, a professor at the Swiss Institute for Experimental Cancer Research, noted that exposure of human lung explants to fresh marijuana or tobacco cigarette smoke evoked abnormalities in DNA synthesis, mitosis, and growth with consequent genetic disturbances that may lead to malignant transformation. The abnormalities were more pronounced following exposure to marijuana than to tobacco smoke. These findings were later confirmed in a similar study. Marijuana smoke also contains benzene, a substance associated with leukemia, and 2-aminonapthalene, which causes bladder cancer.

92. Recent evidence also indicates that marijuana can depress an individual's immune function. The immune system's sensitivity to marijuana depends on the cannabinoid compound and varies among immune cell types. In addition to the various cannabinoids, bacteria present in the plant material can further affect the immune function. A number of microbial contaminants have been isolated from marijuana samples, including pathogenic aspergillus, *Klebsiella pneumoniae, Enterbacter agglomerans,* group D streptococcus, *Enterbacter cloace, Bacillus* sp. and salmonella enteritis. The bacteria were found in both licit and illicit supplies of marijuana. At the Memorial Sloan-Kettering Cancer Center, it is estimated that 60 patients die each year from invasive aspergillus. Aspergillus was cultured from samples of marijuana from patients who developed invasive pulmonary and allergic bronchopulmonary aspergillus. The data supports the theory that marijuana smoking during periods of immunosuppression (as during cancer chemotherapy), may lead to infection. Therefore, because of its own immunosuppression properties, and its propensity for causing infections in immunosuppressed individuals, marijuana smoking may be contraindicated in cancer chemotherapy patients.

93. Studies conducted with respect to passive inhalation of heavy marijuana smoke demonstrate that passive inhalation of a substantial amount of sidestream marijuana can produce subjective effects, plasma levels of THC and urinary cannabinoid metabolites, in subjects similar to those found after the smoking of marijuana. The researchers concluded that with sufficient time and high marijuana smoke conditions, it becomes difficult to distinguish between active smoking and passive inhalation.

94. Marijuana has also produced genetic and non-genetic birth defects in many animal species. Pure THC is not thought to produce permanent alterations of genes in cells studied to date, but other components of cannabis smoke can cause such mutations. When animals of one generation were exposed to cannabis smoke during pregnancy, birth defects were found in the third generation, suggesting that a gene change had been transmitted through second generation animals which were only exposed to cannabis smoke prior to birth. Cannabis smoke has been related to the increased numbers of early fetal deaths, decreased fetal weight, and an increased death rate at birth in study animals. Although there have been some cases reported of deformed babies being born to marijuana smoking mothers, no causal links can be made based upon the limited evidence. Further human research is necessary to establish or rule out such effects. Based upon the insufficient and inconclusive research in this area, pregnant women and those with marginal fertility may be at risk in smoking marijuana, even at moderate levels.

95. Chronic marijuana use may also have a toxic effect on the human brain. Preliminary studies indicate that THC changes the way sensory information gets into and is acted on by the hippocampus. Chronic exposure damages and destroys nerve cells and causes other changes which are identical to normal aging and may be additive to the aging process. Therefore, chronic marijuana use could result in serious or premature memory disorders. The results of these studies are now being confirmed.

96. Animal studies and some human studies have found that in males, sperm count and motility are decreased during cannabis use. In female animals, THC suppresses the secretion of luteinizing hormone. Prolonged suppression would eventually lower gonadal steroid levels. Whether these changes have any effect on human sexual function and fertility is not yet known.

97. In addition to the known and suspected health risks associated with marijuana use, there is also evidence to suggest that tolerance to its therapeutic effects also develops.

98. The National Academy of Sciences found that the dose of marijuana necessary to produce a therapeutic benefit is often close to one that produces an unacceptable frequency of toxic side effects.

99. The severity and frequency of negative side effects experienced from marijuana smoking exceed those caused by accepted medications used to treat glaucoma, emesis and Multiple Sclerosis and spasticity.

100. Because of its unacceptable side effects and undetermined therapeutic utility, smoked marijuana is not recommended for the treatment of glaucoma, emesis, Multiple Sclerosis and spasticity, epileptic seizures and convulsions, asthma, appetite loss or anorexia, alcoholism and drug abuse, pain and inflammation, anxiety, insomnia, migraine headaches, hypertension, depression, infections or tumors.

Conclusion

The Administrator finds that the administrative law judge failed to act as an impartial judge in this matter. He appears to have ignored the scientific evidence, ignored the testimony of highly-credible and recognized medical experts and, instead, relied on the testimony of psychiatrists and individuals who used marijuana. The administrative law judge relied heavily on anecdotal accounts of marijuana use by both physicians and seriously ill persons. The administrative law judge's findings of fact ignored any evidence presented by the Government. For example, in his findings regarding marijuana and nausea and vomiting associated with chemotherapy, Judge Young cites many of the physicians presented by the pro-marijuana parties by name as accepting marijuana as "medically useful." Not once in his

findings or discussion does the judge acknowledge or mention the Government's experts. Not once does the judge mention why he chose to find the pro-marijuana parties' evidence more credible. The administrative law judge failed to acknowledge the position of a major organization of physicians, the American Medical Association; and those of organizations whose existence is dedicated to the treatment and study of the diseases at issue such as the American Cancer Society, the National Academy of Ophthalmology and the National Multiple Sclerosis Society. He chose instead to rely on the testimony of a very small number of physicians. Most significantly, the administrative law judge did not follow the standard for "accepted medical use in treatment in the United States," and "accepted safety for use * * * under medical supervision" established by the Administrator in previous scheduling proceedings. The administrative law judge chose, instead, to develop his own standard for both accepted medical use and accepted safety; standards which were specifically rejected by the Administrator in the scheduling of 3,4-methylenedioxymethamphetamine (MDMA).

The administrative law judge did not even apply his own standard consistently. While the administrative law judge found that marijuana had an accepted medical use in treatment of nausea and vomiting associated with chemotherapy; of spasticity associated with multiple sclerosis and amputation; and of pain associated with hyperparathyroidism; he concluded that it did not have accepted medical use in treatment of glaucoma. His rationale was that in applying his standard of accepted medical use, which is that a "significant minority" of physicians accept marijuana as medically useful, there were not enough physicians to establish such a "significant minority" with respect to glaucoma. In contrast, he found that one physician's opinion was sufficient to establish an accepted medical use of marijuana with regard to hyperparathyroidism, because that was a rare disease.

The Administrator rejects the administrative law judge's findings and conclusions. They were erroneous; they were not based upon credible evidence; nor were they based upon evidence in the record as a whole. Therefore, in this case, they carry no weight and do not represent the position of the agency or its Administrator. The inadequacy of Judge Young's analysis of the case is exemplified by his acceptance of, and reliance upon, irresponsible and irrational statements propounded by the pro-marijuana parties. Such statements include the following: "marijuana is far safer than many of the foods we commonly consume. For example, eating ten raw potatoes can result in a toxic response. By comparison, it is physically impossible to eat enough marijuana to induce death." That such a statement would come from the proponents of marijuana is understandable. To give it the weight of an administrative law judge's finding is appalling.

The Administrator has accepted the agency's findings of fact as his own. In order to conclude that these facts support a conclusion that marijuana remain in Schedule I, they must be applied to the criteria set forth in the Controlled Substances Act for substances in Schedule I.

The three criteria are found at 21 U.S.C. 812(b)(1) and are as follows:

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

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

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

For purposes of this proceeding, the parties stipulated that marijuana has a high potential for abuse. The criteria for substances listed in Schedule II also includes that the drug has a high potential for abuse.

The issue of what "currently accepted medical use in treatment in the United States," and "accepted safety for use * * * under medical supervision" mean, has been the subject of a previous scheduling proceeding involving the drug MDMA. In that proceeding, the Administrator did not adopt Judge Young's recommendation and defined both phrases to mean approved for marketing as safe and effective pursuant to the Food, Drug, and Cosmetic Act. 51 FR 36552, October 8, 1986. The Administrator's decision was reviewed by the United States Court of Appeals for the First Circuit in *Grinspoon* v. *DEA*, 828 F.2d 881 (1987). The Court remanded the matter to the Administrator finding that his standard was too restrictive. The Court did not suggest a standard to be adopted and, instead, stated that "Congress has implicitly delegated to the Administrator the authority to interpret these portions of the CSA* * *" *Grinsooon*, p. 892. The Administrator then published a revised final rule in which he listed several characteristics of a drug or other substance which has an "accepted medical use in treatment in the United States." 53 FR 5156, February 22, 1988. These characteristics are:

1. Scientifically determined and accepted knowledge of its chemistry;
2. The toxicology and pharmacology of the substance in animals;
3. Establishment of its effectiveness in humans through scientifically designed clinical trials;
4. General availability of the substance and information regarding the substance and its use;
5. Recognition of its clinical use in generally accepted pharmacopeia, medical references, journals or textbooks;
6. Specific indications for the treatment of recognized disorders;
7. Recognition of the use of the substance by organizations or associations of physicians; and
8. Recognition and use of the substance by a substantial segment of the medical practitioners in the United States.

These characteristics rely heavily on verifiable scientific data and acceptance by the medical community. These two areas go hand-in-hand, as aptly demonstrated by the record in this proceeding. Most physicians and organizations of physicians rely on scientific data in formulating their opinions regarding the safety and effectiveness of a drug and whether they will provide it for their patients. Many of the experts and organizations who concluded that marijuana did not have an "accepted medical use in treatment in the United States," stated that they reached this conclusion because of the lack of adequate scientific data to support the safety and efficacy of marijuana. The Administrator also notes that the Controlled Substances Act and its legislative history require him to consider scientific evidence in determining the schedule in which a drug should be placed. For example, the Controlled Substances Act at 21 U.S.C. 811(c) lists eight factors to be considered in evaluating the three scheduling criteria. Included among those factors are "scientific evidence of its pharmacological effect, if known" and "the state of current scientific knowledge regarding the drug or other substance." In addition, the Controlled Substances Act requires the Administrator to request a scientific and medical evaluation from the Secretary of Health and Human Services. The Administrator is then bound by the Secretary's recommendation as to scientific and medical matters. 21 U.S.C. 811(b). In this proceeding, the Assistant Secretary for Health has provided the Administrator with an extensive

scientific and medical evaluation in which it was recommended that marijuana remain in Schedule I because there is insufficient scientific and medical evidence to conclude that marijuana is a safe and effective drug.

It is clear from the evidence presented in this proceeding that marijuana does not have the characteristics of a drug which has an "accepted medical use in treatment in the United States." Because of the complex composition of marijuana, containing over 400 separate constituents (many of which have not been tested) varying from plant to plant, the chemistry, toxicology and pharmacology of marijuana is not established. As discussed previously, the effectiveness of marijuana has not been documented in humans with scientifically-designed clinical trials. While many individuals have used marijuana and claim that it is effective in treating their ailments, these testimonials do not rise to the level of scientific evidence. Marijuana is available from the Federal Government to those researchers who obtain proper licensure. However, the evidence suggests that only small numbers of researchers and physicians have obtained marijuana for this purpose, and that some research programs sponsored by states had trouble getting physicians to participate. The vast majority of physicians do not accept marijuana as having a medical use. Marijuana is not recognized as medicine in generally accepted pharmacopeia, medical references, journals or textbooks. As evidenced by expert physician testimony and the statements of many professional medical and research organizations, marijuana is not accepted by organized medicine or a substantial segment of the physician population. The administrative law judge's conclusion that a "respectable minority" of physicians is all that is necessary to establish accepted medical use in treatment in the United States is preposterous. By placing a substance in Schedule II, the Administrator, and through him, the Federal Government, establishes a national standard for drug use. Using the same criteria as medical malpractice cases to determine a national standard of medical acceptance is untenable. It must be recognized that in every profession, including the medical and scientific community, there are those that deviate from the accepted practices of the profession. These deviations may be the beginning of new revolutionary treatments or they may be rejected as quackery. The opinions of those few physicians and scientists are not sufficient to create a finding of national acceptance. The Administrator feels that, in light of the potential risks of declaring a drug has an accepted medical use in treatment in the United States, he must adhere to the strict standard that was established in the MDMA proceeding. It is clear that the evidence conclusively demonstrates that marijuana does not have an accepted medical use in treatment in the United States or an accepted medical use with severe restrictions.

The Administrator's standard for "accepted safety for use * * * under medical supervision" was also stated in the second MDMA final rule published on February 22, 1988. 53 FR 5156. The tests for determining accepted safety of a drug were stated as follows:

> The first requirement in determining safety of a substance is that the chemistry of the substance must be known and reproducible. The next step is to conduct animal toxicity studies to show that the substance will not produce irreversible harm to organs at proposed human doses. Limited clinical trials may then be initiated, but they must be carefully controlled so that adverse effects can be monitored and studies terminated if necessary * * * safety in humans is evaluated as a risk/benefit ratio for a specific use. 53 FR 5158.

It is clear that marijuana cannot meet the criteria set forth above for safety under medical supervision. The chemistry of marijuana is not known and reproducible. The record supports a finding that marijuana plant material is variable from plant to plant. The quantities of the active constituents, the cannabinoids, vary considerably. In addition, the actions and potential risks of several of the cannabinoids have not been studied. Animal toxicity studies with marijuana show several potential risks or hazards of marijuana use, especially when the marijuana is smoked. These hazards have not been evaluated against the benefit or effectiveness of the drug. This is due, in great part, to the fact that marijuana's effectiveness in treating specific medical conditions has not been established by reliable scientific studies. Since a proper risk/benefit ratio cannot be made, the safety of marijuana for medical use cannot be demonstrated. Such lack of information is the basis for the majority of the medical and scientific community, and the Food and Drug Administration, concluding that marijuana does not have "accepted safety for use * * * under medical supervision." The Administrator, therefore, concludes that marijuana lacks "accepted safety for use * * * under medical supervision."

As a final note, the Administrator expresses his displeasure at the misleading accusations and conclusions leveled at the Government and communicated to the public by the pro-marijuana parties, specifically NORML and ACT. These two organizations have falsely raised the expectations of many seriously ill persons by claiming that marijuana has medical usefulness in treating emesis, glaucoma, spasticity and other illnesses. These statements have probably caused many people with serious diseases to experiment with marijuana to the detriment of their own health, without proper medical supervision, and without knowing about the serious side effects which smoking or ingesting marijuana may cause. These are not the Dark Ages. The Congress, as well as the medical community, has accepted that drugs should not be available to the public unless they are found by scientific studies to be effective and safe. To do otherwise is to jeopardize the American public, and take advantage of desperately ill people who will try anything to alleviate their suffering. The Administrator strongly urges the American public not to experiment with a potentially dangerous, mind-altering drug such as marijuana in an attempt to treat a serious illness or condition. Scientific and medical researchers are working tirelessly to develop treatments and drugs to treat these diseases and conditions. As expressed in the record, treatments for emesis (nausea and vomiting) associated with cancer chemotherapy have advanced significantly in the last ten years. Recent studies have shown an over 90 percent rate of effectiveness for the new antiemetic drugs and therapies. NORML and ACT have attempted to perpetrate a dangerous and cruel hoax on the American public by claiming marijuana has currently accepted medical uses. The Administrator again emphasizes that there is insufficient medical and scientific evidence to support a conclusion that marijuana has an accepted medical use for treatment of any condition, or that it is safe for use, even under medical supervision.

Based upon the evidence in the record and the conclusions discussed previously, the Administrator, under the authority vested in the Attorney General by section 201(a) of the Controlled Substances Act (21 U.S.C. 811(a)) and delegated to the Administrator of the Drug Enforcement Administration by regulations of the Department of Justice, 28 CFR 0.100(b), hereby orders that marijuana remain a Schedule I controlled substance as listed in 21 CFR 1308.11(d)(14).

This order is effective December 29, 1989.

Dated: December 21, 1989.
John C. Lawn,
Administrator.
[FR Doc. 89-30126 Filed 12-28-89; 8:45 am]
BILLING CODE 4410-09-M

DEPARTMENT OF LABOR

Employment Standards Administration, Wage and Hour Division

Minimum Wages for Federal and Federally Assisted Construction; General Wage Determination Decisions

General wage determinations decisions of the Secretary of Labor are issued in accordance with applicable law and are based on the information obtained by the Department of Labor from its study of local wage conditions and data made available from other sources. They specify the basic hourly wage rates and fringe benefits which are determined to be prevailing for the described classes of laborers and mechanics employed on construction projects of a similar character and in the localities specified therein.

The determinations in these decisions of prevailing rates and fringe benefits have been made in accordance with 29 CFR Part 1, by authority of the Secretary of Labor pursuant to the provisions of the Davis-Bacon Act of March 3, 1931, as amended (46 Stat. 1494, as amended, 40 U.S.C. 276a) and of other Federal statutes referred to in 29 CFR Part 1, Appendix, as well as such additional statutes as may from time to time be enacted containing provisions for the payment of wages determined to be prevailing by the Secretary of Labor in accordance with the Davis-Bacon Act. The prevailing rates and fringe benefits determined in these decisions shall, in accordance with the provisions of the foregoing statutes, constitute the minimum wages payable on Federal and federally assisted construction projects to laborers and mechanics of the specified classes engaged on contract work of the character and in the localities described therein.

Good cause is hereby found for not utilizing notice and public comment procedure thereon prior to the issuance of these determinations as prescribed in 5 U.S.C. 553 and not providing for delay in the effective date as prescribed in that section, because the necessity to issue current construction industry wage determinations frequently and in large volume causes procedures to be impractical and contrary to the public interest.

General wage determination decisions, and modifications and supersedes decisions thereto, contain no expiration dates and are effective from their date of notice in the **Federal Register**, or on the date written notice is received by the agency, whichever is earlier. These decisions are to be used in accordance with the provisions of 29 CFR Parts 1 and 5. Accordingly, the applicable decision, together with any modifications issued, must be made a part of every contract for performance of the described work within the geographic area indicated as required by an applicable Federal prevailing wage law and 29 CFR Part 5. The wage rates and fringe benefits, notice of which is published herein, and which are contained in the Government Printing Office (GPO) document entitled "General Wage Determinations Issued Under The Davis-Bacon And Related Acts," shall be the minimum paid by contractors and subcontractors to laborers and mechanics.

Any person, organization, or governmental agency having an interest in the rates determined as prevailing is encouraged to submit wage rate and fringe benefit information for consideration by the Department. Further information and self-explanatory forms for the purpose of submitting this data may be obtained by writing to the U.S. Department of Labor, Employment Standards Administration, Wage and Hour Division, Division of Wage Determinations, 200 Constitution Avenue, NW., Room S-3504, Washington, DC 20210.

Modifications to General Wage Determination Decisions

The numbers of the decisions listed in the Government Printing Office document entitled "General Wage Determinations Issued Under the Davis-Bacon and Related Acts" being modified are listed by Volume, State, and page number(s). Dates of publication in the **Federal Register** are in parentheses following the decisions being modified.

VOLUME I

FLORIDA, FL89-45 (January 6, 1989).	p. 206a p. 206c
NEW YORK:	
NY89-2 (January 6, 1989).....	p. 683 pp. 688, 692 p. 693
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NY89-10 (January 6, 1989).....	p. 769 pp. 770

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OREGON, OR89-1 (January 6, 1989).	p. 307 pp. 308-310, p. 316, pp. 323-324
WASHINGTON, WA89-8 (January 6, 1989).	p. 423 pp. 424-425 p. 426a pp. 46-64f

General Wage Determination Publication

General Wage determinations issued under the Davis-Bacon and related Acts, including those noted above, may be found in the Government Printing Office (GPO) document entitled "General Wage Determinations Issued Under The Davis-Bacon And Related Acts". This publication is available at each of the 50 Regional Government Depository Libraries and many of the 1,400 Government Depository Libraries across the country. Subscriptions may be purchased from: Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402, (202) 783-3238

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Federal Register

Wednesday,
April 18, 2001

Part II

Department of Justice

Drug Enforcement Agency

Denial of Petition; Notice

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

Notice of Denial of Petition

By letter dated March 20, 2001, the Drug Enforcement Administration (DEA) denied a petition to initiate rulemaking proceedings to reschedule marijuana. Because DEA believes that this matter is of particular interest to members of the public, the agency is publishing below the letter sent to the petitioner (denying the petition), along with the supporting documentation that was attached to the letter.

Dated: March 28, 2001.

Donnie R. Marshall,

Administrator.

U.S. Department of Justice,

Drug Enforcement Administration,
Washington, D.C. 20537

March 20, 2001.

Jon Gettman:

Dear Mr. Gettman: On July 10, 1995, you petitioned the Drug Enforcement Administration (DEA) to initiate rulemaking proceedings under the rescheduling provisions of the Controlled Substances Act (CSA). Specifically, you petitioned DEA to propose rules, pursuant to 21 U.S.C. 811(a), that would amend the schedules of controlled substances with respect to the following controlled substances: marijuana; tetrahydrocannabinols; dronabinol; and nabilone. Although you grouped these substances together in your petition, the scheduling analysis differs for each. To avoid confusion, DEA is providing you with a separate response for each of the controlled substances that you proposed be rescheduled. This letter responds to your petition to reschedule marijuana.

Summary

You requested that DEA remove marijuana from schedule I based on your assertion that ''there is no scientific evidence that [it has] sufficient abuse potential to warrant schedule I or II status under the [CSA].'' In accordance with the CSA rescheduling provisions, DEA gathered the necessary data and forwarded that information and your petition to the Department of Health and Human Services (HHS) for a scientific and medical evaluation and scheduling recommendation. HHS concluded that marijuana does have a high potential for abuse and therefore recommended that marijuana remain in schedule I. Based on the HHS evaluation and all other relevant data, DEA has concluded that there is no substantial evidence that marijuana should be removed from schedule I. Accordingly, your petition to initiate rulemaking proceedings to reschedule marijuana is hereby denied.

Detailed Explanation

A. Statutory Requirements and Procedural History

The CSA provides that the schedules of controlled substances established by Congress may be amended by the Attorney General in rulemaking proceedings prescribed by the Administrative Procedure Act. 21 U.S.C. 811(a). The Attorney General has delegated this authority to the Administrator of DEA. 28 CFR 0.100.

As you have done, any interested party may petition the Administrator to initiate rulemaking proceedings to reschedule a controlled substance. 21 U.S.C. 811(a); 21 CFR 1308.43(a). Before initiating such proceedings, the Administrator must gather the necessary data and request from the Secretary of HHS a scientific and medical evaluation and recommendation as to whether the controlled substance should be rescheduled as the petitioner proposes. 21 U.S.C. 811(b); 21 CFR 1308.43(d). The Secretary has delegated this function to the Assistant Secretary for Health.[1]

The recommendations of the Assistant Secretary are binding on the Administrator with respect to scientific and medical matters. Id. If the Administrator determines that the evaluations and recommendations of the Assistant Secretary and ''all other relevant data'' constitute substantial evidence that the drug that is the subject of the petition should be subject to lesser control or removed entirely from the schedules, he shall initiate rulemaking proceedings to reschedule the drug or remove it from the schedules as the evidence dictates. 21 U.S.C. 811(b); 21 CFR 1308.43(e). In making such a determination, the Administrator must consider eight factors:

(1) The drug's actual or relative potential for abuse;

(2) Scientific evidence of its pharmacological effect, if known;

(3) The state of current scientific knowledge regarding the drug;

(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) The drug's psychic or physiological dependence liability; and

(8) Whether the drug is an immediate precursor of a substance already controlled under the CSA.

21 USC 811(c).

In this case, you submitted your petition by letter dated March 10, 1995. After gathering the necessary data, DEA referred the petition to HHS on December 17, 1997, and requested from HHS a scientific and medical evaluation and scheduling recommendation. HHS forwarded its scientific and medical evaluation and scheduling recommendation to DEA on January 17, 2001.

B. HHS Scientific and Medical Evaluation and Other Relevant Data Considered by DEA

Attached to this letter is the scientific and medical evaluation and scheduling recommendation that HHS submitted to DEA.[2] Also attached is a document prepared by DEA that specifies other data relevant to your petition that DEA considered.

C. Basis for Denial of Your Petition: The Evidence Demonstrates That Marijuana Does Have A High Potential For Abuse

Your petition rests on your contention that marijuana does not have a ''high potential for abuse'' commensurate with schedule I or II of the CSA. The Assistant Secretary has concluded, based on current scientific and medical evidence, that marijuana does have a high potential for abuse commensurate with schedule I. The additional data gathered by DEA likewise reveals that marijuana has a high potential for abuse. Indeed, when the HHS evaluation is viewed in combination with the additional data gathered by DEA, the evidence overwhelmingly leads to the conclusion that marijuana has a high potential for abuse.

Accordingly, there is no statutory basis for DEA to grant your petition to initiate rulemaking proceedings to reschedule marijuana. For this reason alone, your petition must be denied.

D. A Schedule I Drug With a High Potential For Abuse and No Currently Accepted Medical Use or Safety for Use Must Remain Classified In Schedule I

DEA's denial of your petition is based exclusively on the scientific and medical findings of HHS, with which DEA concurs, that lead to the conclusion that marijuana has a high potential for abuse. Nonetheless, independent of this scientific and medical basis for denying your petition, there is a logical flaw in your proposal that should be noted.

You do not assert in your petition that marijuana has a currently accepted medical use in treatment in the United States or that marijuana has an accepted safety for use under medical supervision. Indeed, the HHS scientific and medical evaluation reaffirms expressly that marijuana has no currently accepted medical use in treatment in the United States and a lack of accepted safety for use under medical supervision.

Nor do you dispute that marijuana is a drug of abuse. That is, you do not contend that marijuana has no potential for abuse such that it should be removed entirely from the CSA schedules. Rather, your contention is that marijuana has less than a ''high potential for abuse'' commensurate with schedules I and II and, therefore, it cannot be classified in either of these two schedules.

Congress established only one schedule—schedule I—for drugs of abuse with ''no currently accepted medical use in treatment in the United States'' and ''lack of accepted safety for use * * * under medical supervision.'' 21 USC 812(b). To be classified in schedules II through V, a drug of abuse

[1] As set for in a memorandum of understanding entered in to by HHS, the Food and Drug Administration (FDA), and the National Institute on Drug Abuse (NIDA), FDA acts as the lead agency within HHS in carrying out the Secretary's scheduling responsibilities under the CAS, with the concurrence of NIDA. 50 FR 9518 (1985).

[2] To avoid confusion, those parts of the HHS document that are not relevant to your petition with respect to marijuana (*i.e.,* those parts that are relevant only to the scheduling of tetrahydrocannabinols, dronabinol, or nabilone) have been redacted from the attachment. The HHS evaluation of these other substances will be addressed when DEA responds (in separate letters) to your petitions with respect to these other substances.

must have a ''currently accepted medical use in treatment in the United States.'' [3] *Id.* This is why the CSA allows practitioners to prescribe only those controlled substances that are listed in schedules II through V. 21 USC 829. Drugs listed in schedule I, by contrast, may not be prescribed for patient use; they may only be dispensed by practitioners who are conducting FDA-approved research and have obtained a schedule I research registration from DEA. 21 USC 823(f); 21 CFR 5.10(a)(9), 1301.18, 1301.32.

That schedule I controlled substances are characterized by a lack of accepted medical use was recently reiterated by Congress, when it declared, in a provision entitled, ''NOT LEGALIZING MARIJUANA FOR MEDICINAL USE'':

It is the sense of the Congress that—

(1) certain drugs are listed on Schedule I of the Controlled Substances Act if they have a high potential for abuse, lack any currently accepted medical use in treatment, and are unsafe, even under medical supervision;

(2) the consequences of illegal use of Schedule I drugs are well documented, particularly with regard to physical health, highway safety, and criminal activity;

(3) pursuant to section 401 of the Controlled Substances Act, it is illegal to manufacture, distribute, or dispense marijuana, heroin, LSD, and more than 100 other Schedule I drugs;

(4) pursuant to section 505 of the Federal Food, Drug and Cosmetic Act, before any drug can be approved as a medication in the United States, it must meet extensive scientific and medical standards established by the Food and Drug Administration to ensure it is safe and effective;

(5) *marijuana and other Schedule I drugs have not been approved by the Food and Drug Administration to treat any disease or condition.*

* * * * *

Pub. L. No. 105–277, Div. F., 112 Stat. 2681–760 to 2681–761 (1998) (emphasis added).

Thus, when it comes to a drug that is currently listed in schedule I, if it is undisputed that such drug has no currently accepted medical use in treatment in the United States and a lack of accepted safety for use under medical supervision, and it is further undisputed that the drug has at least some potential for abuse sufficient to warrant control under the CSA, the drug must remain in schedule I. In such circumstances, placement of the drug in schedules II through V would conflict with the CSA since such drug would not meet the criterion of ''a currently accepted medical use in treatment in the United States.'' 21 USC 812(b).

Therefore, even if one were to assume, theoretically, that your assertions about marijuana's potential for abuse were correct (*i.e.,* that marijuana had some potential for abuse but less than the ''high potential for abuse'' commensurate with schedules I and II), marijuana would not meet the criteria for placement in schedules III through V since it has no currently accepted medical use in treatment in the United States—a determination that is reaffirmed by HHS in the attached medical and scientific evaluation.

For the foregoing reasons, your petition to reschedule marijuana cannot be granted under the CSA and is, therefore, denied.

Sincerely,

Donnie R. Marshall,
Administrator.
Attachments.

Department of Health and Human Services,

Office of the Secretary, Office of the Public Health and Science, Assistant Secretary for Health, Surgeon General, Washington, D.C. 20201.

January 17, 2001.

Mr. Donnie R. Marshall,
Deputy Administrator, Drug Enforcement Administration, Washington, D.C. 20537.

Dear Mr. Marshall: In response to your request dated December 17, 1997, and pursuant to the Controlled Substances Act (CSA), 21 U.S.C. § 811 (b), (c), and (f), the Department of Health and Human Services (DHHS) recommends that marijuana * * * continue to be subject to control under Schedule I. * * * Marijuana and the tetrahydrocannabinols are currently controlled under Schedule I of the CSA. Marijuana continues to meet the three criteria for placing a substance in Schedule I of the CSA under 21 U.S.C. 812(b)(1). As discussed in the attached analysis, marijuana has a high potential for abuse, has no currently accepted medical use in treatment in the United States, and has a lack of accepted safety for use under medical supervision. Accordingly, HHS recommends that marijuana * * * continue to be subject to control under Schedule I of the CSA.

You will find enclosed two documents prepared by FDA's Controlled Substance Staff that are the bases for the recommendations.

Sincerely yours,

David Satcher,
Assistant Secretary for Health and Surgeon General.
Enclosure.

Basis for the Recommendation for Maintaining Marijuana in Schedule I of the Controlled Substances Act

A. Background

On July 10, 1995, Mr. Jon Gettman submitted a petition to the Drug Enforcement Administration (DEA) requesting that proceedings be initiated to repeal the rules and regulations that place marijuana and the tetrahydrocannabinols in Schedule I of the Controlled Substances Act (CSA) and dronabinol and nabilone in Schedule II of the CSA. The petition contends that evidence of abuse potential is insufficient for each substance or class of substances to be controlled in Schedule I or II of the CSA. In December 1997, the DEA Administrator requested that the Department of Health and Human Services (DHHS) develop scientific and medical evaluations and recommendations as to the proper scheduling of the substances at issue, pursuant to 21 U.S.C. 811(b).

This document responds to the portion of the petition that concerns marijuana * * *.

In accordance with 21 U.S.C. 811(b), the DEA has gathered information, and the Secretary of DHHS has considered eight factors in a scientific and medical evaluation, to determine how to schedule and control marijuana (Cannabis sativa) under the CSA. The eight factors are: actual or relative potential for abuse, scientific evidence of pharmacological effects, scientific knowledge about the drug or substance in general, history and current patterns of abuse, the scope and duration and significance of abuse, the risk (if any) to public health, psychic or physiologic dependence liability, and whether the substance is an immediate precursor of a substance that is already controlled. If appropriate, the Secretary must also make three findings—related to a substance's abuse potential, legitimate medical use, and safety or dependence liability—and then a recommendation. This evaluation presents scientific and medical knowledge under the eight factors, findings in the three required areas, and a recommendation.

Administrative responsibilities for evaluating a substance for control under the CSA are performed by the Food and Drug Administration (FDA), with the concurrence of the National Institute on Drug Abuse (NIDA), as described in the Memorandum of Understanding (MOU) of March 8, 1985 (50 FR 9518–20).

Pursuant to 21 U.S.C. 811(c), the eight factors pertaining to the scheduling of marijuana are considered below. The weight of the scientific and medical evidence considered under these factors supports the three findings that: (1) Marijuana has a high potential for abuse, (2) marijuana has no currently accepted medical use in treatment in the United States, and (3) there is a lack of accepted evidence about the safety of using marijuana under medical supervision.

B. Evaluating Marijuana Under the Eight Factors

This section presents scientific and medical knowledge about marijuana under the eight required factors.

[3] A controlled substance in schedule II must have either ''a currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions.'' 21 USC 812(b)(2)(B).

1. Its Actual or Relative Potential for Abuse

The CSA defines marijuana as the following:

> All parts of the plant Cannabis Sativa L., whether growing or not; the seeds thereof; the resin extracted from any part of such plant; and every compound, manufacture, salt, derivative, mixture, or preparation of such plant, its seeds or resin. Such term does not include the mature stalks of such plant, fiber produced from such stalks, oil or cake made from the seeds of such plant, any other compound, manufacture, salt, derivative, mixture, or preparation of such mature stalks (except the resin extracted therefrom), fiber, oil, or cake, or the sterilized seed of such plant which is incapable of germination. 21 U.S.C. 802(16).

The term ''abuse'' is not defined in the CSA. However, the legislative history of the CSA suggests the following in determining whether a particular drug or substance has a potential for abuse:

a. Individuals are taking the substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community.

b. There is a significant diversion of the drug or substance from legitimate drug channels.

c. Individuals are taking the substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such substances.

d. The substance is so related in its action to a substance already listed as having a potential for abuse to make it likely that it will have the same potential for abuse as such substance, 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. Comprehensive Drug Abuse Prevention and Control Act of 1970, H.R. Rep. No. 91–1444, 91st Cong., Sess. 1 (1970) reprinted in U.S.C.C.A.N. 4566, 4603.

In considering these concepts in a variety of scheduling analyses over the last three decades, the Secretary has analyzed a range of factors when assessing the abuse liability of a substance. These factors have included the prevalence and frequency of use in the general public and in specific sub-populations, the amount of the material that is available for illicit use, the ease with which the substance may be obtained or manufactured, the reputation or status of the substance ''on the street'', as well as evidence relevant to population groups that may be at particular risk.

Abuse liability is a complex determination with many dimensions. There is no single test or assessment procedure that, by itself, provides a full and complete characterization. Thus, no single measure of abuse liability is ideal. Scientifically, a comprehensive evaluation of the relative abuse potential of a drug substance can include consideration of the drug's receptor binding affinity, preclinical pharmacology, reinforcing effects, discriminative stimulus effects, dependence producing potential, pharmacokinetics and route of administration, toxicity, assessment of the clinical efficacy-safety database relative to actual abuse, clinical abuse liability studies and the public health risks following introduction of the substance to the general population. It is important to note that abuse may exist independent of a state of physical dependence, because drugs may be abused in doses or in patterns that do not induce physical dependence.

Animal data and epidemiological data are both used in determining a substance's abuse liability. While animal data may help the Secretary draw conclusions on the abuse liability of a substance, data regarding human abuse, if available, is given greater weight. For example, even if a compound fails to display abuse liability in animal laboratory testing, positive evidence of abuse liability in humans is given greater weight. Epidemiological data can also be an important indicator of actual abuse and may, in some circumstances, be given greater weight than laboratory data. Thus, in situations where the epidemiological data indicates that a substance is abused, despite the lack of positive abuse liability indications in animal or human laboratory testing, the abuse liability determination may rest more heavily on the epidemiological data. Finally, evidence of clandestine production and illicit trafficking of a substance are also important factors to consider as this evidence sheds light on both the demand for a substance as well as the ease with which it can be obtained.

The Secretary disagrees with Mr. Gettman's assertion that ''[t]he accepted contemporary legal convention for evaluating the abuse potential of a drug or substance is the relative degree of self-administration the drug induces in animal subjects.'' As discussed above, self-administration tests that identify whether a substance is reinforcing in animals are but one component of the scientific assessment of the abuse potential of a substance. Positive indicators of human abuse liability for a particular substance, whether from laboratory studies or epidemiological data, are given greater weight than animal studies suggesting the same compound has no abuse potential.

Throughout his petition, Mr. Gettman argues that while many people ''use'' marijuana, few ''abuse'' it. He appears to equate abuse with the level of physical dependence and toxicity resulting from marijuana use. Thus, he appears to be arguing that a substance that causes only low levels of physical dependence and toxicity must be considered to have a low potential for abuse. The Secretary does not agree with this argument. Physical dependence and toxicity are not the only factors that are considered in determining a substance's abuse potential. The actual use and frequency of use of a substance, especially when that use may result in harmful consequences such as failure to fulfill major obligations at work or school, physical risk-taking, or even substance-related legal problems, are indicative of a substance's abuse potential.

a. *There is evidence that individuals are taking the substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community.*

Marijuana is a widely used substance. The pharmacology of the psychoactive constituents of marijuana (including delta^{9}-THC, the primary psychoactive ingredient in marijuana) has been studied extensively in animals and humans and is discussed in more detail below in Section 2, ''Scientific Evidence of its Pharmacological Effects, if Known.'' Although it is difficult to determine the full extent of marijuana abuse, extensive data from the National Institute on Drug Abuse (NIDA) and from the Substance Abuse Mental Health Services Administration (SAMHSA) are available. These data are discussed in detail in Section 4 ''Its History and Current Pattern of Abuse;'' Section 5, ''The Scope, Duration, and Significance of Abuse;'' and Section 6, ''What, if any Risk There is to the Public Health.''

According to the National Household Survey on Drug Abuse (NHSDA), of the 14.8 million Americans who used illicit drugs on a monthly basis in 1999, 11.2 million used marijuana. In 1998, 1.6 million children between the ages of 12 and 17 used marijuana for the first time. (See the discussion of the 1999 NHSDA in Section 4). A 1999 survey of 8th, 10th, and 12th grade students indicates that marijuana is the most widely used illicit drug in this age group. By 12th grade, 37.8% of students report having used marijuana in the past year, and 23.1% report using it monthly. (See the

discussion of the Monitoring the Future Study in Section 4). Primary marijuana abuse accounts for 13% of the admissions to treatment facilities for substance abuse, with 92% of those admitted having used marijuana for the first time by age 18. (See discussion of the Treatment Episode Data Set in Section 4).

The Drug Abuse Warning Network (DAWN) is a national probability survey of hospitals with emergency departments (EDs). DAWN is designed to obtain information on ED episodes that are induced by or related to the use of an illegal drug or the non-medical use of a legal drug. DAWN recently reported 87,150 ED drug mentions for marijuana/hashish in 1999, representing 16 % of all drug-related episodes in 1999. (See discussion of DAWN in Section 4). In 1999, DAWN data show that out of 664 medical examiner marijuana-related episodes, there were 187 deaths in persons who had used marijuana alone. While marijuana has a low level of toxicity when compared to other drugs of abuse, there are a number of risks resulting from both acute and chronic use of marijuana. These risks are discussed in full in sections 2 and 6 below.

b. *There is significant diversion of the substance from legitimate drug channels.*

Because cannabis is currently available through legitimate channels for research purposes only, there is limited legitimate use of this substance and thus limited potential for diversion. The lack of significant diversion of investigational supplies may also result from the ready availability of cannabis of equal or greater potency through illicit channels.

The magnitude of the demand for marijuana is, however, evidenced by the Drug Enforcement Administration (DEA) / Office of National Drug Control Policy (ONDCP) statistics. Data on marijuana seizures can often highlight trends in the overall trafficking patterns. The DEA's Federal-Wide Drug Seizure System (FDSS) provides information on total federal drug seizures. FDSS reports total federal seizures of 699 metric tons of marijuana in fiscal year 1997, 825 metric tons in fiscal year 1998 and 1,175 metric tons in fiscal year 1999 (ONDCP, 2000).

c. *Individuals are taking the substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such substances.*

The 1998 NHSDA suggests that 6.8 million individuals use marijuana on a weekly basis (SAMHSA, 1998), confirming that marijuana has reinforcing properties for many individuals. The FDA has not approved a new drug application for marijuana, although research under several INDs is currently active. Based on the large number of individuals who use marijuana, it can be concluded that the majority of individuals using cannabis do so on their own initiative, not on the basis of medical advice from a practitioner licensed to administer the drug in the course of professional practice.

d. *The substance is so related in its action to a substance already listed as having a potential for abuse to make it likely that it will have the same potential for abuse as such substance, 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.*

Two drug products that contain cannabinoid compounds that are structurally related to the active components in marijuana are already regulated under the CSA. These are Marinol (dronabinol, delta^9-THC), which is a Schedule III drug, and nabilone, which is a Schedule II drug. All other cannabinoid compounds that are structurally related to the active components in marijuana are listed as Schedule I drugs under the CSA. Cannabinoid compounds constitute a distinct pharmacological class that is unrelated to other drugs currently listed in the CSA. The primary psychoactive compound in botanical marijuana is delta^9-tetrahydrocannabinol (delta^9-THC). Other cannabinoids also present in the marijuana plant likely contribute to the psychoactive effects. Individuals administer the constituents of marijuana by burning the material and inhaling (smoking) many of its combustible and vaporized products. The route of administration of a drug is one component of its abuse potential. Most psychoactive drugs exert their maximum subjective effects when blood levels of the drug are rapidly increased. Inhalation of drugs permits a rapid delivery and distribution of the drug to the brain. The intense psychoactive drug effect, which can be rapidly achieved by smoking, is often called a ''rush'' and generally is considered to be the effect desired by the abuser. This effect explains why marijuana abusers prefer the inhalation, intravenous or intranasal routes rather than oral routes of administration. Such is also the case with cocaine, opium, heroin, phencyclidine, and methamphetamine (Wesson & Washburn, 1990).

2. Scientific Evidence of Its Pharmacological Effects, If Known

We concur with the petitioner that there is abundant scientific data available on the neurochemistry, toxicology, and pharmacology of marijuana. This section includes a scientific evaluation of marijuana's neurochemistry and pharmacology, central nervous system effects including human and animal behavior, pharmacodynamics of central nervous system effects, cognitive effects, cardiovascular and autonomic effects, endocrine system effects and immunological system effects. The overview presented below relies upon the most current research literature on cannabinoids.

Neurochemistry and Pharmacology of Marijuana

To date, a total of 483 natural constituents have been identified in marijuana of which approximately 66 belong to the general group known as cannabinoids (Ross and ElSohly, 1995). The cannabinoids appear to be unique to marijuana, and most of those occurring naturally have already been identified. Within the cannabinoids, delta^9-tetrahydrocannabinol (delta^9-THC) is considered the major psychoactive constituent of marijuana. Since the elucidation of the structure and discovery of the function of delta^9-THC, in 1964 by Gaoni and Mechoulam, cannabis and cannabinoid research has flourished. Substantial discoveries on the pharmacology, biochemistry and behavioral mechanisms of action of the cannabinoids have been accomplished, and laid the scientific foundations for a better understanding of the effects of marijuana.

There is conclusive evidence of the existence of at least two cannabinoid receptors, CB_1 and CB_2, and it is now known that some of the pharmacological effects of cannabinoids are mediated through activation of these receptors. The cannabinoid receptors belong to the G-protein-coupled receptors family and present a typical seven transmembrane-spanning domain structure. Many G-protein coupled receptors are linked to adenylate cyclase, and stimulation of these receptors might result, either in inhibition or activation of adenylate cyclase, depending on the receptor system. Cannabinoid receptors are linked to an inhibitory G protein (Gi), meaning that when activated, inhibition of the activity of adenylate cyclase occurs, thus preventing the conversion of ATP to the second messenger cyclic AMP (cAMP). Examples of inhibitory-coupled receptors include opioid,

muscarinic," $_2$-adrenoreceptors, dopamine (D_2) and serotonin (5-HT_1) among others. The pharmacological relevance of the adenylate cyclase inhibition has been difficult to determine (Adams and Martin, 1996).

Advances in molecular biology allowed the cloning of a cannabinoid receptor (Matsuda *et al.,* 1990), first from rat brain origin followed by the cloning of the human receptor (Gerard *et al.,* 1991) therefore offering definitive evidence for a specific cannabinoid receptor. Autoradiographic studies have provided information on the distribution of cannabinoid receptors. CB_1 receptors are present in the brain and spinal cord and in certain peripheral tissues. The distribution pattern of these receptors within the central nervous system is heterogeneous. It is believed that the localization of these receptors in various regions of the brain, such as basal ganglia, cerebellum, hippocampus and cerebral cortex, may explain cannabinoid interference with movement coordination and effects on memory and cognition. Concentration of CB_1 receptors is considerably lower in peripheral tissues than in the central nervous system (Henkerham *et al.,* 1990 and 1992). CB_2 receptors have been detected only outside the central nervous system. Their occurrence has been shown to be primarily in immune tissues such as leukocytes, spleen and tonsils and it is believed that the CB_2-type receptor is responsible for mediating the immunological effects of cannabinoids (Galiegui *et al.,* 1995).

Recently it has been shown that CB_1 but not CB_2 receptors inhibit N- and Q type calcium channels and activate inwardly rectifying potassium channels. Inhibition of the N-type calcium channels decreases neurotransmitter release from several tissues and this may the mechanism by which cannabinoids inhibit acetylcholine, noradrenaline and glutamate release from specific areas of the brain. These effects might represent a potential cellular mechanism underlying the antinociceptive and psychoactive effects of cannabinoids (Ameri, 1999).

Several synthetic cannabinoid agonists have been synthesized and characterized and selective antagonists for both receptors have been identified. In 1994, SR–141716A, the first selective antagonist with CB_1 selectivity was identified, and more recently the selective CB_2 receptor antagonist, SR-144528, was described (Rinaldi-Carmona *et al.,* 1994 and 1998). In general, antagonists have proven to be invaluable tools in pharmacology. They allow the identification of key physiological functions by the receptors, through the blockade of their responses.

Delta^9-THC displays similar affinity for CB_1 and CB_2 receptors but behaves as a weak agonist for CB_2 receptors as judged by inhibition of adenylate cyclase. The identification of synthetic cannabinoid ligands deprived of the typical THC-like psychoactive properties, that selectively bind to CB_2 receptors, supports the idea that the psychotropic effects of cannabinoids are mediated through the activation of CB_1-receptors (Hanus *et al.,* 1999). Furthermore, cannabinoid agonists such as delta^9-THC and the synthetic ones, WIN–55,212–2 and CP–55,940, produce hypothermia, analgesia, hypoactivity and cataplexy. These effects are reversed by the selective CB_1 antagonist, SR–141716A, providing good evidence for the involvement of a CB_1 receptor mediated mechanism.

In addition, the discovery of the endogenous cannabinoid receptor agonists, anandamide and arachidonyl glycine (2–AG) confirmed the belief of a central cannabinoid neuromodulatory system. Indeed, cannabinoid and their endogenous ligands are present in central as well as peripheral tissues. Mechanisms for the synthesis and metabolism of anandamide have been described. The physiological roles of endogenous cannabinoids are not yet fully characterized, although it has been the target of large research efforts (Martin *et al.,* 1999).

In conclusion, progress in cannabinoid pharmacology, including the characterization of the cannabinoid receptors, isolation of endogenous cannabinoid ligands, synthesis of agonists and antagonists with diverse degree of affinity and selectivity for cannabinoid receptors, have provided the foundation for the elucidation of the specific effects mediated by cannabinoids and their roles in psychomotor disorders, memory, cognitive functions, analgesia, antiemesis, intraocular and systemic blood pressure modulation, broncodilation, and inflammation.

The reinforcing properties of a number of commonly abused drugs such as amphetamine, cocaine, alcohol, morphine and nicotine, have been explained by the effects of these drugs in the activation of dopaminergic pathways in certain areas of the brain and in particular the mesolimbic dopaminergic system (Koob, 1992). It has been demonstrated that delta^9-THC increases dopamine activity in reward relevant circuits in the brain (French, 1997; Gessa, *et al.* 1998), but the mechanism of these effects and the relevance of these findings in the context of the abuse potential of marijuana is still unknown.

Central Nervous System Effects

Human Behavioral Effects

As with other psychoactive drugs, the response that an individual has to marijuana is dependent on the set (psychological and emotional orientation) and setting (circumstances) under which the individual takes the drug. Thus, if an individual uses marijuana while in a happy state of mind among good friends, the responses are likely to be interpreted as more positive than if that individual uses the drug during a crisis while alone.

The mental and behavioral effects of marijuana can vary widely among individuals, but common responses, described by Wills (1998) and others (Adams and Martin 1996; Hollister 1986a, 1988a; Institute of Medicine 1982) are listed below:

(1) Dizziness, nausea, tachycardia, facial flushing, dry mouth and tremor can occur initially

(2) Merriment, happiness and even exhilaration at high doses

(3) Disinhibition, relaxation, increased sociability, and talkativeness

(4) Enhanced sensory perception, giving rise to increased appreciation of music, art and touch

(5) Heightened imagination leading to a subjective sense of increased creativity

(6) Time distortions

(7) Illusions, delusions and hallucinations are rare except at high doses

(8) Impaired judgement, reduced co-ordination and ataxia, which can impede driving ability or lead to an increase in risk-taking behavior

(9) Emotional lability, incongruity of affect, dysphoria, disorganized thinking, inability to converse logically, agitation, paranoia, confusion, restlessness, anxiety, drowsiness and panic attacks may occur, especially in inexperienced users or in those who have taken a large dose

(10) Increased appetite and short-term memory impairment are common

Humans demonstrate a preference for higher doses of marijuana (1.95% delta^9-THC) over lower doses (0.63% delta^9-THC) (Chaitand Burke, 1994), similar to the dose preference exhibited for many other drugs of abuse.

Animal Behavioral Effects

- Predictors of Reinforcing Effects (Self-Administration and Conditioned Place Preference)

One indicator of whether a drug will be reinforcing in humans is the self-administration test in animals. Self-

administration of marijuana, LSD, sigma receptor agonists, or cholinergic antagonists is difficult to demonstrate in animals. However, when it is known that humans voluntarily consume a particular drug for its pleasurable effects, the inability to establish self-administration with that drug in animals has no practical importance. This is because the animal test is only useful as a rough predictor of human behavioral response in the absence of naturalistic data. Thus, the petitioner is incorrect that the accepted legal convention for abuse potential is self-administration in animals and that because marijuana does not induce self-administration in animals, it has a lower abuse potential than drugs that easily induce self-administration in animals. Similarly, the petitioner is incorrect that the difficulty in inducing self-administration of marijuana in animals is due to a lack of effect on dopamine receptors. In fact, dopamine release can be stimulated indirectly by marijuana, following direct action of the drug on cannabinoid receptors. However, it is important to note that while self-administration in animals has been correlated with dopamine function, both pleasurable and painful stimuli can evoke dopaminergic responses. Dopamine functioning does not determine scheduling under the CSA.

Naïve animals will not typically self-administer cannabinoids when they must choose between saline and a cannabinoid. However, a recent report shows that when squirrel monkeys are first trained to self-administer intravenous cocaine, they will continue to bar-press at the same rate when THC is substituted for cocaine, at doses that are comparable to those used by humans who smoke marijuana (Tanda *et al.,* 2000). This effect was blocked by the cannabinoid receptor antagonist, SR 141716. These data demonstrate that under specific pretreatment conditions, an animal model of reinforcement by cannabinoids now exists for future investigations. Additionally, mice have been reported to self-administer WIN 55212, a CB_1 receptor agonist with a non-cannabinoid structure (Martellotta *et al.,* 1998). There may be a critical dose-dependent effect, though, since aversive effects, rather than reinforcing effects, have been described in rats with high doses of WIN 55212 (Chaperon *et al.,* 1998) as well as delta^9-THC (Sanudo-Pena *et al.,* 1997). The cannabinoid antagonist, SR 141716, counteracted these aversive effects.

The conditioned place preference (CPP) test also functions as a predictor of reinforcing effects. Animals show CPP to cannabinoids, but only at mid-dose levels. However, cannabinoid antagonists also induce CPP, suggesting that occupation of the cannabinoid receptor itself, may be responsible.

• Drug Discrimination Studies

Animals, including monkeys and rats (Gold *et al.,* 1992) as well as humans (Chait, 1988) can discriminate cannabinoids from other drugs or placebo. Discriminative stimulus effects of delta^9-THC are pharmacologically specific for marijuana-containing cannabinoids (Balster and Prescott, 1992, Barrett *et al.,* 1995, Browne and Weissman, 1981, Wiley *et al.,* 1993, Wiley *et al.,* 1995). Additionally, the major active metabolite of delta^9-THC, 11-OH-delta^9-THC, also generalized to the stimulus cue elicited by delta^9-THC (Browne and Weissman, 1981). Twenty-two other cannabinoids found in marijuana also fully substituted for delta^9-THC. The discriminative stimulus effects of the cannabinoid group appear to provide unique effects because stimulants, hallucinogens, opioids, benzodiazepines, barbiturates, NMDA antagonists and antipsychotics have not been shown to substitute for delta^9-THC.

Pharmacodynamics of CNS Effects

Psychoactive effects occur within seconds after smoking marijuana, while the onset of effects after oral administration is 30–60 min. After a single moderate smoked dose, most mental and behavioral effects are measurable for approximately 4 to 6 hours (Hollister 1986, 1988). Venous blood levels of delta^9-THC or other cannabinoids correlate poorly with intensity of effects and character of intoxication (Agurell *et al.* 1986; Barnett *et al.* 1985; Huestis *et al.* 1992a). There does not appear to be a ''hangover'' syndrome following acute administration of marijuana containing 2.1% delta^9-THC (Chait, 1985).

We agree with the petitioner that clinical studies do not demonstrate tolerance to the ''high'' from marijuana. This may be related to recent electrophysiological data showing that the ability of THC to increase neuronal firing in the ventral tegmental area (a region known to play a critical role in drug reinforcement and reward) is not reduced following chronic administration of the drug (Wu and French, 2000). On the other hand, tolerance can develop in humans to marijuana-induced cardiovascular and autonomic changes, decreased intraocular pressure, sleep and sleep EEG, mood and certain behavioral changes (Jones *et al.,* 1981).

Repeated use of many drugs leads to the normal physiological adaptations of tolerance and dependence and is not a phenomenon unique to drugs of abuse. Down-regulation of cannabinoid receptors has been suggested as the mechanism underlying tolerance to the effects of marijuana (Rodriguez de Fonseca *et al.,* 1994, Oviedo *et al.,* 1993). By pharmacological definition, tolerance does not indicate the physical dependence liability of a drug.

Physical dependence is a condition resulting from the repeated consumption of certain drugs. Discontinuation of the drug results in withdrawal signs and symptoms known as withdrawal or abstinence syndrome. It is believed that the withdrawal syndrome probably reflects a rebound of certain physiological effects that were altered by the repeated administration of the drug. These pharmacological events of physical dependence and withdrawal are not associated uniquely with drugs of abuse. Many medications such as antidepressants, beta-blockers and centrally acting antihypertensive drugs that are not associated with addiction can produce these effects after abrupt discontinuation.

Some authors describe a marijuana withdrawal syndrome consisting of restlessness, irritability, mild agitation, insomnia, sleep EEG disturbances, nausea and cramping that resolves in days (Haney *et al.,* 1999). This syndrome is mild compared to classical alcohol and barbiturate withdrawal phenomena, which may include agitation, paranoia, and seizures. Marijuana withdrawal syndrome has more frequently been reported in adolescents who were admitted for substance abuse treatment or under research conditions upon discontinuation of daily administration.

According to the American Psychiatric Association, Diagnostic and Statistical Manual (DSM–IV–TR™, 2000), the distinction between occasional use of cannabis and cannnabis dependence or abuse can be difficult to make because social, behavioral, or psychological problems may be difficult to attribute to the substance, especially in the context of use of other substances. Denial of heavy use is common, and people appear to seek treatment for cannabis dependence or abuse less often than for other types of substance-related disorders.

Although pronounced withdrawal symptoms can be provoked from the administration of a cannabinoid antagonist in animals who had received chronic THC administration, there is no overt withdrawal syndrome behaviorally in animals under conditions of natural discontinuation following chronic THC administration.

This may be the result of slow release of cannabinoids from adipose storage, as well as the presence of the major metabolite, 11-OH-delta^9-THC, which is also psychoactive.

Cognitive Effects

Acute administration of smoked marijuana impairs performance on tests of learning, associative processes, and psychomotor behavior (Block *et al.,* 1992). These data demonstrate that the short-term effects of marijuana can interfere significantly with an individual's ability to learn in the classroom or to operate motor vehicles. Administration of 290 ug/kg delta^9-THC in a smoked marijuana cigarette by human volunteers impaired perceptual motor speed and accuracy, two skills that are critical to driving ability (Kurzthaler *et al.,* 1999). Similarly, administration of 3.95% delta^9-THC in a smoked marijuana cigarette increased dysequilibrium measures as well as the latency in a task of simulated vehicle braking at a rate comparable to an increase in stopping distance of 5 feet at 60 mph (Liguori *et al.,* 1998).

The effects of marijuana may not resolve fully until at least a day after the acute psychoactive effects have subsided. A study at the National Institute on Drug Abuse (NIDA) showed residual impairment on memory tasks 24 hours after volunteer subjects had smoked 0, 1, or 2 marijuana cigarettes containing 2.57% delta^9-THC on two occasions the previous day (Heishman *et al.,* 1990). However, later studies at NIDA showed that there were no residual alterations in subjective or performance measures the day after subjects were exposed to 1.8%, or 3.6% smoked delta^9-THC, indicating that the residual effects of smoking a single marijuana cigarette are minimal (Fant *et al.,* 1998). A John Hopkins study examined marijuana's effects on cognition on 1,318 participants over a 15-year period and reported there were no significant differences in cognitive decline between heavy users, light users, and nonusers of cannabis, nor any male-female differences. The authors concluded that ''these results * * * seem to provide strong evidence of the absence of a long-term residual effect of cannabis use on cognition.'' (Lyketsos *et al.,* 1999).

Age of first use may be a critical factor in persistent impairment resulting from chronic marijuana use. Individuals with a history of marijuana-only use that began before the age of 16 were found to perform more poorly on a visual scanning task measuring attention than individuals who started using marijuana after that age (Ehrenreich *et al.,* 1999). However, the majority of early-onset marijuana users do not go on to become heavy users of marijuana, and those that do tend to associate with delinquent social groups (Kandel and Chen, 2000).

An individual's drug history may play a role in the response that person has to marijuana. Frequent marijuana users (greater than 100 times) were better able to identify a drug effect from low dose delta^9-THC than infrequent users (less than 10 times) and were less likely to experience sedative effects from the drug (Kirk and deWit, 1999). This difference in experiential history may account for data showing that reaction times are not altered by acute administration of marijuana in long term marijuana users (Block and Wittenborn, 1985), suggesting that behavioral adaptation or tolerance can occur to the acute effects of the drug in the absence of evidence for dependence.

The impact of *in utero* marijuana exposure on a series of cognitive tasks had been studied in children at different stages of development. Differences in several cognitive domains distinguished the 4-year-old children of heavy marijuana users. In particular, memory and verbal measures were negatively associated with maternal marijuana use (Fried and Watkinson, 1987). Maternal marijuana use was predictive of poorer performance on abstract/visual reasoning tasks, although it was not associated with an overall lowered IQ in 3-year old children (Griffith *et al.,* 1994). At 6 years of age, prenatal marijuana history was associated with an increase in omission errors on a vigilance task, possibly reflecting a deficit in sustained attention, was noted (Fried *et al.,* 1992). Recently, it had been speculated that prenatal exposure may affect certain behaviors and cognitive abilities that fall under the construct termed executive function, that is, not associated with measures of global intelligence. It was postulated that when tests evaluate novel problem-solving abilities as contrasted to knowledge, there is an association between executive function and intelligence. In a recent study (Fried *et al.,* 1998), the effect of prenatal exposure in 9–12 year old children was analyzed, and similarly to what was shown in other age groups, *in utero* marijuana exposure was negatively associated with executive function tasks that require impulse control, visual analysis and hypothesis testing and it was not associated with global intelligence.

Cardiovascular and Autonomic Effects

Single smoked or oral doses of delta^9-THC ingestion produce tachycardia and unchanged or increased blood pressure (Capriotti *et al.,* 1988, Benowitz and Jones, 1975). However, prolonged delta^9-THC ingestion produces significant heart rate slowing and blood pressure lowering (Benowitz and Jones, 1975). Both plant-derived cannabinoids and the endogenous ligands have been shown to elicit hypotension and bradycardia via activation of peripherally located CB_1 receptors (Wagner *et al.,* 1998). The mechanism of these effects were suggested in that study to include presynaptic CB_1 receptor mediated inhibition of norepinephrine release from peripheral sympathetic nerve terminals, with the possibility of additional direct vasodilation via activation of vascular cannabinoid receptors.

Impaired circulatory responses to standing, exercise, Valsalva maneuver, and cold pressor testing following THC administration suggest a state of sympathetic insufficiency. Tolerance developed to the orthostatic hypotension, possibly related to plasma volume expansion, but did not develop to the supine hypotensive effects. During chronic marijuana ingestion, nearly complete tolerance was shown to have developed to the tachycardia and psychological effects when subjects were challenged with smoked marijuana. Electrocardiographic changes were minimal despite the large cumulative dose of THC. (Benowitz and Jones, 1975)

Cardiovascular effects of smoked or oral marijuana have not been shown to result in any health problems in healthy and relatively young users. However, marijuana smoking by older patients, particularly those with some degree of coronary artery or cerebrovascular disease, is postulated to pose greater risks, because of the resulting increased cardiac work, increased catecholamines, carboxyhemoglobin, and postural hypotension (Benowitz and Jones 1981; Hollister 1988).

As a comparison, the cardiovascular risks associated with use of cocaine are quite serious, including cardiac arrhythmias, myocardial ischemia, myocarditis, aortic dissection, cerebral ischemia, stroke and seizures.

Respiratory Effects

Transient bronchodilation is the most typical effect following acute exposure to marijuana. The petitioner is correct that marijuana does not suppress respiration in a manner that leads to death. With long-term use of marijuana, there can be an increased frequency of pulmonary illness from chronic bronchitis and pharyngitis. Large-airway obstruction, as evident on pulmonary function tests, can also occur with

chronic marijuana smoking, as can cellular inflammatory histopathological abnormalities in bronchial epithelium (Adams and Martin 1996; Hollister 1986).

The low incidence of carcinogenicity may be related to the fact that intoxication from marijuana does not require large amounts of smoked material. This may be especially true today since marijuana has been reported to be more potent now than a generation ago and individuals typically titrate their drug consumption to consistent levels of intoxication. Several cases of lung cancer in young marijuana users with no history of tobacco smoking or other significant risk factors have been reported (Fung *et al.* 1999). However, a recent study (Zhang *et al.,* 1999) has suggested that marijuana use may dose-dependently interact with mutagenic sensitivity, cigarette smoking and alcohol use to increase the risk of head and neck cancer. The association of marijuana use with carcinomas remains controversial.

Endocrine System Effects

In male human volunteers, neither smoked THC (18 mg/marijuana cigarette) nor oral THC (10 mg t.i.d. for 3 days and on the morning of the fourth day) altered plasma prolactin, ACTH, cortisol, luteinizing hormone or testosterone levels (Dax *et al.,* 1989). Reductions in male fertility by marijuana are reversible and only seen in animals at concentrations higher than those found in chronic marijuana users.

Relatively little research has been performed on the effects of experimentally administered marijuana on human female endocrine and reproductive system function. Although suppressed ovulation and other ovulatory cycle changes occur in nonhuman primates, a study of human females smoking marijuana in a research hospital setting did not find hormone or menstrual cycle changes like those in monkeys that had been given delta^{9}-THC (Mendelson *et al.,* 1984a).

THC reduces binding of the corticosteroid dexamethasone in hippocampal tissue from adrenalectomized rats, suggesting a direct interaction with the glucocorticoid receptor. Chronic THC administration also reduced the number of glucocorticoid receptors. Acute THC releases corti-costerone, but tolerance developed with chronic THC administration. (Eldridge *et al.,* 1991)

Immune System Effects

Immune functions can be enhanced or diminished by cannabinoids, dependent on experimental conditions, but the effects of endogenous cannabinoids on the immune system are not yet known. The concentrations of THC that are necessary for psychoactivity are lower than those that alter immune responses.

A study presented by Abrams and coworkers at the University of California, San Francisco at the XIII International AIDS Conference investigated the effect of marijuana on immunological functioning in 62 AIDS patients who were taking protease inhibitors. Subjects received one of three treatments, three times a day: Smoked marijuana cigarette containing 3.95% THC; oral tablet containing THC (2.5 mg oral dronabinol); or oral placebo. There were no changes in HIV RNA levels between groups, demonstrating no short-term adverse virologic effects from using cannabinoids. Additionally, those individuals in the cannabinoid groups gained more weight than those in the placebo group (3.51 kg from smoked marijuana, 3.18 kg from dronabinol, 1.30 kg from placebo) (7/13/00, Durban, South Africa).

3. The State of Current Scientific Knowledge Regarding the Drug or Other Substance

This section discusses the chemistry, human pharmacokinetics, and medical uses of marijuana.

Chemistry

According to the DEA, three forms of cannabis (that is, Cannabis sativa L. and other species) are currently marketed illicitly in the U.S.A. These cannabis derivatives include marijuana, hashish and hashish oil.

Each of these forms contains a complex mixture of chemicals. Among these components the twenty-one carbon terpenes found in the plant as well as their carboxylic acids, analogues, and transformation products are known as cannabinoids (Agurell *et al.,* 1984, 1986; Mechoulam, 1973). The cannabinoids appear to be unique to marijuana and most of the naturally-occurring have been identified. Among the cannabinoids, delta^{9}-tetrahydrocannabinol (delta^{9}-THC, alternate name delta^{1}-THC) and delta-8-tetrahydrocannabinol (delta^{8}-THC, alternate name delta^{6}-THC) are the only compounds in the plant, which show all of the psychoactive effects of marijuana. Because delta^{9}-THC is more abundant than delta^{8}-THC, the activity of marijuana is largely attributed to the former, which is considered the main psychoactive cannabinoid in cannabis. Delta^{8}-THC is found only in few varieties of the plant (Hively *et al.,* 1966). Other cannabinoids, such as cannabidiol (CBD) and cannabinol (CBN), has been characterized. CBD is not considered to have cannabinol-like psychoactivity, but is thought to have significant anticonvulsant, sedative, and anxiolytic activity (Adams and Martin, 1996; Agurell *et al.,* 1984, 1986; Hollister, 1986).

Marijuana is a mixture of the dried flowering tops and leaves from the plant (Agurell *et al.* 1984; Graham 1976; Mechoulam 1973) and is variable in content and potency (Agurell *et al.* 1986; Graham 1976; Mechoulam 1973). Marijuana is usually smoked in the form of rolled cigarettes. The other cannabis forms are also smoked. Potency of marijuana, as indicated by cannabinoid content, has been reported to average from as low as one to two percent to as high as 17 percent.

Delta^{9}-THC is an optically active resinous substance, insoluble in water and extremely lipid soluble. Chemically is known as (6aR-trans)-6a,7,8,10a-tetrahydro-6,6,9-trimethyl-3-pentyl-6H-dibenzo-[b,d]pyran-1-ol or (-)-delta^{9}-(trans)-tetrahydrocannabinol. The pharmacological activity of delta^{9}-THC is stereospecific; the (-)-trans isomer is 6–100 times more potent than the (+)-trans isomer (Dewey *et al.,* 1984).

The concentration of delta^{9}-THC and other cannabinoids in marijuana varies greatly depending on growing conditions, parts of the plant collected (flowers, leaves stems, etc), plant genetics, and processing after harvest (Adams and Martin , 1996; Agurell *et al.,* 1984; Mechoulam, 1973). Thus, there are many variables that can influence the strength, quality and purity of marijuana as a botanical substance. In the usual mixture of leaves and stems distributed as marijuana, the concentration of delta^{9}-THC ranges from 0.3 to 4.0 percent by weight. However, specially grown and selected marijuana can contain 15 percent or even more delta^{9}-THC. Thus, a one-gram marijuana cigarette might contain as little as 3 milligrams or as much as 150 milligrams or more of delta^{9}-THC among several other cannabinoids. As a consequence, the clinical pharmacology of pure delta^{9}-THC may not always be expected to have the same clinical pharmacology of smoked marijuana containing the same amount of delta^{9}-THC (Harvey, 1985). Also, the lack of consistency of concentration of delta^{9}-THC in botanical marijuana from diverse sources makes the interpretation of clinical data very difficult. If marijuana is to be investigated more widely for medical use, information and data regarding the chemistry, manufacturing and specifications of marijuana must be developed. 21 CFR 314.50(d)(1)

describes the data and information that should be included in the chemistry, manufacturing and controls section of a new drug application (NDA) to be reviewed by FDA.

Hashish consists of the cannabinoid-rich resinous material of the cannabis plant, which is dried and compressed into a variety of forms (balls, cakes *etc.*). Pieces are then broken off, placed into pipes and smoked. Cannabinoid content in hashish has recently been reported by DEA to average 6 percent.

Hash oil is produced by extracting the cannabinoids from plant material with a solvent. Color and odor of the extract vary, depending on the type of solvent used. Hash oil is a viscous brown or amber-colored liquid that contains approximately 15 percent cannabinoids. One or two drops of the liquid placed on a cigarette purportedly produce the equivalent of a single marijuana cigarette.

Human Pharmacokinetics

Marijuana is generally smoked as a cigarette (weighing between 0.5 and 1.0 gram), or in a pipe. It can also be taken orally in foods or as extracts of plant material in ethanol or other solvents. Pure preparations of delta^9-THC and other cannabinoids can be administered by mouth, rectal suppository, intravenous injection, or smoked.

The absorption, metabolism, and pharmacokinetic profile of delta^9-THC (and other cannabinoids) in marijuana or other drug products containing delta^9-THC are determined by route of administration and formulation (Adams and Martin 1996; Agurell *et al.* 1984, 1986). When marijuana is administered by smoking, delta^9-THC in the form of an aerosol in the inhaled smoke is absorbed within seconds. The delta^9-THC is delivered to the brain rapidly and efficiently as would be expected of a very lipid-soluble drug. The delta^9-THC bioavailability from smoked marijuana, i.e., the actual absorbed dose as measured in blood, varies greatly among individuals. Bioavailability can range from one percent to 24 percent with the fraction absorbed rarely exceeding 10 to 20 percent of the delta^9-THC in a marijuana cigarette or pipe (Agurell *et al.* 1986; Hollister 1988a). This relatively low and quite variable bioavailability results from significant loss of delta^9-THC in side-stream smoke, from variation in individual smoking behaviors, from cannabinoid pyrolysis, from incomplete absorption of inhaled smoke, and from metabolism in the lungs. A smoker's experience is likely an important determinant of the dose that is actually absorbed (Herning *et al.* 1986; Johansson *et al.* 1989). Venous blood levels of delta^9-THC or other cannabinoids correlate poorly with intensity of effects and character of intoxication (Agurell *et al.* 1986; Barnett *et al.* 1985; Huestis *et al.* 1992a).

After smoking, venous levels of delta^9-THC decline precipitously within minutes, and within an hour are about 5 to 10 percent of the peak level (Agurell *et al.,* 1986, Huestis *et al.,* 1992a, 1992b). Plasma clearance of delta^9-THC is approximately 950 mL/min or greater, thus approximating hepatic blood flow. The rapid disappearance of delta^9-THC from blood is largely due to redistribution to other tissues in the body, rather than to metabolism (Agurell *et al.,* 1984, 1986). Metabolism in most tissues is relatively slow or absent. Slow release of delta^9-THC and other cannabinoids from tissues and subsequent metabolism results in a long elimination half-life. The terminal half-life of delta^9-THC is estimated to range from approximately 20 hours to as long as 10 to 13 days, though reported estimates vary as expected with any slowly cleared substance and the use of assays of variable sensitivities.

In contrast, following an oral dose of delta^9-THC or marijuana, maximum delta^9-THC and other cannabinoid blood levels are attained after 2 to 3 hours (Adams and Martin 1996; Agurell *et al.* 1984, 1986). Oral bioavailability of delta^9-THC, whether pure or in marijuana, is low and extremely variable, ranging between 5 and 20 percent (Agurell *et al.* 1984, 1986). There is inter-and intra-subject variability, even when repeatedly dosed under controlled and ideal conditions. The low and variable oral bioavailability of delta^9-THC is a consequence of its first-pass hepatic elimination from blood and erratic absorption from stomach and bowel. Because peak effects are slow in onset, typically one or two hours after an oral dose, and variable in intensity, it is more difficult for a user to titrate the oral delta^9-THC dose than with marijuana smoking. When smoked, the active metabolite, 11-hydroxy-delta^9-THC, probably contributes little to the effects since relatively little is formed, but after oral administration, metabolite levels produced may exceed that of delta^9-THC and thus contribute greatly to the pharmacological effects of oral delta^9-THC or marijuana. Delta^9-THC is metabolized via microsomal hydroxylation to more than 80, active and inactive, metabolites (Lemberger *et al.,* 1970, Lemberger *et al.,* 1972a, 1972b) of which the primary active metabolite was 11-OH-delta^9-THC. This metabolite is approximately equipotent to delta^9-THC in producing marijuana-like subjective effects (Agurell *et al.,* 1986, Lemberger and Rubin, 1975). Following oral administration of radioactive-labeled delta^9-THC, it has been confirmed that delta^9-THC plasma levels attained by the oral route are low relative to those levels after smoking or intravenous administration. The half-life of delta^9-THC has been determined to be 23–28 hours in heavy marijuana users, but 60–70 hours in naive users (Lemberger *et al.,* 1970).

Characterization of the pharmacokinetics of delta^9-THC and other cannabinoids from smoked marijuana is difficult (Agurell *et al.*, 1986, Herning *et al.*, 1986, Heustis *et al.*, 1992a) in part because a subject's smoking behavior during an experiment cannot be easily controlled or quantified by the researcher. An experienced marijuana smoker can titrate and regulate the dose to obtain the desired acute psychological effects and to avoid overdose and/or minimize undesired effects. Each puff delivers a discrete dose of delta^9-THC to the body. Puff and inhalation volume changes with phase of smoking, tending to be highest at the beginning and lowest at the end of smoking a cigarette. Some studies found frequent users to have higher puff volumes than less frequent marijuana users. During smoking, as the cigarette length shortens, the concentration of delta^9-THC in the remaining marijuana increases; thus, each successive puff contains an increasing concentration of delta^9-THC.

Cannabinoid metabolism is extensive. There are at least 80 probable biologically inactive, but not completely studied, metabolites formed from delta^9-THC (Agurell *et al.*, 1986; Hollister, 1988a). In addition to the primary active metabolite, 11-hydroxy-delta^9-THC, some inactive carboxy metabolites have terminal half-lives of 50 hours to 6 days or more. The latter substances serve as long term markers of earlier marijuana use in urine tests. Most of the absorbed delta^9-THC dose is eliminated in feces, and about 33 percent in urine. Delta^9-THC enters enterohepatic circulation and undergoes hydroxylation and oxidation to 11-nor-9-carboxy-delta^9-THC. The glucuronide is excreted as the major urine metabolite along with about 18 nonconjugated metabolites. Frequent and infrequent marijuana users are similar in the way they metabolize delta^9-THC (Agurell *et al.*, 1986).

Medical Uses for Marijuana

FDA has not approved a new drug application for marijuana, although there are several INDs currently active. There is suggestive evidence that

marijuana may have beneficial therapeutic effects in relieving spasticity associated with multiple sclerosis, as an analgesic, as an antiemetic, as an appetite stimulant and as a bronchodilator, but there is no data from controlled clinical trials to support a new drug application for any of these indications. Data of the risks and potential benefits of using marijuana for these various indications must be developed to determine whether botanical marijuana, or any cannabinoid in particular, has a therapeutic role.

In February 1997, a NIH-sponsored workshop analyzed available scientific information and concluded that ''in order to evaluate various hypotheses concerning the potential utility of marijuana in various therapeutic areas, more and better studies would be needed'' (NIH, 1997). In addition, in March 1999, the Institute of Medicine (IOM) issued a detailed report that supports the absolute need for evidence-based research into the effects of marijuana and cannabinoid components of marijuana, for patients with specific disease conditions. The IOM report also emphasized that smoked marijuana is a crude drug delivery system that exposes patients to a significant number of harmful substances and that ''if there is any future for marijuana as a medicine, it lies in its isolated components, the cannabinoids and their synthetic derivatives.'' As such, the IOM recommended that clinical trials should be conducted with the goal of developing safe delivery systems (Institute of Medicine, 1999). Additionally, State-level public initiatives, including referenda in support of the medical use of marijuana have generated interest in the medical community for high quality clinical investigation and comprehensive safety and effectiveness data.

The Department of Health and Human Services (DHHS) is committed to providing ''research-grade marijuana for studies that are the most likely to yield usable, essential data'' (DHHS, 1999). The opportunity for scientists to conduct clinical research with botanical marijuana has increased due to changes in the process for obtaining botanical marijuana from the National Institute on Drug Abuse, the only legal source of the drug for research. Studies published in the current medical literature demonstrate that clinical research with marijuana is being conducted in the US under FDA-authorized Investigational New Drug applications. In May 1999, DHHS provided guidance on the procedures for providing research-grade marijuana to scientists who intend to study marijuana in scientifically valid investigations and well-controlled clinical trials (DHHS, 1999). This action was prompted by the increasing interest in determining through scientifically valid investigations whether cannabinoids have medical use.

4. Its History and Current Pattern of Abuse

To assess drug abuse patterns and trends, data from different sources such as National Household Survey on Drug Abuse (NHSDA), Monitoring the Future (MTF), Drug Abuse Warning Network (DAWN), and Treatment Episode Data Set (TEDS) have been analyzed. These indicators of marijuana use in the United States are described below:

National Household Survey on Drug Abuse

The National Household Survey on Drug Abuse (NHSDA, 1999) is conducted by the Department of Health and Human Service's Substance Abuse and Mental Health Services Administration (SAMHSA) annually. This survey has been the primary source of estimates of the prevalence and incidence of alcohol, tobacco and illicit drug use in the US. It is important to note that this survey identifies whether an individual used a drug during a certain period, but not the amount of the drug used on each occasion. The survey is based on a nationally representative sample of the civilian, non-institutionalized population 12 years of age and older. Persons excluded from the survey include homeless people who do not use shelters, active military personnel, and residents of institutional group quarters, such as jails and hospitals. In 1999, 66,706 individuals were interviewed.

According to the 1999 NHSDA, illicit drug use involved approximately 14.8 million Americans (6.7% of the US population) on a monthly basis. The most frequently used illicit drug was marijuana, with 11.2 million Americans (5.1% of the US population) using it monthly. The 1999 NHSDA no longer provides data on the weekly or daily use of any drug, so these statistics are unavailable for marijuana. The NHSDA estimated that 76.4 million Americans (34.6% of the population) have tried marijuana at least once during their lifetime. Thus, 14.7% of those who try marijuana go on to use it monthly. NHSDA data from 1999 show that 57% of illicit drug users only use marijuana on a monthly basis, which corresponds to 8.44 million persons (3.8% of the US population). However, there are no data available on marijuana-only use as a percent of use of any drug.

An estimated 2.3 million persons of all ages used marijuana for the first time in 1998, of whom 1.6 million were between the ages of 12–17. (Information on when people first used a substance is collected on a retrospective basis, so this information is always one year behind information on current use.) This represents a slight reduction in new marijuana users from 1997, when the rate was 2.6 million people of all ages and 1.8 million for those 12–17 years old. Trends for marijuana use were similar to the trends for any illicit use. There were no significant changes between 1998 and 1999 for any of the four age groups, but an increasing trend since 1997 among young adults age 18–25 years (12.8 % in 1997, 13.8 % in 1998, and 16.4 % in 1999) and a decreasing trend since 1997 for youths age 12–17 years (9.4 % in 1997, 8.3 % in 1998, and 7.0 % in 1999).

Monitoring the Future

Monitoring the Future (MTF, 1999) is a national survey that tracks drug use trends among American adolescents. The MTF has surveyed 8th, 10th and 12th graders every spring in randomly selected U.S. schools since 1975 for 12th graders and since 1991 for 8th and 10th graders. This survey is conducted by the Institute for Social Research at the University of Michigan under a grant from NIDA. The 1999 sample sizes were 17,300, 13,900, and 14,100 in 8th, 10th, and 12th grades, respectively. In all, about 45,000 students in 433 schools participated. Because multiple questionnaire forms are administered at each grade level, and because not all questions are contained in all forms, the numbers of cases upon which a particular statistic are based can be less than the total sample.

Comparisons between the MTF and students sampled in the NHSDA (described above) have generally shown NHSDA prevalence to be lower than MFT estimates, in which the largest difference occurred with 8th graders. The MTF survey showed the use of illegal drugs by adolescents leveled off in 1997 and then declined somewhat for most drugs in 1998. Also, the 1998-year survey showed that for the first time since 1991 an increase in the percentage of 8th graders who said marijuana is a risk to their health.

Illicit drug use among teens remained steady in 1999 in all three grades, as did the use of a number of important specific drugs such as marijuana, amphetamines, hallucinogens taken as a class, tranquilizers, heroin, and alcohol. Marijuana is the most widely used illicit drug. For 1999, the annual prevalence rates in grades 8, 10, and 12,

respectively, are 17%, 32%, and 38%. Current monthly prevalence rates are 9.7%, 19.4% and 23.1%. (See Table 1), whereas current daily prevalence rates (defined as the proportion using it on 20 or more occasions in the prior thirty days) are 1.4%, 3.8%, and 6.0%.

TABLE 1.—TRENDS IN ANNUAL AND MONTHLY PREVALENCE OF USE OF VARIOUS DRUGS FOR EIGHTH, TENTH, AND TWELFTH GRADERS

[Entries are precentages]

Grade	Annual			30-Day		
	1997	1998	1999	1997	1998	1999
Any illicit drug (a)						
8th	22.1	21.0	20.5	12.9	12.1	12.2
10th	38.5	35.0	35.9	23.0	21.5	22.1
12th	42.4	41.4	42.1	26.2	25.6	25.9
Any illicit drug other than cannabis (a)						
8th	11.8	11.0	10.5	6.0	5.5	5.5
10th	18.2	16.6	16.7	8.8	8.6	8.6
12th	20.7	20.2	20.7	10.7	10.7	10.4
Marijuana/hashish						
8th	17.7	16.9	16.5	10.2	9.7	9.7
10th	34.8	31.1	32.1	20.5	18.7	19.4
12th	38.5	37.5	37.8	23.7	22.8	23.1
Cocaine						
8th	2.8	3.1	2.7	1.1	1.4	1.3
10th	4.7	4.7	4.9	2.0	2.1	1.8
12th	5.5	5.7	6.2	2.3	2.4	2.6
Heroin (b)						
8th	1.3	1.3	1.4	0.6	0.6	0.6
10th	1.4	1.4	1.4	0.6	0.7	0.7
12th	1.2	1.0	1.1	0.5	0.5	0.5

Source. The Monitoring the Future Study, the University of Michigan.

a. For 12th graders only: Use of ''any illicit drug'' includes any use of marijuana, LSD, other hallucinogens, crack, other cocaine, or heroin, or any use of other opiates, stimulants, barbiturates, or tranquilizers not under a doctor's orders. For 8th and 10th graders: The use of other opiates and barbiturates has been excluded, because these younger respondents appear to over-report use (perhaps because they include the use of nonprescription drugs in their answers).

b. In 1995, the heroin question was changed in three of six forms for 12th graders and in two forms for 8th and 10th graders. Separate questions were asked for use with injection and without injection. Data presented here represents the combined data from all forms. In 1996, the heroin question was changed in the remaining 8th and 10th grade forms.

Drug Abuse Warning Network (DAWN)

The Drug Abuse Warning Network (DAWN, 1998) is a national probability survey of hospitals with emergency departments (EDs) designed to obtain information on ED episodes that are induced by or related to the use of an illegal drug or the non-medical use of a legal drug. The DAWN system provides information on the health consequences of drug use in the United States as manifested by drug-related visits to emergency departments (ED episodes). DAWN captures the non-medical use of a substance either for psychological effects, dependence, or suicide attempt. The ED data come from a representative sample of hospital emergency department's which are weighted to produce national estimates. As stated in DAWN methodology, ''the terms 'ED drug abuse episode' or 'ED episode' refer to any ED visit that was induced by or related to drug abuse. Similarly, the terms 'ED drug mention' or 'ED mention' refer to a substance that was mentioned in a drug abuse episode. Up to 4 substances can be reported for each ED episode. Thus, the number of ED mentions will always equal or exceed the number of ED episodes.''

Many factors can influence the estimates of ED visits, including trends in the ED usage in general. Some drug users may have visited EDs for a variety of reasons, some of which may have been life threatening, whereas others may have sought care at the ED for detoxification because they needed certification before entering treatment. It is important to note that the variable ''Motive'' applies to the entire episode and since more than one drug can be mentioned per episode, it may not apply to the specific drug for which the tables have been created. DAWN data do not distinguish the drug responsible for the ED visit from others used concomitantly. The DAWN report itself states, ''Since marijuana/hashish is frequently present in combination with other drugs, the reason for the ED contact may be more relevant to the other drug(s) involved in the episode.''

In 1999, there were an estimated 554,932 drug-related ED episodes and 1,015,206 ED drug mentions from these drug-related episodes. Nationally, the number of ED episodes and mentions remained relatively stable from 1998 to 1999. The 4 drugs mentioned most frequently in ED reports—alcohol-in-combination (196,277 mentions), cocaine (168,763), marijuana/hashish (87,150), and heroin/morphine (84,409)—were statistically unchanged from 1998 to 1999. Marijuana/hashish mentions represented 16% of all drug-related episodes in 1999. For adolescent patients age 12–17, there was no statistical change from 1998 to 1999 in drug use for any drug category (Table 2). There was no a statistically significant change in the number of marijuana/hashish mentions, heroin/morphine of cocaine from 1998 to 1999.

TABLE 2.—ESTIMATED NUMBER OF EMERGENCY DEPARTMENT DRUG EPISODES, DRUG MENTIONS AND MENTIONS FOR SELECTED DRUGS FOR TOTAL COTERMINOUS US BY YEAR FOR 1997–1999

	1997	1998	1999
Drug episodes	527,058	542,544	554,932
Drug mentions	943,937	982,856	1,015,206
Cocaine	161,087	172,014	168,763
Heroin/Morphine	72,010	77,645	84,409
Marijuana/Hashish	64,744	76,870	87,150

Source: Office of applied studies, SAMHSA, Drug Abuse Warning Network, 1999 (03/2000 update). Note: These estimates are based on a representative sample of non-federal, short-stay hospitals with 24-hour emergency departments in the U.S.

There were no statistically significant increases in marijuana/hashish mentions on the basis of age, gender, or race/ethnicity subgroups between 1998 and 1999, although a 19% increase in marijuana/hashish mentions (from 22,907 to 27,272) among young adults age 18 to 25 was observed.

Approximately 15 percent of the emergency department marijuana/hashish mentions involved patients in the 6–17 years of age, whereas this age group only accounts for less than 1 percent of the emergency department heroin/morphine and approximately 2 percent of the cocaine emergency department mentions. Most of the emergency department heroin/morphine and cocaine mentions involved subjects in the 26–44 years of age range.

Marijuana/hashish is likely to be mentioned in combination with other substances, particularly with alcohol and cocaine. Marijuana use as a single drug accounted for approximately 22% of the marijuana episodes. Single use of cocaine and heroin accounted for 29% and 47% of the cocaine and heroine episodes respectively.

The petitioner asserts that ''common household painkillers'' and benzodiazepines produce more ED visits than marijuana and that marijuana users are no more likely to be seen in EDs

than other chronic drug users. DAWN data do not confirm the petitioner's assertions. For 1999, the estimated rate of mentions of selected drugs per 100,000 population is 69.4 for cocaine, 35.8 for marijuana/hashish, 34.7 for heroin/morphine, 17.5 for alprazolam/diazepam/lorazepam, and 16.9 for aspirin/acetaminophen. The estimated rate of mentions of marijuana/hashish per 100,000 population is similar to that of heroin/morphine, but approximately twice that of aspirin/acetaminophen and that of alprazolam/diazepam/lorazepam. However, marijuana estimated rate of mentions/100,000 population is approximately half that of cocaine.

These drugs are easily distinguished by the motivation for their use. In 1999, marijuana/hashish mentions were related to episodes in which the motive for drug intake was primarily dependence (34.2%) followed by recreational use (28%), suicide (11.5%) and other psychic effects (8.1%). DAWN defines ''psychic effects'' as a conscious action to use a drug to improve or enhance any physical, emotional, or social situation or condition. The use of a drug for experimentation or to enhance a social situation, as well as the use of drugs to enhance or improve any mental, emotional, or physical state, is reported to DAWN under this category. Examples of the latter include anxiety, stay awake, help to study, weight control, reduce pain and to induce sleep. A different pattern is observed for tranquilizers (alprazolam/diazepam/lorazepam) and aspirin/acetamipnophen. Alprazolam/diazepam/lorazepam mentions were primarily related to episodes where the motive for drug intake was primarily suicide (approximately 58%), followed by dependence (approximately 17%), other psychic effects (approximately 11%), and recreational use (approximately 5%). For the use of aspirin/acetaminophen the primary motive of the episode was suicide (80%), other psychic effects (9%) and recreational use (2%).

DAWN also collects information on drug-related deaths from selected medical examiner offices from more than 40 metropolitan areas. In 1997 and 1998, there were 678 and 595 marijuana-related death mentions, representing 7.1 and 5.9 percent of the total drug abuse deaths for each year respectively. Medical examiner data also showed that in the majority of the mentions, marijuana was used concomitantly with cocaine, heroin and alcohol.

Treatment Episode Data Set

The Treatment Episode Data Set (TEDS, 1998) system is part of SAMHSA's Drug and Alcohol Services Information System (Office of Applied Science, SAMHSA). TEDS comprises data on treatment admissions that are routinely collected by States in monitoring their substance abuse treatment systems. The TEDS report provides information on the demographic and substance use characteristics of the 1.5 million annual admissions to treatment for abuse of alcohol and drugs in facilities that report to individual State administrative data systems. It is important to note that TEDS is an admission-based system, and TEDS admissions do not represent individuals, because a given individual admitted to treatment twice within a given year would be counted as two admissions. TEDS includes facilities that are licensed or certified by the State substance abuse agency to provide substance abuse treatment and that are required by the States to provide TEDS client-level data. Facilities that report TEDS data are those that receive State alcohol and/or drug agency funds for the provision of alcohol and/or drug treatment services. The primary goal for TEDS is to monitor the characteristics of treatment episodes for substance abusers.

Primary marijuana abuse accounted for 13% of TEDS admissions in 1998, the latest year for which data are available. In general, most of the individuals admitted for marijuana were white young males. Marijuana use began at an early age among primary marijuana admissions and more than half of the admitted patients had first used marijuana by the age of 14 and 92% by the age of 18. More than half of marijuana treatment admissions were referred through the criminal justice system.

Approximately one-third of those who were admitted for primary marijuana abuse use the drug daily. Between 1992 and 1998, the proportion of admissions for primary marijuana use increased from 6% to 13%, whereas the proportion of admissions for primary cocaine use declined from 18% in 1992 to 15% in 1998. The proportion of opiate admissions increased from 12% in 1992 to 15% in 1998 and alcohol accounted for about half (47%) of all TEDS admissions in 1998. Marijuana has not been associated with other drugs in 30.8% of the primary marijuana admissions that corresponds to 4.1% of all admissions. Secondary use of alcohol was reported by 38.2% of the marijuana admissions and secondary cocaine use was reported by 4% of admissions for primary marijuana abuse. The combination marijuana/alcohol/cocaine accounts for 8.5% of marijuana primary admissions and 1.1% of all admissions.

The TEDS Report concludes that, ''Overall, TEDS admissions data confirm that those admitted to substance abuse treatment have problems beyond their dependence on drugs and alcohol, being disadvantaged in education and employment when compared to the general population after adjusting for age, gender, and race/ethnicity distribution differences between the general population and the TEDS. It is not possible to conclude cause and effect from TEDS data—whether substance abuse precedes or follows the appearance of other life problems—but the association between problems seems clear.''

NIDA's Community Epidemiology Work Group (CEWG, 1999)

The CEWG is a network composed of epidemiologic and ethnographic researchers from major metropolitan areas of the United States and selected countries from abroad that meets semiannually to discuss the current epidemiology of drug abuse. Large-scale databases used in analyses include TEDS; DAWN; the Arrestee Drug Abuse Monitoring (ADAM) program funded by the National Institute of Justice; information on drug seizures, price, and purity from the Drug Enforcement Administration; Uniform Crime Reports maintained by the Federal Bureau of Investigation and Poison Control Centers. These data are enhanced with qualitative information obtained from ethnographic research, focus groups, and other community-based sources. Although data from TEDS and DAWN have been previously discussed this document, the analysis offered by the CEWG gives a more descriptive overview of individual geographical areas. In 1999, marijuana indicators were stable in 17 of the 21 CEWG areas. Indicators were mixed in two areas (Atlanta and Baltimore) and increased in two (Los Angeles and St. Louis). Despite the stability of certain indicators, marijuana abuse remains a serious problem in CEWG areas. In Atlanta, marijuana is the second most prevalent drug on the market and is increasingly used by a wide variety of people mostly white males and young adolescents. In St. Louis, marijuana indicators are increasing and DAWN marijuana ED mentions rose 33.3% from the last half of 1998 to the first half of 1999. Treatment admissions rose 40.1% from the second half of 1998 to the first

half of 1999, and another 9.6% in the second half of 1999.

In recent years, the proportion of primary marijuana abusers entering drug abuse treatment programs has been increasing in many CEWG cities. For example, between 1998 and the first semester of 1999, drug treatment admissions for primary marijuana abuse increased from 15.2% to 20.3% in Atlanta. In the first half of 1999, primary marijuana abusers represented 18.8% of drug treatment admissions in New York City compared with 16.6% in the first half of 1998. In the first half of 1999, primary marijuana abuse represented 41.2% of all drug treatment admissions in Denver and totaled 3,179. The number of primary marijuana admissions in St. Louis increased dramatically in the first half of 1999, representing 40.8% of treatment admissions.

The CEWG reports an increase in problems associated with marijuana that they attribute to the drug's greater availability/potency, its relative low cost, and a public attitude that use of marijuana is less risky than use of other drugs.

5. The Scope, Duration, and Significance of Abuse

According to the National Household Survey on Drug Abuse and the Monitoring the Future study, marijuana remains the most extensively used illegal drug in the US, with 34.6% of individuals over age 12 (76.4 million) and 49.7% of 12th graders having tried it at least once in their lifetime. While the majority of individuals (85.3%) who have tried marijuana do not use the drug monthly, 11.2 million individuals (14.7%) report that they used marijuana within the past 30 days. An examination of use among various age cohorts demonstrates that monthly use occurs primarily among college age individuals, with use dropping off sharply after age 25.

The Drug Abuse Warning Network data show that among 18–25 year olds, there was a 19% increase in 1999 for marijuana emergency department mentions. The fact that this age cohort had the greatest degree of acute adverse reactions to marijuana might be expected given that this group has the largest prevalence of marijuana use. Marijuana was commonly associated with alcohol and cocaine.

According to 1999 DAWN data, there were 187 deaths mentions where marijuana was the only drug reported, out of the total 664 medical examiners episodes involving marijuana in 1999. In the majority of the medical examiners episodes marijuana was associated with alcohol, cocaine, and morphine.

Data from the Treatment Episode Data Set confirm that 69% of admissions to drug treatment programs for primary marijuana abuse also had concurrent use of alcohol and other drugs. The TEDS report also emphasizes that individuals who are admitted for drug treatment have multiple disadvantages in education and employment compared to the general population. Individuals most likely to develop dependence on marijuana have a higher rate of associated psychiatric disorders or are socializing with a delinquent crowd.

6. What, if Any, Risk There is to the Public Health

The risk to the public health as measured by quantifiers such as emergency room episodes, marijuana-related deaths, and drug treatment admissions is discussed in full in sections 1, 4, and 5 above. Accordingly, this section focuses on the health risks to the individual user. All drugs, both medicinal and illicit, have a broad range of effects on the individual user that are dependent on dose and duration of usage. It is not uncommon for a FDA approved drug product to produce adverse effects even at doses in the therapeutic range. Such adverse responses are known as ''side effects''. When determining whether a drug product is safe and effective for any indication, FDA performs a thorough risk-benefit analysis to determine whether the risks posed by the drug product's potential or actual side effects are outweighed by the drug product's potential benefits. As marijuana is not approved for any use, any potential benefits attributed to marijuana use have not been found to be outweighed by the risks. However, cannabinoids have a remarkably low acute lethal toxicity despite potent psychoactivity and pharmacologic actions on multiple organ systems.

The consequences of marijuana use and abuse are discussed below in terms of the risk from acute and chronic use of the drug to the individual user (IOM, 1999) (see also the discussion of the central nervous system effects, cognitive effects, cardiovascular and autonomic effects, respiratory effects, and the effect on the immune system in Section 2):

Risks from acute use of marijuana:

Acute use of marijuana causes an impairment of psychomotor performance, including performance of complex tasks, which makes it inadvisable to operate motor vehicles or heavy equipment after using marijuana. People who have or are at risk of developing psychiatric disorders may be the most vulnerable to developing dependence on marijuana. Dysphoria is a potential response in a minority of individuals who use marijuana.

Risks from chronic use of marijuana:

Marijuana smoke is considered to be comparable to tobacco smoke in respect to increased risk of cancer, lung damage, and poor pregnancy outcome. An additional concern includes the potential for dependence on marijuana, which has been assessed to be rare among the general population but more common among adolescents with conduct disorder and individuals with psychiatric disorders. Although a distinctive marijuana withdrawal syndrome has been identified, it is mild and short-lived.

The Diagnostic and Statistical Manual (DSM–IV–SR, 2000) of American Psychiatric Association states that the consequences of cannabis abuse are as follows:

> [P]eriodic cannabis use and intoxication can interfere with performance at work or school and may be physically hazardous in situations such as driving a car. Legal problems may occur as a consequence of arrests for cannabis possession. There may be arguments with spouses or parents over the possession of cannabis in the home or its use in the presence of children. When psychological or physical problems are associated with cannabis in the context of compulsive use, a diagnosis of Cannabis Dependence, rather than Cannabis Abuse, should be considered.

Individuals with Cannabis Dependence have compulsive use and associated problems. Tolerance to most of the effects of cannabis has been reported in individuals who use cannabis chronically. There have also been some reports of withdrawal symptoms, but their clinical significance is uncertain. There is some evidence that a majority of chronic users of cannabinoids report histories of tolerance or withdrawal and that these individuals evidence more severe drug-related problems overall. Individuals with Cannabis Dependence may use very potent cannabis throughout the day over a period of months or years, and they may spend several hours a day acquiring and using the substance. This often interferes with family, school, work, or recreational activities. Individuals with Cannabis Dependence may also persist in their use despite knowledge of physical problems (*e.g.,* chronic cough related to smoking) or psychological problems (*e.g.,* excessive sedation and a decrease in goal-oriented activities resulting from repeated use of high doses).

7. Its Psychic or Physiologic Dependence Liability

Tolerance can develop to marijuana-induced cardiovascular and autonomic changes, decreased intraocular pressure, sleep and sleep EEG, mood and behavioral changes (Jones *et al.,* 1981). Down-regulation of cannabinoid receptors has been suggested as the mechanism underlying tolerance to the effects of marijuana (Rodriguez de Fonseca *et al.,* 1994). Pharmacological tolerance does not indicate the physical dependence liability of a drug.

In order for physical dependence to exist, there must be evidence for a withdrawal syndrome. Although pronounced withdrawal symptoms can be provoked from the administration of a cannabinoid antagonist in animals who had received chronic THC administration, there is no overt withdrawal syndrome behaviorally in animals under conditions of natural discontinuation following chronic THC administration. The marijuana withdrawal syndrome is distinct but mild compared to the withdrawal syndromes associated with alcohol and heroin use, consisting of symptoms such as restlessness, mild agitation, insomnia, nausea and cramping that resolve after 4 days (Budney *et al.,* 1999; Haney *et al.,* 1999). These symptoms are comparable to the decreased vigor, increased fatigue, sleepiness, headache, and reduced ability to work seen with caffeine withdrawal (Lane *et al.,* 1998). However, marijuana withdrawal syndrome has only been reported in adolescents who were inpatients for substance abuse treatment or in individuals who had been given marijuana on a daily basis during research conditions. Physical dependence on marijuana is a rare phenomenon compared to other psychoactive drugs and if it develops, it is milder when marijuana is the only drug instead of being used in combination with other drugs.

TEDS data for 1998 show that 37.9% of admissions for treatment for primary marijuana use met DSM IV criteria for cannabis dependence, whereas 27.7% met DSM IV criteria for cannabis abuse. Taken in the context of the total number of admissions, a DSM IV diagnosis for cannabis dependence represented 6.6%, and a diagnosis for cannabis abuse represented 4.9%, of all subjects admitted to treatment. In contrast, opioid and cocaine dependence was the DSM diagnosis of 12.2% and 12.6% of all admissions, respectively. (See Section 6 regarding marijuana abuse and dependence).

According to the NHSDA, data discussed above in Section 1, 6.8 million Americans used marijuana weekly in 1998. In addition, the DAWN data discussed in Section 4 indicates that 34.2% of the 87,150 ED marijuana mentions in 1999 were related to episodes in which the motive for drug intake was primarily dependence. It should be emphasized that the patient-reported ''motive'' for the drug intake applies to the entire episode and since more than one drug can be mentioned per episode, it may not apply to one specific drug. DAWN data do not distinguish the drug responsible for the ED visit from others used concomitantly. Finally, the CEWG data discussed in Section 4 above reports an increase in the proportion of primary marijuana users entering drug abuse treatment programs. Thus, there is evidence among a certain proportion of marijuana users for a true psychological dependence syndrome.

8. Whether the Substance is an Immediate Precursor of a Substance Already Controlled Under This Article

Marijuana is not an immediate precursor of another controlled substance.

C. Findings and Recommendation

After considering the scientific and medical evidence presented under the eight factors above, FDA finds that marijuana meets the three criteria for placing a substance in Schedule I of the CSA under 21 U.S.C. 812(b)(1). Specifically:

1. Marijuana Has a High Potential for Abuse

11.2 million Americans used marijuana monthly in 1999 and 1998 data indicate that 6.8 million Americans used marijuana weekly. A 1999 study indicates that by 12th grade, 37.8% of students report having used marijuana in the past year, and 23.1 % report using it monthly. In 1999, 87,150 emergency department episodes were induced by or related to the use of marijuana/hashish, representing 16% of all drug-related episodes. The primary motive for drug intake in 34.2 % of those episodes was reported to be dependence. DAWN data from that same year show that out of 664 medical examiner episodes involving marijuana, marijuana was the only drug reported in 187 deaths. In recent years, the proportion of primary marijuana abusers entering drug abuse treatment programs has been increasing in major U.S. cities, ranging from 19% in New York City to 41% in St. Louis and Denver.

Data show that humans prefer higher doses of marijuana to lower doses, demonstrating that marijuana has dose-dependent reinforcing effects. Marijuana has relatively low levels of toxicity and physical dependence as compared to other illicit drugs. However, as discussed above, physical dependence and toxicity are not the only factors to consider in determining a substance's abuse potential. The large number of individuals using marijuana on a regular basis and the vast amount of marijuana that is available for illicit use are indicative of widespread use. In addition, there is evidence that marijuana use can result in psychological dependence in a certain proportion of the population.

2. Marijuana Has No Currently Accepted Medical Use in Treatment in the United States

The FDA has not approved a new drug application for marijuana. The opportunity for scientists to conduct clinical research with marijuana has increased recently due to the implementation of DHHS policy supporting clinical research with botanical marijuana. While there are INDs for marijuana active at the FDA, marijuana does not have a currently accepted medical use for treatment in the United States nor does it have an accepted medical use with severe restrictions.

A drug has a ''currently accepted medical use'' if all of the following five elements have been satisfied:

a. The drug's chemistry is known and reproducible;

b. There are adequate safety studies;

c. There are adequate and well-controlled studies proving efficacy;

d. The drug is accepted by qualified experts; and

e. The scientific evidence is widely available.

Alliance for Cannabis Therapeutics v. DEA, 15 F.3d 1131, 1135 (D.C. Cir. 1994).

Although the chemistry of many cannabinoids found in marijuana have been characterized, a complete scientific analysis of all the chemical components found in marijuana has not been conducted. Safety studies for acute or subchronic administration of marijuana have been carried out through a limited number of Phase 1 clinical investigations approved by the FDA, but there have been no studies that have scientifically assessed the efficacy of marijuana for any medical condition. A material conflict of opinion among experts precludes a finding that marijuana has been accepted by qualified experts. At this time, it is clear

that there is not a consensus of medical opinion concerning medical applications of marijuana.

Alternately, a drug can be considered to have ''a currently accepted medical use with severe restrictions'' (21 U.S.C. 812(b)(2)(B)). Although some evidence exists that some form of marijuana may prove to be effective in treating a number of conditions, research on the medical use of marijuana has not progressed to the point that marijuana can be considered to have a ''currently accepted medical use with severe restrictions.''

3. There Is a Lack of Accepted Safety for Use of Marijuana Under Medical Supervision

There are no FDA-approved marijuana products. Marijuana does not have a currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions. As discussed earlier, the known risks of marijuana use are not outweighed by any potential benefits. In addition, the agency cannot conclude that marijuana has an acceptable level of safety without assurance of a consistent and predictable potency and without proof that the substance is free of contamination. If marijuana is to be investigated more widely for medical use, information and data regarding the chemistry, manufacturing and specifications of marijuana must be developed. Therefore, FDA concludes that, even under medical supervision, marijuana has not been shown to have an acceptable level of safety.

FDA therefore recommends that marijuana be maintained in Schedule I of the CSA.

References

Adams, I.B., and Martin, B.R. Cannabis: Pharmacology and toxicology in animals and humans. Addiction 1996, 91(11):1585–1614.

Agurell, S., Dewey, W.L., and Willett, R.E., eds. The Cannabinoids: Chemical, Pharmacologic, and Therapeutic Aspects. New York: Academic Press, 1984.

Agurell, S.; Halldin, M.; Lindgren, J.E.; Ohlsson, A.; Widman, M.; Gillespie, H.; and Hollister, L. Pharmacokinetics and metabolism of delta 1-tetrahydrocannabinol and other cannabinoids with emphasis on man. Pharmacol Rev. 1986, 38(1), 21–43.

Ameri, A. The effects of cannabinoids on the brain. Progress in Neurobiology 1999, 58(4), 315–348.

Balster, R.L., Prescott, W.R.,) 9-Tetrahydrocannabinol discrimination in rats as a model for cannabis intoxication. Neurosci. & Biobehav. Rev. 1992, 16(1), 55–62.

Barnett, G.; Licko, V.; and Thompson, T. Behavioral pharmacokinetics of marijuana. Psychopharmacology 1985, 85(1), 51–56.

Budney AJ, Novy PL, Hughes JR. Marijuana withdrawal among adults seeking treatment for marijuana dependence. Addiction 1999, 94(9):1311–22 Community Epidemiology Work Group, National Institutes of Health, National Institute on Drug Abuse, Epidemiologic Trends in Drug Abuse, Volume I: Highlights and Executive Summary, June 2000, http://www.nida.nih.gov/CEWG/pubs.html

Department of Health and Human Services. Announcement of the Department of Health and Human Services Guidance on Procedures for the Provision of Marijuana for Medical Research. May 21, 1999. (*http://grants.nih.gov/grants/guide/notice-files/not99–091.html*).

Drug Abuse Warning Network. Year-End 1999 Emergency Department Data from the Drug Abuse Warning Network. Department of Health and Human Services. Substance Abuse and Mental Health Services Administration. National Clearinghouse for Alcohol and Drug information. Rockville, MD.

Drug Abuse Warning Network. Annual Medical Examiner Data 1998. Department of Health and Human Services. Substance Abuse and Mental Health Services Administration. National Clearinghouse for Alcohol and Drug information. Rockville, MD.

DSM–IV–TR 2000: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision 4th Edition—Text Revision American Psychiatric Association, Publisher: American Psychiatric Press, Incorporated, Pub. Date: July 2000, Edition Desc: 4th Edition—Text Revision.

Dewey, W. L., Martin, B. R., May, E. L. Cannabinoid stereoisomers: pharmacological effects. In Smith, D. F. (Ed.) CRC Handbook of stereoisomers: drugs in psychopharmacology, 317–326 (Boca Raton, FL, CRC Press), 1984.

Fried, P. A., Watkinson, B. 36- and 48-month neurobehabioral follow-up of children prenatally exposed to marijuana, cigarettes and alcohol. J. Dev. Behav. Pediatr. 1987, 8, 318–326.

Fried, P. A., Watkinson, B., Gray, R. A follow-up study of attentional behavior in 6-year-old children exposed prenatally to marihuana, cigarettes and alcohol. Neurotoxicol. Teratol. 1992, 14, 299–311.

Fried, P. A., Watkinson, B., Gray, R. Differential effects on cognitive functioning in 9- to 12-year olds prenatally exposed to cigarettes and marihuana. Neurotoxicol. Teratol. 1998, 20(3), 293–306.

French, E.D. Delta9-Tetrahydrocannabinol excites rat VTA dopamine neurons through activation of cannabinoid CB1 but not opioid receptors. Neurosci Lett 1997, 226, 159–162.

Fung, M., Gallagher, C., Machtay, M. Lung and aeo-digestive cancers in young marijuana smokers. Tumori 1999, 85 (2), 140–142.

Galiegui, S.; Mary, S.; Marchand, J.; Dussossoy, D.; Carriere, D.; Carayon, P.; Bouaboula, M; Shire, D.; Le Fur, g.; Casellas, P. Expression of central and peripheral cannabinoid receptors in human immune tissues and leukocyte subpopulations. Eur J Biochem. 1995, 232(1), 54–61.

Gaoni, Y., Mechoulam, R. Isolation, structure, and partial synthesis of an active constituent of hashish. J. Am. Chem. Soc. 1964, 86, 1646–1947.

Gerard, C. M., Mollereau, C., Vassart, G., Parmentier, M. Molecular cloning of a human cannabinoid receptor which is also expressed in testis. : Biochem J. 1991, 279, 129–34.

Gessa, G.L., Melis, M., Munoni, A.L., Diana, M. Cannabinoids activate mesolimbic dopamine neurons by an action on cannabinoid CB1 receptors. Eur J Pharmacol 1998, 341(1), 39–44.

Graham, J.D.P., ed. Cannabis and Health. New York: Academic Press, 1976.

Griffith, D. R., Azuma, S. D., Chasnoff, I. J. Three-year outcome of children exposed prenatally to drugs. J. Am. Acad. Child Adolesc. Psychiatry 1994, 33, 20–27.

Haney M, Ward AS, Comer SD, Foltin RW, Fischman MW. Abstinence symptoms following smoked marijuana in humans. Psychopharmacology (Berl) 1999, 141(4):395–404.

Hanus, L., Breuer, A., Tchilibon, S., Shiloah, S., Goldenberg, D., Horowitz, M., Pertwee, R.G., Roos, R. A., Mechoulam, R., Fride, E. HU–308: a specific agonist for CB(2), a peripheral Cannabinoid receptor. Proc. Natl. Acad. Sci. USA 1999, 96, 14228–33.

Harvey, D.J., ed. Satellite Symposium on Cannabis (3rd: 1984: Oxford, England) Marihuana '84: Proceedings of the Oxford Symposium on Cannabis. Washington, DC: IRL Press, 1985.

Herkenham, M. Cannabinoid receptor localization in brain: Relationship to motor and reward systems. In: Kalivas, P.W., and Samson, H.H., eds. The neurobiology of drug and alcohol addiction. Ann N Y Acad Sci 1992, 654, 19–32.

Herkenham, M., Lynn, A.B., Little, M.D., Johnson, M.R., Melvin, L.S., de Costa, B.R., Rice, K.C. Cannabinoid receptor localization in Brain. Proc. Natl. Acad. Sci. USA. 1990, 87, 1932–1936.

Herning, R.I.; Hooker, W.D.; and Jones, R.T. Tetrahydrocannabinol content and differences in marijuana smoking behavior. Psychopharmacology 1986, 90(2):160–162.

Hively, R.L., Mosher, W.A., Hoffman, F.W. Isolation of trans-)9-tetrahydrocannabinol from marihuana. J. Am. Chem. Soc. 1966, 88, 1832–1833.

Hollister, L.E. Health aspects of cannabis. Pharmacological Rev. 1986, 38, 1–20.

Hollister, L.E. Cannabis. (Literature review). Acta Psychiatr Scand (Suppl) 1988, 78, 108–118.

Huestis, M.A., Sampson, A.H., Holicky, B.J., Henningfield, J.E., Cone, E.J. Characterization of the absorption phase of marijuana smoking. Clin. Pharmacol. Ther. 1992a, 52, 31–41.

Huestis, M.A.; Henningfield, J.E.; and Cone,

E.J. Blood Cannabinoids. 1. Absorption of THC and formation of 11-OH-THC and THC COOH during and after smoking marijuana. J Anal Toxicol 1992b, 16(5), 276–282.
Johansson, E.; Halldin, M.M.; Agurell, S.; Hollister, L.E.; and Gillespie, H.K. Terminal elimination plasma half-life of delta 1-tetrahydrocannabinol (delta 1-THC) in heavy users of marijuana. Eur J Clin Pharmacol 1989, 37(3), 273–277.
Jones, R.T.; Benowitz, N.L.; and Herning, R.I. Clinical relevance of cannabis tolerance and dependence. J Clin Pharmacol 1981, 21,143S–152S.
Koob, G.F. Neural mechanisms of drug reinforcement. Ann. N Y Acad Sci 1992, 654, 171–191.
Lane JD, Phillips-Bute BG. Caffeine deprivation affects vigilance performance and mood. Physiol Behav 1998 65, 171–5.
Lemberger L., Rubin A. The physiologic disposition of marihuana in man, Life Sci. 1975,17, 1637–42.
Lemberger L., Silberstein, S.D., Axelrod, J., Kopin, I.J. Marihuana: studies on the disposition and metabolism of delta-9-tetrahydrocannabinol in man. Science 1970, 170, 1320–1322.
Lemberger L., Weiss, J.L., Watanabe, A.M., Galanter, I.M., Wyatt, R.J., Cardon, P. V. Delta-9-tetrahydrocannabinol: temporal correlation of the psychological effects and blood levels after various routes of administration. New Eng. J. Med. 1972a, 286(13), 685–688.
Lemberger, L., Crabtree, R.E., Rowe, H.M. 11-Hydroxy-)9-tetrahydrocannabinol: pharmacology, disposition and metabolism of a major metabolite of marihuana in man. Science 1972b, 177, 62–63.
Martin, B.R.; Mechoulam, R., Razdan, R.K. Discovery and characterization of endogenous cannabinoids. Life Sci. 1999, 65, 573–595.
Matsuda, L.A., Lolait, S.J., Brownstein, M.J., Young, A.C., Bonner, T.I. Structure of a cannabinoid receptor and functional expression of the cloned cDNA. Nature 1990, 346, 561–564.
Mechoulam, R. Cannabinoid chemistry. In Mechoulam, R. (ED.) Marijuana, pp.2–88 (New York, NY, Academic Press, Inc.), 1973.
Monitoring the Future. National Results on Adolescent Drug Use. Overview of 1999 Key findings, 1999. Department of Health and Human services. National Institute on Drug Abuse. Rockville, MD. (*http://monitoringthe*future.org)
National Institutes of Health (NIH). Workshop on the medical Utility of Marijuana, February 19–20, 1997. (*www.nih.gov/news/medmarijuana/MedicalMarijuana.htm*)
NHSDA. Summary of Findings from the 1999 National Household Survey on Drug Abuse. Office of Applied Studies. Department of Health and Human services. Substance Abuse and Mental Health Services Administration. National Clearinghouse for Alcohol and Drug information. Rockville, MD.
Office of National Drug Control Policy. The National Drug Control Strategy: 2000 Annual Report. Superintendent of Documents, Mail Stop: SSOP, Washington, DC.
Oviedo, A., Glowa, J., Herkenham, M. Chronic cannabinoid administration alters cannabinoid receptor binding in rat brain: a quantitative autoradiographic study. Brain Res. 1993, 616, 293–302.
Rinaldi-Carmona, M., Barth F., Heaulme, M., Shire, D., Calandra, B., Congy, C., Martinez, S., Maruani, J., Neliat, G., Caput, D., et al. SR141716A, a potent and selective antagonist of the brain cannabinoid receptor. FEBS Letters 1994, 350, 240–244.
Rinaldi-Carmona M, Barth F, Millan J, Derocq JM, Casellas P, Congy C, Oustric D, Sarran M, Bouaboula M, Calandra B, Portier M, Shire D, Breliere JC, Le Fur GL, SR 144528, the first potent and selective antagonist of the CB_2 cannabinoid receptor. J Pharmacol Exp Ther. 1998 , 284(2), 644–50.
Rodriguez de Fonseca F, Gorriti, M.A., Fernandez-Ruiz, J.J., Palomo, T., Ramos, J.A. Downregulation of rat brain cannabinoid binding sites after chronic delta 9-tetrahydrocannabinoil treatment. Phamacol. Biochem. Behav. 1994, 47 (1), 33–40.
Ross, S.A. and ElSohlyy, M.A. Constituents of Cannabis Sativa L. XXVIII. A review of the natural constituents:1980–1994. Zagazig J. Pharm. Sci. 1995, 4 (2), 1–10.
Sanudo-Pena M.C., Tsou, K., Delay, E.R., Hohman, A.G., Force, M., Walker, J.M. Endogenous cannabinoids as an aversive or counter-rewarding system in the rat. Neurosci. Lett., 223, 125–128, 1997.
Treatment Episode Data Set (TEDS): 1993–1998. National Admissions to Substance Abuse Treatment Services. Department of Health and Human services. Substance Abuse and Mental Health Services Administration. National Clearinghouse for Alcohol and Drug information. Rockville, MD.
Wesson, D.R.; Washburn, P. Current patterns of drug abuse that involve smoking. In Research Findings on Smoking of Abused Substances, Chiang, C.N.; Hawks, R.L. (ED.) NIDA Research Monograph, 99:5–11, 1990.

Additional Scientific Data Considered by the Drug Enforcement Administration in Evaluating Jon Gettman's Petition To Initiate Rulemaking Proceedings To Reschedule Marijuana

Drug and Chemical Evaluation Section, Office of Diversion Control, Drug Enforcement Administration, March 2001

Introduction

On July 10, 1995, Jon Gettman petitioned the Drug Enforcement Administration (DEA) to initiate rulemaking proceedings to reschedule marijuana. Marijuana is currently listed in schedule I of the Controlled Substances Act (CSA).

Mr. Gettman proposed that DEA promulgate a rule stating that ''there is no scientific evidence that [marijuana has] sufficient abuse potential to warrant schedule I or II status under the [CSA].''

In accordance with the CSA, DEA gathered the necessary data and, on December 17, 1997, forwarded that information along with Mr. Gettman's petition to the Department of Health and Human Services (HHS) for a scientific and medical evaluation and scheduling recommendation. On January 17, 2001, HHS forwarded to DEA its scientific and medical evaluation and scheduling recommendation. The CSA requires DEA to determine whether the HHS scientific and medical evaluation and scheduling recommendation and ''all other relevant data'' constitute substantial evidence that the drug should be rescheduled as proposed in the petition. 21 U.S.C. 811(b). This document contains an explanation of the ''other relevant data'' that DEA considered.

In deciding whether to grant a petition to initiate rulemaking proceedings, DEA must consider eight factors specified in 21 U.S.C. 811(c). The information contained in this document is organized according to these eight factors.

(1) Its Actual or Relative Potential for Abuse

Evaluation of the abuse potential of a drug is obtained, in part, from studies in the scientific and medical literature. There are many preclinical indicators of a drug's behavioral and psychological effects that, when taken together, provide an accurate prediction of the human abuse liability. Specifically, these include assessments of the discriminative stimulus effects, reinforcing effects, conditioned stimulus effect, effects on operant response rates, locomotor activity, effects on food intake and other behaviors, and the development of tolerance and dependence (cf., Brady *et al.,* 1990; Preston *et al.,* 1997). Clinical studies of the subjective and reinforcing effects in substance abusers, interviews with substance abusers, clinical interviews with medical professionals, and epidemiological studies provide quantitative data on abuse liability in humans and some indication of actual abuse trends (cf., deWit and Griffiths, 1991).

Evidence of actual abuse and patterns of abuse are obtained from a number of substance abuse databases, and reports of diversion and trafficking. Specifically, data from Drug Abuse Warning Network (DAWN), Poison

Control Centers, System To Retrieve Investigational Drug Evidence (STRIDE), seizures and declarations from U.S. Customs, DEA Drug Theft Reports and other diversion and trafficking data bases are indicators of the pattern, scope, duration and significance of abuse.

Reinforcing Effects in Animals

As described by the petitioner, the preponderance of preclinical studies using animal models had, to recently, shown that Δ^9-THC had minimal activity in behavioral paradigms predictive of reinforcing efficacy (*i.e.,* self-administration paradigms; Harris *et al.,* 1974; Pickens et al., 1973; Deneau and Kaymakcalan, 1971). In general, Δ^9-THC had been shown to be relatively ineffective in maintaining self-administration behavior by either the intravenous or oral routes (Kaymakcalan, 1973; Harris *et al.,* 1974; Carney *et al.,* 1977; Mansbach *et al.,* 1994). Under limited experimental parameters, Δ^9-THC self-administration was demonstrated after animals were either first trained to self-administer PCP, after a chronic cannabinoid history was established or when maintained at 80% reduced body weight (Pickens *et al.,* 1973; Deneau and Kaymakcalan, 1971; Takahashi and Singer, 1979). However, Tanda, Munzar and Goldberg of the Intramural Preclinical Pharmacology Section of the NIDA (2000) have clearly demonstrated that THC can act as a strong reinforcer of drug-taking behavior in an experimental animal model, the squirrel monkey, as it does in humans. The self-administration behavior was comparable in intensity to that maintained by cocaine under identical conditions and was obtained using a range of doses similar to those self-administered by humans smoking a single marijuana cigarette.

Although the neuropharmacological actions of Δ^9-THC suggest a powerful brain substrate underlying its rewarding and euphorigenic effects, behavioral studies of Δ^9-THC's rewarding effects had been inconclusive. Several reasons for the previous inability by a number of laboratories to demonstrate self-administration of Δ^9-THC in animals may be its relatively slow-onset, its long-lasting behavioral effects and its insolubility in physiological saline or water for injection (Mansbach *et al.,* 1994). Similar findings have been found in the animal literature with nicotine—an avid reinforcer in humans. The strength of THC, like nicotine, as a reinforcer in animals may be more dependent on supplementary strengthening by ancillary stimuli than is the case for other drugs (cf. Henningfield, 1984).

In other behavioral and pharmacological tests used to assess reinforcing efficacy, Δ^9-THC produced significant effects. Specifically, Δ^9-THC augments responding for intracranial self-stimulation by decreasing the reinforcing threshold for brain stimulation reward. It also dose-dependently enhances dopamine efflux in forebrain nuclei associated with reward and this enhanced efflux occurs locally in the terminal fields within brain reward pathways (Gardner and Lowinson, 1991; Gardner, 1992; Chen *et al.,* 1993, 1994). In conditioned place preference procedures, Δ^9-THC (2.0 and 4.0 mg/kg, i.p.) produced significant dose-dependent increases in preference for the drug paired chamber, the magnitude of which was similar to that seen with 5.0 mg/kg cocaine and 4.0 mg/kg morphine (Leprore *et al.,* 1995). However, Δ^9-THC also produced a conditioned place aversion and conditioned taste aversion (Leprore *et al.,* 1995; Parker and Gillies, 1995). The development of taste aversions with drug administrations that also produce place preferences have been described as somewhat of a ''drug paradox'' by Goudie; however, this has been found to occur within the ''therapeutic window'' of all known drugs of abuse (cf Goudie, 1987). Goudie has concluded that drugs can possess both reinforcing and aversive properties at the same doses. This fact may underlie the reciprocal relationship between the behavioral effects of THC, CBD, and THC+CBD combinations, discussed below.

Drug Discrimination in Animals

Preclinical drug discrimination studies with Δ^9-THC are predictive of the subjective effects of cannabinoid drugs in humans and serve as animal models of marijuana and THC intoxication in humans (Balster and Prescott, 1992; Wiley *et al.,* 1993b, 1995). In a variety of species it has been found that Δ^9-THC shares discriminative stimulus effects with cannabinoids that bind to CNS cannabinoid receptors with high affinity (Compton *et al.,* 1993; Järbe *et al.,* 1989; Gold *et al.,* 1992; Wiley *et al.,* 1993b, 1995b; Järbe and Mathis, 1992) and that are psychoactive in humans (Balster and Prescott, 1992). Furthermore, recent studies show that the discriminative stimulus effects of Δ^9-THC are mediated via the CB_1 receptor subtype (Pério *et al.,* 1996).

Chronic Δ^9-THC administration to rats produced tolerance to the discriminative stimulus effects of Δ^9-THC, but not to its response rate disruptions. Specifically, tolerance to the stimulus effects of Δ^9-THC increased 40-fold when supplemental doses of up to 120 mg/kg/day Δ^9-THC were administered under conditions of suspended training (Wiley *et al.,* 1993a).

The discriminative stimulus effects of Δ^9-THC appear to be pharmacologically specific as non-cannabinoid drugs typically do not elicit cannabimimetic effects in drug discrimination studies (Browne and Weissman, 1981; Balster and Prescott, 1992, Gold *et al.,* 1992; Barrett *et al.,* 1995; Wiley *et al.,* 1995a). Furthermore, these studies show that high doses of Δ^9-THC produce marked response rate disruption, immobility, ataxia, sedation and ptosis in rhesus monkeys and rats (Wiley *et al.*, 1993b; Gold *et al.*, 1992; Martin *et al.*, 1995).

Clinical Abuse Potential

Both marijuana and THC can serve as positive reinforcers in humans. Marijuana and Δ^9-THC produced profiles of behavioral and subjective effects that were similar regardless of whether the marijuana was smoked or taken orally, as marijuana in brownies, or orally as THC-containing capsules, although the time course of effects differed substantially. There is a large clinical literature documenting the subjective, reinforcing, discriminative stimulus, and physiological effects of marijuana and THC and relating these effects to the abuse potential of marijuana and THC (*e.g.,* Chait *et al.*, 1988; Lukas *et al.*, 1995; Kamien *et al.*, 1994; Chait and Burke, 1994; Chait and Pierri, 1992; Foltin *et al.*, 1990; Azorlosa *et al.*, 1992; Kelly *et al.*, 1993, 1994; Chait and Zacny, 1992; Cone *et al.*, 1988; Mendelson and Mello, 1984).

These listed studies represent a fraction of the studies performed to evaluate the abuse potential of marijuana and THC. In general, these studies demonstrate that marijuana and THC dose-dependently increases heart rate and ratings of ''high'' and ''drug liking'', and alters behavioral performance measures (*e.g.,* Azorlosa *et al.,* 1992; Kelly *et al.,* 1993, 1994; Chait and Zacny, 1992; Kamien *et al.,* 1994; Chait and Burke, 1994; Chait and Pierri, 1992; Foltin *et al.,* 1990; Cone *et al.,* 1988; Mendelson and Mello, 1984). Marijuana also serves as a discriminative stimulus in humans and produces euphoria and alterations in mood. These subjective changes were used by the subjects as the basis for the discrimination from placebo (Chait *et al.,* 1988).

In addition, smoked marijuana administration resulted in multiple brief episodes of euphoria that were paralleled by rapid transient increases in EEG alpha power (Lukas *et al.,* 1995);

these EEG changes are thought to be related to CNS processes of reinforcement (Mello, 1983).

To help elucidate the relationship between the rise and fall of plasma THC and the self-reported psychotropic effects, Harder & Rietbrock (1997) measured both the plasma levels of THC and the psychological ''high'' obtained from smoking a marijuana cigarette containing 1% THC. As can be seen from these data, a rise in plasma THC concentrations results in a corresponding increase in the subjectively reported feelings of being ''high''. However, as THC levels drop the subjectively reported feelings of ''high'' remain elevated. The subjective effects seem to lag behind plasma THC levels. Similarly, Harder and Rietbrock compared lower doses of 0.3% THC-containing and 0.1% THC-containing cigarettes in human subjects.

As can be clearly seen by these data, even low doses of marijuana, containing 1%, 0.3% and even 0.1% THC, typically referred to as ''non-active'', are capable of producing subjective reports and physiological markers of being ''high'.

THC and its major metabolite, 11-OH-THC, have similar psychoactive and pharmacokinetic profiles in man (Wall *et al.,* 1976; DiMarzo *et al.,* 1998; Lemberger *et al.,* 1972). Perez-Reyes *et al.* (1972) reported that THC and 11-OH-THC were equipotent in generating a ''high'' in human volunteers. However, the metabolite, 11-OH-THC, crosses the blood-brain barrier faster than the parent THC compound (Ho *et al.,* 1973; Perez-Reyes *et al.,* 1976). Therefore, the changes in THC plasma concentrations in humans may not be the best predictive marker for the subjective and physiological effects of marijuana in humans. Cocchetto et al. (1981) have used hysteresis plots to clearly demonstrate that plasma THC concentration is a poor predictor of simultaneous occurring physiological (heart rate) and psychological (''high'') pharmacological effects. Cocchetto et al. demonstrated that the time course of tachycardia and psychological responses lagged behind the plasma THC concentration-time profile. As recently summarized by Martin & Hall (1997, 1998)

> There is no linear relationship between blood [THC] levels and pharmacological effects with respect to time, a situation that hampers the prediction of cannabis-induced impairment based on THC blood levels (p90).

Physical Dependence in Animals

There are reports that abrupt withdrawal from Δ^9-THC can produce a mild spontaneous withdrawal syndrome in animals, including increased motor activity and grooming in rats, decreased seizure threshold in mice, increased aggressiveness, irritability and altered operant performance in rhesus monkeys (cf., Pertwee, 1991). The failure to observe profound withdrawal signs following abrupt discontinuation of the drug may be due to Δ^9-THC's long half-life in plasma and slowly waning levels of drug that continue to permit receptor adaptation.

Recently the discovery of a cannabinoid receptor antagonist demonstrates that a profound precipitated withdrawal syndrome can be produced in Δ^9-THC tolerant animals after twice daily injections (Tsou *et al.,* 1995) or continuous infusion (Aceto *et al.,* 1995, 1996).

Physical Dependence in Humans

Signs of withdrawal in humans have been demonstrated after studies with marijuana and Δ^9-THC. Although the intensity of the withdrawal syndrome is related to the daily dose and frequency of administration, in general, the signs of Δ^9-THC withdrawal have been relatively mild (cf., Pertwee, 1991). This withdrawal syndrome has been compared to that of short-term, low dose treatment with opioids, sedatives, or ethanol, and includes changes in mood, sleep, heart rate, body temperature, and appetite. Other signs such as irritability, restlessness, tremor, mild nausea, hot flashes and sweating have also been noted (cf., Jones, 1980, 1983).

Chait, Fischman, & Schuster (1985) have demonstrated an acute withdrawal syndrome or ''hangover'' occurring approximately 9 hours after a single marijuana smoking episode. Significant changes occurred on two subjective measures and on a time production task. In 1973, Cousens & DiMascio reported a similar ''hangover'' effect from acute administrations of Δ^9-THC. The hangover phenomenon or continued ''high'', in the Cousens & DiMascio study, occurred 9 hrs after drug administration and was associated with some residual temporal disorganization, as well. These residual or hangover effects may mimic the withdrawal syndrome, both qualitatively and quantitatively, which is expressed after chronic marijuana exposure. This acute hangover may reflect a true acute withdrawal syndrome similar to that experienced from high acute alcohol intake. The presence of an acute withdrawal syndrome after drug administration has been suggested to represent a physiological compensatory rebound by which chronic administration of the drug will eventually potentiate and produce dependence and the potential for continued abuse (Gauvin, Cheng & Holloway, 1993).

Crowley *et al.* (1998) screened marijuana users for DSM–IIIR dependence criteria. Of the 165 males and 64 female patients that met the criteria, 82.1% were found to have co-morbid conduct disorders; 17.5% had major depression; and 14.8% had a diagnosis of attention-deficit/hyperactivity disorder. These results also showed that most patients claimed to have ''serious problems'' from cannabis use. The data also indicated that for adolescents with conduct problems, cannabis use was not benign, and that the drug served as a potent reinforcer for further cannabis usage, producing dependence and withdrawal.

Kelly & Jones (1992) quantified concentrations of THC and its metabolites in both plasma and urine after a 5 mg intravenous dose of THC was administered to frequent and infrequent marijuana smokers. The frequent smokers were users who smoked marijuana almost daily for at least two years. The infrequent smokers were users who smoked marijuana no more than two to three times per month but had done so for at least two years. Pharmacokinetic parameters after intravenously administered THC revealed no significant differences between frequent and infrequent marijuana users on area under the time-effect curve (AUC), volume of distribution, elimination half-lives of parent THC and metabolites in plasma and urine. There were also no group differences in metabolic or renal clearances. The authors concluded that there was no evidence for metabolic or dispositional tolerance between the two groups of subjects. Kelly and Jones also reported that tolerance was not evident in heart rate, diastolic blood pressure, skin temperature, and the degree of psychological ''high'' from the i.v. administration of THC.

In two separate reports, Haney et al. have recently described abstinence symptoms of an acute withdrawal syndrome following high (30 mg q.i.d.) and low (20 mg q.i.d) dose administrations of oral THC (Haney et al., 1999a) and following 5 puffs of high (3.1%) and low (1.8%) THC-containing smoked marijuana cigarettes (Haney et al., 1999b). Abstinence from oral THC increased ratings of ''anxious'', ''depressed'', and ''irritable'', and decreased the reported quantity and quality of sleep and decreased food intake by 20–30% compared to baseline. Abstinence from as low as 5 controlled puffs of active marijuana smoking increased ratings of ''anxious'', ''irritable'' and ''stomach pain'', and

significantly decreased food intake. The 5 controlled puffs of 5 second duration each were drawn from 2 separate marijuana cigarettes (3 puffs from one, 2 puffs from the other. The smoke was held for 40 seconds and then exhaled. All subjects reported significant increases on subjective measures of ''high'', ''good drug effect'', and ''stimulated'', as well as ''mellow'', ''content'', and ''friendly'' as a result of this limited and controlled draw of THC. Both of these studies have delineated a withdrawal syndrome from concentrations of THC significantly lower than those reported in any other previous study and, for the first time, clearly identified a marijuana withdrawal syndrome detected at low levels of THC exposure that do not produce tolerance. The abstinence syndrome was not limited to subjective state changes but was also quantified using a cognitive/memory test battery.

In a related study, Khouri *et al* (1999) found that long-term heavy marijuana users became more aggressive during abstinence from marijuana than did former or infrequent users. Previous dependence studies have relied largely on patients' subjective reports of a range of symptoms. Khouri *et al.* examined a single symptom—aggression. The authors concluded that marijuana abstinence is associated with unpleasant behavioral symptoms that may contribute to continued marijuana use.

Kouri & Pope (2000) examined three groups of marijuana users during a 28-day supervised abstinence period. Current marijuana users experienced significant increases in anxiety, irritability, physical tension, and physical symptoms and decreases in mood and appetite during marijuana withdrawal. These symptoms were most pronounced during the initial 10 days of abstinence, bust some were present for the entire 28-day withdrawal period. The findings from this study reveal that chronic heavy users of marijuana experience a number of withdrawal symptoms during abstinence and clearly demonstrate a ''marijuana dependence syndrome'' in humans.

These data suggest that dependence on THC may in fact be an important consequence of repeated, daily exposure to cannabinoids and that daily marijuana use may be maintained, at least in part, by the alleviation of abstinence symptoms. Relevant to the present petition, the Haney *et al.* study is the first report demonstrating this syndrome with extremely low concentrations of THC.

Results of THC Dose Comparison Studies

There are reports in the scientific literature that evaluated dose-related subjective and reinforcing effects of Cannabis sativa in humans. These studies have assessed the subjective and reinforcing effects of cannabis cigarettes containing different potencies of THC and/or which have manipulated the THC dose by varying the volume of THC smoke inhaled (Azorlosa *et al.*, 1992; Lukas *et al.*, 1995; Chait *et al.*, 1988; Chait and Burke, 1994; Kelly *et al.*, 1993).

Chait *et al.* (1988) studied the discriminative stimulus effects of smoked marijuana cigarettes containing THC contents of 0%, 0.9%, 1.4%, 2.7%. Marijuana smokers were trained to discriminate smoked marijuana from placebo using 4 puffs of a 2.7%-THC cigarettes. Subjective ratings of ''high'', and physiological measures (*i.e.,* heart rate) were significantly and dose-dependently increased after smoking the 0.9%, 1.4%, 2.7%.

Marijuana cigarettes containing 1.4% THC completely substituted for 2.7%-THC on drug identification tasks, however, 0.9%-THC did not. The authors found that the onset of discriminative stimulus effects was within 90 seconds after smoking began (after the first two puffs). Since the 1.4%-THC cigarette substituted for 2-puffs of the 2.7%-THC cigarette, the authors estimate that an inhaled dose of THC as low as 3 mg can produce discriminable subjective effects.

Similarly, Lukas *et al.* (1995) reported that marijuana cigarettes containing either 1.26% or 2.53% THC produced significant and dose-dependent increases in level of intoxication and euphoria in male occasional marijuana smokers. Four of the six subjects that smoked the 1.26%-THC cigarette reported marijuana effects and 75% of these subjects reported euphoria. All six of the subjects that smoked 2.53% THC reported marijuana effects and euphoria. Peak levels of self-reported intoxication occurred at 15 and 30 minutes after smoking and returned to control levels by 90–105 minutes. There was no difference between latency to or duration of euphoria after smoking either the 1.26% or 2.53% THC cigarettes. The higher dose-marijuana cigarette produced a more rapid onset and longer duration of action than the lower dose marijuana cigarette (1.26% THC). Plasma THC levels peaked 5–10 minutes after smoking began; the average peak level attained after the low- and high-dose marijuana cigarette was 36 and 69 ng/ml respectively.

In order to determine marijuana dose-effects on subjective and performance measures over a wide dose range, Azorlosa *et al.* (1992) evaluated the effects of 4, 10, or 25 puffs from marijuana cigarettes containing 1.75 or 3.55% THC in seven male moderate users of marijuana. Orderly dose-response curves were produced for subjective drug effects, heart rate, and plasma concentration, as a function of THC content and number of puffs. After smoking the 1.75% THC cigarette, maximal plasma THC levels were 57 ng/ml immediately after smoking, 18.3 ng/ml 15 minutes after smoking, 10.3 ng/ml 30 minutes after smoking, and 7.7 ng/ml 45 minutes after smoking.

The study also showed that subjects could smoke more of the low THC cigarette to produce effects that were similar to the high THC dose cigarette (Azorlosa *et al.*, 1992). There were nearly identical THC levels produced by 10-puff low-THC cigarette (98.6 ng/ml) and 4-puff high THC cigarette (89.4 ng/ml). Similarly, the subjective effects ratings, including high, stoned, impaired, confused, clear-headed and sluggish, produced under the 10 puff low- and high-THC and 25 puff low-THC conditions did not differ significantly from each other.

As with most drugs of abuse, higher doses of marijuana are preferred over lower dose. Although not preferred, these lower doses still produce cannabimimetic effects. Twelve regular marijuana smokers participated in a study designed to determine the preference of a low potency (0.64%-THC) vs. a high potency (1.95%-THC) marijuana cigarette (Chait and Burke, 1994). The subjects first sampled the marijuana of two different potencies in one session, then chose which potency and how much to smoke. During sampling sessions, there were significant dose-dependent increases in heart rate and subjective effects, including ratings of peak ''high'', strength of drug effects, stimulated, and drug liking. During choice sessions, the higher dose marijuana was chosen over the lower dose marijuana on 87.5% of occasions. Not surprising, there was a significant positive correlation between the total number of cigarettes smoked and the ratings of subjective effects, strength of drug effect, drug ''liking'', expired air carbon monoxide, and heart rate increases. The authors state it is not necessary valid to assume that the preference observed in the present study for the high-potency marijuana was due to greater CNS effects from its higher THC content. The present study found that the low- and high-potency marijuana cigarettes also differ on

several sensory dimensions; the high-potency THC was found to be reported as ''fresher'' and ''hotter''. Other studies found that marijuana cigarettes containing different THC contents varied in sensory dimensions (cf., Chait *et al.*, 1988; Nemeth-Coslett *et al.*, 1986).

As summarized by Martin & Hall for the United Nations only a small amount of cannabis (*e.g.* 2–3 mg of available THC) is required to produce a brief pleasurable high for the occasional user and a single joint may be sufficient for two or three individuals. Using these data and those of Harder & Reitbroch (1997, above), a one gram cigarette containing 1% THC containing cannabis, would contain 10 mg of THC—a dose well capable of producing a social high.

Carlini *et al.* (1974) examined 33 subjects who smoked marijuana cigarettes with different ratios of constituent cannabinoids. The plant containing 0.82% THC produced larger than expected results based on the estimates from the THC content.

Smoking a 250 mg cigarette containing 5.0 mg of Δ^9-THC induced more reactions graded 3 and 4 than 10 or 20 mg of Δ^9-THC. It was further observed that the psychological effects (subjective ''high'') started around 10 min after the end of the inhalation, and reached a maximum 20 to 30 min later, subsiding within 1 to 3 hrs. The peak of psychological disturbances, therefore, did not coincide in time with the peak of pulse rate effects. Carlini *et al.,* suggested that other constituents of the marijuana were interacting synergistically with the THC to potentiate the subjective response induced by the smoking of the cigarette. Karniol and colleagues (1973, 1974) have clearly demonstrated that cannabidiol (CBD) blocks some of the effects induced by THC, such as increased pulse rates and disturbed time perception. More importantly, CBD blocked some of the psychological effects of THC, but not by altering the quantitative or intensity of the psychological reactions. CBD seemed better able to block the aversive effects of THC. CBD changed the symptoms reported by the subjects in such a way that the anxiety component produced by THC administration was actually reduced. The animal subjects of one study showed greater analgesia scores with a CBD+THC combination (1973) and the human subjects from the other study (1974) showed less anxiety and panic but reported more pleasurable effects. CBD may be best seen as an ''entourage'' compound (Mechoulam, Fride, DiMarzo, 1998) which is administered along with THC and results in a functional potentiation of THC's behavioral and subjective effects. This potentiation can be in both the intensity and/or duration of the high induced by marijuana. According to Paris & Nahas (1984) the CBD:THC ratio in industrial or fiber type hemp is 2:1. Relevant to the current petition, the CBD:THC ratio producing the greatest increase in euphoria in the Karniol, *et al.* studies was 2:1 (60:30 mg).

Jones & Pertwee (1972) were first to report that the presence of cannabidiol inhibited the metabolism of THC and its active metabolite. These data were soon replicated by Nilsson *et al.,* (1973). Bronheim *et al.,* (1995) examined the effects of CBD on the pharmacokinetic profile of THC content in both blood and brains of mice. CBD pretreatments produced a modest elevation in THC-blood levels; area under the kinetics curve of THC was increased by 50% as a function of decreased clearance. CBD pretreatments also modestly increased the C_{max}, AUC, and half-life of the major THC metabolites in the blood. The THC kinetics function showed a 7- to 15-fold increase in the area under the curve, a 2- to 4-fold increase in the half-life, as well as the t_{max}. CBD pretreatments resulted in large increases in area under the curves and half-lives of all the THC metabolites in the mice brains. The inhibition of the metabolism of THC and its psychoactive metabolites by CBD may underlie the potentiation in the subjective effects of THC by CBD in humans.

In addition to THC, hemp material contains a variety of other substances (*e.g.,* Hollister, 1974), including other cannabinoids such as cannabidiol (CBD) and cannabinol (CBN). One comprehensive review described the activities of 300 cannabinoid compound in preclinical models (Razdan, 1986). Since CBD is always present in preparations of cannabis, it may represent a high CBD:THC ratio in the case of low THC cannabis. Therefore, it is important to understand the interactions of cannabidiol and Δ^9-THC.

Structure-activity studies of cannabinoid compounds characterized cannabidiol in relationship to Δ^9-THC and other cannabinoids (Martin et al., 1981; Little *et al.,* 1988). These and other studies have found that cannabidiol was inactive and did not produce neuropharmacological effects or discriminative stimulus, subjective effects and behavioral effects predictive of psychoactive subjective effects (Howlett, 1987; Howlett *et al.,* 1992; c.f., Hiltunen and Järbe, 1986; Perez-Reyes *et al.,* 1973; Zuardi *et al.,* 1982; Karniol *et al.,* 1974).

Other studies have reported that cannabidiol has cannabinoid properties, including anticonvulsant effects in animal and human models (Consroe *et al.,* 1981; Carlini & Cunha, 1981; Doyle and Spence, 1995), hypnotic effects (Monti, 1977), anxiolytic effects (Musty, 1984; Onaivi, Geen, & Martin, 1990; Guimarães *et al.,* 1990; 1994) and rate-decreasing effects on operant behavior (Hiltunen *et al.,* 1988).

Experiments with cannabidiol in combination with THC have found that certain behavioral responses induced by THC (*i.e.,* operant, schedule-controlled responding) were attenuated by cannabidiol (Borgen and Davis, 1974; Brady and Balster, 1980; Consroe *et al.,* 1977; Dalton *et al.,* 1976; Kraniol and Carlini, 1973; Karniol *et al.,* 1974; Welburn *et al.,* 1976; Zuardi and Karniol, 1983; Zuardi *et al.,* 1981, 1982; Hiltunen *et al.,* 1988). However, other affects produced by THC are augmented or prolonged by the combined administration of CBD and THC or marijuana extract (Chesher and Jackson, 1974; Hine *et al.,* 1975a,b; Fernandes *et al.,* 1974; Karniol and Carlini, 1973; Musty and Sands, 1978; Zuardi and Karniol, 1983; Zuardi *et al.,* 1984). Still other studies did not report any behavioral interaction between the CBD and THC (Bird *et al.,* 1980; Browne and Weissman, 1981; Hollister and Gillespie, 1975; Järbe and Henricksson, 1974; Järbe *et al.,* 1977; Mechoulam *et al.,* 1970; Sanders *et al.,* 1979; Ten Ham and DeLong, 1975).

A study to characterize the interaction between CBD and THC was conducted using preclinical drug discrimination procedures. Rats and pigeons trained to discriminate the presence or absence of THC, and tested with CBD administered alone and in combinations with THC (Hiltunen and Järbe, 1986).

Specifically, in rats trained to discriminate 3.0 mg/kg, i.p. THC, CBD (30.0 mg/kg) was administered alone and in combination with THC (0.3 and 1.0 mg/kg, i.p.). In pigeons trained to discriminate 0.56 mg/kg, i.m. THC, CBD (17.5 mg/kg) was administered alone and in combination with THC (0.1, 0.3, and 0.56 mg/kg, i.m.). CBD prolonged the discriminative stimulus effects of THC in rats, but did not change the time-effect curve for THC in pigeons. In pigeons, the administration of CBD did not produce any differential effect under a fixed ratio schedule of reinforcement (Hiltunen and Järbe, 1986).

These data suggest that CBD may somehow augment or prolong the actions of THC in rats and had no effect in pigeons. In the present study, the CBD/THC ratios ranged from 30:1 to 100:1 in rats and enhanced the stimulus

effects of THC. However, similar CBD/THC ratios in pigeons (31:1, 58:1 and 175:1) did not result in any changes to THC's discriminative stimulus or response rate effects (Hiltunen and Järbe, 1986).

It should be noted that cannabidiol can be easily converted to delta-9- and delta-8-tetrahydrocannabinol. Even industrial hemp plant material (leaves), containing high concentrations of CBD, can be treated in clandestine laboratories to convert the CBD to delta-9-tetrahydrocannabinol (Mechoulam, 1973) converting a supposedly innocuous weed into a potent smoke product.

In conclusion, the ''entourage'' compound, cannabidiol, does contribute to all of the effects ascribed to THC, however it also appears to lack cannabimimetic properties. However, there is no credible scientific evidence that CBD is a pharmacological antagonist at the cannabinoid receptor (Howlett, Evans, & Houston, 1992). There is clear evidence that CBD can functionally antagonize some of the aversive effects of THC (Dewey, 1986). The data from the scientific literature cited above, clearly demonstrate the ability of CBD to modify some very specific effects of THC. Most importantly, relative to the euphorigenic effects of THC (which contributes to its abuse liability), CBD appears to potentiate the psychological or subjective effects of THC by potentiating the blood and brain THC and 11-OH-THC levels and by functionally blocking the aversive (anxiety-like) properties of THC.

Abuse Liability Summary

Preclinical and clinical experimental data demonstrate that marijuana and ''Δ^9-THC have similar abuse liabilities (*i.e.,* drug discrimination, self-administration, subjective effects). Both preclinical and clinical studies show that discontinuation of either marijuana or ''Δ^9-THC administration produces a mild withdrawal syndrome. The effects of THC are dose-dependent and several studies have found that low-potency THC is behaviorally active and can produce cannabimimetic-like subjective and physiological effects.

Actual Abuse

There are dozens of data collection and reporting systems that are useful for monitoring the United States' problem with abuse of licit and illicit substances. These data collection and reporting systems provide quantitative data on many factors related to abuse of a particular substance, including incidence, pattern, consequence and profile of the abuser of specific substances (cf., Larsen *et al.,* 1995).

Evidence of actual abuse is defined by episodes/mentions in the databases indicative of abuse/dependence. Some of the databases that are utilized by DEA to provide data relevant to actual abuse of a substance include the Drug Abuse Warning Network (DAWN), National Household Survey on Drug Abuse, Monitoring the Future survey, FDA's Spontaneous Adverse Events Reports, the American Association of Poison Control Centers database and reports of the Community Epidemiology Work Group (CEWG).

Drug trafficking and diversion data provide strong evidence that a drug or other substance is being abused. In order to determine the pattern, incidence, and consequences of abuse and the demographics of abusers of a particular substance to be controlled, DEA relies on data collected from a number of sources, including the United States government as well as state and local law enforcement groups. Information from these sources often provides a first indication of an emerging pattern of abuse of a particular drug or substance, and when taken together with other data sources provide strong evidence that can be used in determining a substance's placement in the schedules listed in the CSA.

The evidence from epidemiological studies conclude that marijuana use alone and in combination with other illicit drugs is increasing. The most recent ''Monitoring the Future Study'', documented increases in lifetime, annual and current (within the past 30 days) and daily use of marijuana by eighth and tenth graders; this increasing trend began in the early 1990's.

Similarly, according the NIDA's ''National Household Survey'', marijuana use is increasing with the greatest increase among the younger age groups (12–17 years of age). The frequency of marijuana use in the past year increases significantly among 12–17 year olds. This survey also found that youths who used marijuana at least once in their lives were more likely to engage in violent or other antisocial behaviors.

Marijuana is the most readily available illicit drug in the United States. Cannabis is cultivated in remote locations and frequently on public lands. Major domestic outdoor cannabis cultivation areas are found in California, Hawaii, Kentucky, New York and Tennessee. Significant quantities of marijuana were seized from indoor cultivation operations; there were 3,532 seizures in 1996 compared to 3,348 seized in 1995. Mexico is the major source of foreign marijuana, along with lesser amounts from Colombia and Jamaica (NNICC, 1996).

Domestically, marijuana is distributed by groups or individuals, ranging from large sophisticated organizations with controlled cultivation and interstate trafficking, to small independent traffickers at the local level.

(2) Scientific Evidence of Its Pharmacological Effects, If Known

Cannabis sativa is unique in that it is the only botanical source of the terpenophenolic substances referred to as cannabinoids which are responsible for the psychoactive effects of Cannabis. There are roughly 60 different cannabinoids found in Cannabis (Nahas, 1984; Murphy & Bartke, 1992; Agurell, Dewey & Willette, 1984) but the psychoactive properties of Cannabis are attributed to one or two of the major cannabinoid substances, namely delta-9-tetrahydrocannabinol and delta-8-tetrahydrocannabinol. In fresh, carefully dried marijuana, up to 95% of their cannabinoids are present as (-)-delta-9-(trans)-tetrahydrocannabinol carboxylic acid (Nahas, 1984; Murphy & Bartke, 1992; Agurell, Dewey & Willette, 1984). The acid form is not psychoactive, but is readily decarboxylated upon heating to yield delta-9-tetrahydrocannabinol (neutral form). Therefore, plant material could be very high in its ''pro-drug'' acid form and very low in neutral form but still be very potent when smoked.

There are two primary factors that influence THC content: genetic predisposition and environmental influences. Genetic factors are considered predominant in determining cannabinoid content, although, fluctuations in weather conditions have greatly enhanced or diminished the THC content.

Paris & Nahas (1984) have admonished that marijuana is not a single uniform plant like many of those encountered in nature, but a rather deceptive weed with several hundred variants. The intoxicating substances prepared from Cannabis vary considerably in potency according to the varying mixtures of different parts of the plant, and according to the techniques of fabrication. According to Paris & Nahas, this basic botanical fact has been overlooked by physicians and educators, who have written about marijuana as a simple, single substance, which uniformly yields a low concentration of a single intoxicant. In addition to changes due to its own genetic plasticity, marijuana has been modified throughout the ages by environmental factors and human manipulations, and is not yet a

stabilized botanical species (Paris & Nahas, 1984).

According to Paris & Nahas (1984) the terminology used by Fetterman *et al.* (1970, 1971) is somewhat misleading, especially with respect to their contention that environmental factors, including climate, are not as important as heredity in determining the cannabinoid content of cutigens. The analyses of Fetterman *et al.,* (1970) were performed according to the technique by Doorenbos *et al.,* (1971) on plant materials from variants that had been cut at the stem beneath the lowest leaves and air-dried. Seeds, bracts, flowers, leaves and small stems were then stripped from the plant. Most of the small stems were removed by a 10-mesh screen, and the seeds were eliminated with a mechanical seed separator. This preparation of marijuana contains less seed and stem than most of the illicit material available in the United States. Cannabinoids were then extracted from the plant material and analyzed by standard techniques.

Other systems of separating Cannabis into drug, intermediate and non-drug type have been developed. These are typically determined by chemical analyses based upon the method described by Doorenbos (1971) which utilizes manicured portions of the Cannabis plant only in determining percent concentration.

Cannabis sativa has been referred to as a widely distributed and unstabilized species. Cannabis exhibits extreme polymorphism (ability to alter, change) in different varieties, dependent upon many factors. For example, there are at least twenty strains which are cultivated for fiber. There have been many attempts to classify Cannabis as a function of intoxicant properties or fiber properties. Such classification efforts are dependent upon the age of the sample. And there is no totally reliable classification system based on a single chemical analysis. The plasticity of the genus has prevented the development of such a system (Turner *et al.* 1980a,b).

In a study where twelve strains of Cannabis were grown out of doors in Southern England (Fairbairn and Liebmann, 1974, Fairbairn *et al.,* 1971), the following were determined:

1. Warm climate are not necessary for high THC content.

2. There is considerable THC content variation within and between plants.

3. Quantitative results of tetrahydrocannabinol concentration (THC) are highly dependent upon the specific plant part sampled, the stage of growth and the size of sample.

4. Certain strains of Cannabis can be THC or cannabidiol (CBD) rich which does not seem to be dependent upon environmental conditions.

5. However, growing the same strain of Cannabis under different lighting conditions can produce plants that range from 2.4 to 4.42% THC concentration (based upon an analysis of the upper leaves). And finally,

6. THC concentration are dramatically higher on dried flowering or vegetative tops of the plants relative to middle or lower portions.

In a similar study on the characterization of Cannabis accessions with regard to cannabinoid content, vis-a-vis other plant characters (deMeijer, 1992), it was determined that:

1. There exists considerable variation within and among accessions for cannabinoid content;

2. Mean cannabinoid content is strongly affected by year of cultivation;

3. There is no strict relationship between chemical and non-chemical traits; and,

4. It is uncommon, but some accessions combine high bark fiber content and considerable psychoactive potency.

In 1993 de Meijer reported the results of a government (Netherlands) funded industrial hemp project designed to investigate the stem quality, yield, and a comparative analysis to wood fibers. deMeijer found that the commercial grade industrial hemp seeds, germplasms derived from <0.3% THC chemovars, demonstrated a significant variation in the average THC content which ranged from 0.06 to 1.77% in the female dry leaf matter. deMeijer concluded by stating,

> Although high bark fiber content does not necessarily exclude high THC content, most fiber cultivars have very low THC content and thus possess no psychoactive potency

While the data from his own study refutes these conclusions he does conclude that the industrial hemp plant does not preclude high THC content.

A review of these and other studies in the scientific literature, indicate that THC concentrations vary within portions of the Cannabis plant (Hanus *et al.,* 1989, 1975). In some studies, the concentration of THC can increase as much as 100% from leafy to flowering portions of the same plant. THC concentrations are known to be elevated on the upper portions of the plant. In a study published by Fairbairn and Liebmann, (1974) there was considerable variations between the flowering tops (bracts, flowers, immature fruits at the ends of shoots) and leafy portions of some specimens. THC content decreases with age and length of leaves (Paris & Nahas, 1984, p 25). The lower, more developed leaves have a low cannabinoid content and the top leaves have a high cannabinoid content, especially when they are associated with the bracts of the plant. Cannabinoids are localized in the upper third of the ''stalk'' and in the flowers. Therefore, the THC content of specific portions of a plant, which on a whole plant basis did not exceed 1%, could significantly exceed this threshold. Very few marijuana users actually ''smoke'' the leaves. It is the colas or the flowering portions of the plants which are utilized and these are exactly the portions of the plant which would be expected to have the highest concentration of THC.

It is clearly recognized that Cannabis presents a high degree of genetic plasticity which results in extreme polymorphism in its different varieties. The hemp first grown in the United States for fiber was of European origin. The type basic to modern American fiber production, known as Kentucky, came originally from China. In Europe, there are five to six varieties with one considered ''exceptional''—the Kymington. The plasticity of the European fiber variety has been clearly shown (Bouquet, 1951; Hamilton, 1912, 1915). European cultigens planted in dry, warm areas of Egypt to supply fiber for rope-making were found to produce, within several generations, plants with high psycho-active ingredients and very little fiber. Cannabis sativa's botanical and chemical characteristics change markedly as a result of environmental factors and human manipulation. Doorenbos *et al.,* (1971) cultivated a Mexican and Turkish variant in Mississippi for three consecutive generations. During that period, the Δ^9-THC content did not change in the Mexican variant but increased in the Turkish variant. In the more controlled environment of a phytotron (light, humidity, and nutrition controlled), Braut-Boucher (1978), Braut-Boucher & Petiard (1981), Braut-Boucher, Paris, & Cosson (1977) and Paris *et al.,* (1975) found that the cannabinoid concentrations rose over a similar three year period. The concentrations rose more sharply in cool environments (22–12°C: day-night) than in warm environments (32–12°C). Some authors have hypothesized that immediate environmentally caused changes are individual plant reactions, whereas the progressive changes over generations are linked with whole populations and constitute a true natural selection. Whether this evolution is caused by a change of genetic equilibrium (caused by the environment), or by a

modification of the genetic capacity (over time), is impossible to say (Paris & Nahas, 1984).

In 1974 through 1976 the University of Mississippi cultivated 7 variants of 12 Cannabis plants discovered and collected in 1973 from different areas of Mexico. Cannabinoid content was analyzed weekly during the cultivation period. Turner, Elsohly, Lewis, Lopez-Santibanez & Carranza (1982) summarized their findings as follows:

> In 1974, vegetative plants of ME–H, ME–K, ME–L, ME–N and ME–O, at 13 weeks of age had higher Δ^9-THC content that at weeks 12 and 14. They showed minimum Δ^9-THC content at week 15. For the most part, 1974 staminate and pistillate plants grown in Mississippi produced a low Δ^9-THC concentration * * *.

In all variants, the average Δ^9-THC was higher in 1976 than in 1974. Also, a greater fluctuation of Δ^9-THC was observed in 1976 than in 1974.

These results further establish that Cannabis Sativa L. is not a stable hybrid plant, but rather, represents characteristics more similar to an unstable weed.

Marijuana chemistry is complex and cannot be simplified or extrapolated from any one or two ''active compounds''. As early as 1974 this fact was recognized by the United Nations Division on Narcotic Drugs (UN Doc, 1974). As highlighted by Turner (1980), the chemistry of THC is not the chemistry of marijuana and the pharmacology of marijuana is not the pharmacology of THC. Recent findings do suggest that the interactions between cannabinoids is one of many critical factors in the analysis of the psychopharmacology of marijuana.

According to Jones (1980), because of exposure to a wide range of plant material and the cultural labeling (almost like advertising) of much of the marijuana experience, marijuana users are particularly subject to the effects of nonpharmacological variables that alter the subjective response to marijuana intoxication (Jones 1971, 1980; Cappell & Pliner, 1974; Becker 1967). As reviewed by Jones (1971), a number of studies suggest that experienced marijuana users are more subject to ''placebo reactions'; that is, a degree of intoxication disproportionate to the THC content of the material. This seems particularly true if the individuals are exposed to low potency marijuana (<1.0% THC). Jones believes that this is a result of experience and practice at recognizing minimal physiologic cues together with the smell, taste and other sensations associated with smoking a marijuana cigarette (Jones 1980, 1971). Becker 1967 and Cappell & Pliner (1974) have described a number of psychological factors (expectancy, social setting, *etc.*) that appear to synergistically interact to help generate the subjective experiences engendered by marijuana smoking.

Domino, Rennick, & Pearl (1976) administered THC injected into tobacco cigarettes to male volunteers. Similar to findings described by Isbell *et al.,* (1967) they report that 50 µg of THC into the cigarettes produced a ''social high'', while 250 µg/kg was ''hallucinogenic''. Taking 80 kg as the mean weight of their subjects the authors concluded that a 4.0 mg total THC dose produced a ''social high''; a hallucinogenic dose was 20 mg total THC by inhalation. A standard 1g cigarette of 1% THC fibre-type hemp provides 10 mg of THC. Even allowing for a 50% loss of THC from sidestream smoke and pyrolysis, smoking this cigarette provides more than enough THC to produce a ''social high''.

In 1968 Weil, Norman, & Nelsen described a set of studies examining the physiological and psychological aspects of smoked marijuana. The first batch of Mexican grown marijuana used in the study was found to contain only 0.3% THC by weight. The potency of this product was considered to be ''low'' by the experimenters on the basis of the doses needed to produce symptoms of intoxication in the chronic users. This low potency marijuana was able to produce a ''high'', but only with two 1 gram cigarettes. A second batch was used in later studies. Weil, Norman, & Nelsen report that marijuana assayed at 0.9% THC (a quantity slightly less than the 1% THC limit set forth by the petitioners) was rated by the chronic users in the study to be ''good, average'' marijuana, neither exceptionally strong nor exceptionally weak compared to the usual supplies. Users consistently reported symptoms of intoxication after smoking about 0.5 grams of the 0.9% THC containing marijuana (half a joint). With the high dose of marijuana (2.0 grams of 0.9% THC containing marijuana) all chronic users became ''high'' by their own accounts and in the judgment of experimenters who had observed many persons under the influence of marijuana.

Agurell & Leander (1971) examined the physiological and psychological effects of low THC-containing cannabis in experienced users. They reported that 14–29% of the cannabinoid content of the cigarette was transferred to the main stream smoke. Based on qualitative and quantitative analyses, Agurell & Leander demonstrated that as little as 3–5 mg of THC was needed to be absorbed by the lung in order to produce a ''normal biological high''. Further, they found that as little as 1 mg of absorbed THC was discriminable by all of their chronic user subjects.

In 1982, Barnett, Chiang, Perez-Reyes, & Owens had six subjects smoke a 1% THC-containing (industrial hemp, as defined by the petitioner) marijuana cigarette. Significant heart rate and subjective measures of ''high'' were measured for 2 hours after each cigarette.

In 1971 Jones reported on the wide variability in THC concentrations found in street samples:

> Specimens gathered in the midwestern United States contained only 0.1—0.5% THC. Thirty specimens selected from seized samples in the Bureau of Narcotics and Dangerous Drugs Laboratory in San Francisco all contained less than 1% THC. Samples from the State of California Bureau of Narcotic enforcement analyzed in our laboratory contained as little as 0.1% THC and a maximum of 0.9% * * * In a survey done in Ontario, Canada, Marshman and Gibbons found that of 36 samples alleged to be marijuana with high cannabinoid content, 34% contained no marijuana at all, and much of the rest was cut with other plant substances. A generous assumption is that marijuana generally available in the United States averages about 1.0% THC.

It must be acknowledged that the THC content of domestically grown and imported marijuana has increased since these reports. However, the description by Weil, Zinberg & Nelson (1968), Agurell & Leander (1971), Jones (1971) and Barnett *et al.* (1982) highlight the historical importance of low THC concentrations contained in marijuana which provided the basis for the marijuana culture that developed in the 1970s. The incident described by Jones was not an isolated case of the inadvertent misrepresentation of the THC content of marijuana extracts. Caldwell *et al.,* (1969) found that the NIMH-supplied marijuana that they reported to have contained 1.3% THC was analyzed by two independent laboratories and found to contain as little as 0.2 to 0.5% THC. Similarly, according to Paton & Pertwee (1973) the THC content of material used by Clark & Nakashima (1968), Weil *et al.,* (1968), Weil & Zinberg (1969), and Crancer *et al.,* (1969) must be expected to be one-third to one-sixth less than stated. This means that the positive results of all of these studies were the result of a surprisingly low THC-containing (<1.0%) marijuana. The early scientific data on the subjective effects of marijuana were generated with these samples by experienced smokers smoking material in this potency range. These experienced marijuana smokers were reporting that these marijuana

samples were of ''average quality'' (Mechoulam, 1973).

In an early study, Jones (1971) utilized 1 gram of plant material with a THC concentration of 0.9% (9 mg of THC). Experienced marijuana smokers were asked to freely smoke marijuana cigarettes for 10 minutes. The smoking topography of the smokers widely varied and was not controlled in this set of experiments. Subjects were asked to smoke the entire cigarette. Subjective state was measured by asking the subjects to make global estimates of his degree of intoxication on a 0–100 scale. A score of 0 was defined as ''sober'' and a score of 100 as the most intoxicated or most ''stoned'' they had ever been in any social situation. At the end of the session (about 3 hrs), the subject also filled out a 272-item symptom checklist (SDEQ: subjective drug effects questionnaire) which taps some of the more unusual emotional, perceptual and cognitive effects produced by psychoactive drugs. The mean potency rating was 61 for the marijuana containing only 9 mg of THC. There was a tremendous range in the rating made by individual smokers. Jones concluded that the smokers may obtain intermittent reinforcement from THC but where much of the behavior and subsequent response is maintained by ''conditioned reinforcers'' such as the whole ritual of lighting up, the associated stimuli of smell, taste, visual stimuli and so on.

Manno, Kiplinger, Haine, Bennett, & Forney (1970) asked subjects to smoke an entire 1 gram cigarette containing 1% THC (10 mg; low potency). The subjects were told to take 2 to 4 seconds to inhale and to hold the draw for 30 to 60 seconds. The expired smoke was collected and analyzed for THC content, as well. During the experiment the subjects smoked the entire cigarette; in all cases, less than 0.5 mg of THC remained in the residue of each cigarette. Manno *et al.* reported that the quantity of THC or other cannabinols present in a marijuana cigarette was not a reliable indicator of the amount of cannabinols that were delivered in the smoke of the cigarette. Controlled smoking experiments through a manufactured smoking machine demonstrated that approximately 50% of the Δ^9-THC originally present in the cigarette was delivered unchanged in the smoke. Manno et al. concluded that a dose of approximately 5 mg of Δ^9-THC was delivered which was estimated to be an administered dose in the range of 50 to 75 µg per kilogram. These low potency marijuana cigarettes produced significant motor and mental performance measures on the pursuit meter test, delayed auditory feedback, verbal output, reverse reading, reverse counting, progressive counting, simple addition, subtraction, addition +7, subtract +7, and color differentiation. These low potency cigarettes also produced significant pulse rate increases and significant increases on a somatic symptoms checklist. Unsolicited verbal comments from the subjects verified that the subjects were ''high'' on these low potency marijuana cigarettes.

Kiplinger, Manno, Rodda, Forney, Haine, Ease, & Richards (1971) conducted a randomized block, double-blind study designed to establish a dose-response analysis of the THC content in marijuana using a variety of behavioral and subjective effects measures. Marijuana cigarettes were manufactured to deliver doses of 0, 6.25, 12.5, 25, and 50 µg/kg of Δ^9-THC. Based on an average 70 kg man, the total delivered doses of THC were 0, 0.43, 0.875, 1.75, and 3.5 mg. Based on the assumption of a 50% loss of THC from pyrolysis and sidestream smoke these doses would be equivalent to smoking cigarettes containing 0, 0.08%, 0.16%, 0.3%, and 0.7% THC containing hemp. The lower concentrations of THC were used because these doses are found in the weaker ''hemp'' or fiber type marijuana commonly grown in the United States. All doses of THC, including the two lowest doses, increased the subjective ratings on both the ARCI and Cornell Medical Indexes, produced heart-rate increases, increased motoric decrements in pursuit meter, and produced decrements in mental performance using the delayed auditory feedback test. Most importantly, 80% of subjects correctly identified the lowest dose (6.25 µg/kg; 0.43 mg THC) as active marijuana. The authors suggested that even lower doses might have measurable effects. Holtzman (1971) has suggested that one of the best predictors of a drug's abuse liability is the identification of the substance as ''drug-like'' by experienced drug users. The identification of the lowest dose of marijuana in the Kiplinger et al. and the other studies, discussed above, clearly suggests that industrial ''fiber-type'' marijuana has abuse potential.

Many of the studies examining the behavioral effects of marijuana in animals have chosen to administer THC because of the difficulties in controlling and administering exact doses within and between subjects when using pyrolyzed forms of marijuana to animals. Accurate small-animal smoke delivery systems are not yet available. The lack of water solubility of Δ^9-THC has made its administration and absorption a difficult problem for pharmacologists. Many different methods for suspending, solubilizing, or emulsifying Δ^9-THC have been used. None of these methods are without difficulty and without influence on absorption and pharmacological activity. The fact that many methods have been used by various investigators makes quantitative comparisons difficult.

Δ^9-THC is the primary active ingredient of marijuana that produces the subjective ''high'' associated with smoking the plant material and is the chemical basis for cannabis abuse. Studies in several species of laboratory animals, including rhesus monkeys, rats and pigeons, have found pharmacological specificity for Δ^9-THC at the cannabinoid receptors, and for cannabinoid drugs that bind with high affinity to brain cannabinoid receptors, and is psychoactive in humans and animals (Browne and Weissman, 1981; Balster and Prescott, 1992; Compton *et al.,* 1993; Wiley *et al.,* 1995a,b). In general, the doses that produce its acute therapeutic effects and its cannabimimetic effects are similar (Devine *et al.,* 1987; Consroe and Sandyk, 1992).

Central Nervous System Effects

It has been reported that in man, doses above 1 milligram of Δ^9-THC absorbed by smoking marijuana are sufficient to cause a ''high'' (Agurell *et al.,* 1986). Further, Agurell *et al.* (1986) suggested based on mouse data, that a pronounced ''high'' would be caused by the presence of as little as 10 micrograms of Δ^9-THC in the brain, immediately after smoking a marijuana cigarette. These conclusions, based on a diverse array of pharmacokinetic studies, suggest that ''fiber-type'' marijuana clearly has the capacity to deposit these levels of THC into the brain of man soon after smoking a 1% THC-containing marijuana cigarette (assuming the typical ''joint'' of 1 g, with 10mg THC). Δ^9-THC exerts its most prominent effects on the CNS and the cardiovascular system.

Administration of Δ^9-THC via smoked cannabis is associated with decrements in motivation, cognition, judgement, memory, motor coordination, and alterations in perception (especially time perception), sensorium, and mood (cf., Jaffe, 1993). Most commonly Δ^9-THC produces an increase in well-being and euphoria accompanied by feelings of relaxation and sleepiness. The consequences produced by Δ^9-THC-induced behavioral impairments can greatly impact the public health and safety, given that individuals may be

attending school, working, or driving a motor vehicle under the influence of the drug (*i.e.,* marijuana).

Preclinical studies show that Δ9-THC produces decrements in short-term memory, as evidenced by disruptions in acquisition and performance of maze behavior, conditioned emotional responses, and passive avoidance responses, impairment on the retention in delayed matching and alternation tests, and increases in resistance to extinction (Drew and Miller, 1974, Nakamura *et al.,* 1991; Jäarbe and Mathis, 1992; Lichtman and Martin, 1996). Recent studies in rats found that these Δ9-THC-induced impairments in spatial working memory were reversible after long abstinence (Nakamura *et al.,* 1991) and can be blocked by the cannabinoid receptor antagonist SR141716A (Lichtman and Martin, 1996).

Memory disturbances are one of the well-documented effects of ''Δ9-THC and marijuana on human behavior (Mendelson *et al.,* 1974; Jaffe, 1993; Hollister, 1986; Chait and Pierri, 1992). Clinical investigators of Δ9-THC and marijuana's effects in memory have suggested that the drug produces a deficit in memory for recent events, and inhibition of the passage of memory from short-term to long-term storage (Drew and Miller, 1974; Darley 1973a,b).

Heishman, Huestis, Henningfield, & Cone (1990) demonstrated cognitive performance decrements in marijuana smokers. Performance remained impaired on arithmetic and recall tests on the day after smoke administration. The authors suggested that performance decrements from smoking two to four marijuana cigarettes may be evident for 24 to 31 hours. These data identify a particular set of performance decrements which characterize a marijuana-induced abstinence syndrome in man.

Cardiovascular Effects

In humans, Δ9-THC produces an increase in heart rate, an increase in systolic blood pressure while supine, decreases in blood pressure while standing, and a marked reddening of the conjunctivae (cf., Jaffe, 1993). The increase in heart rate is dose-dependent and its onset and duration varies but lags behind the peak of Δ9-THC levels in the blood.

Respiratory Effects

Marijuana smoking produces inflammation, edema, and cell injury in the tracheobronchial mucosa of smokers and may be a risk factor for lung cancer (Sarafian *et al.,* 1999). Smoke from marijuana has been shown to stimulate intermediate levels of reactive oxygen species. A brief, 30-minute exposure to marijuana smoke, regardless of the THC content, also induced necrotic cell death that increased steadily up to 48 hours after administration. Sarafian *et al.,* concluded that marijuana smoke containing THC is a potent source of cellular oxidative stress that could contribute significantly to cell injury and dysfunction in the lungs of smokers.

The low incidence of carcinogenicity may be related to the fact that intoxication from marijuana does not require large amounts of smoked material. This may be especially true today since marijuana has been reported to be more potent now than a generation ago and individuals typically titrate their drug consumption to consistent levels of intoxication. However, several cases of lung cancer in young marijuana users with no have been reported (Fung *et al.,* 1999).

However, a recent study (Zhang *et al.,* 1999, below) has suggested that marijuana use may dose-dependently interact with mutagenic sensitivity, cigarette smoking and alcohol use to increase the risk of head and neck cancer. THC is known to suppress macrophage natural killer cells and T-lymphocytes and reduce resistance to viral and bacterial infections. As shown below, Zhu *et al.,* demonstrated that THC probably interacts with the T-cell cannabinoid CB2 receptor to produce these effects. As shown in the figure, below, these researchers found that THC promoted tumor growth in two immunocompetent mice lines. In two different weakly immunogenic murine lung cancer models, intermittent administration of THC led to accelerated growth of tumor implants compared with treatment with placebo alone. The immune inhibitory cytokines IL–10 and TGF-beta were augmented, while IFN-gamma was down-regulated at both the tumor site and in the spleens of THC-treated mice. This has been the first clear demonstration that THC promotes tumor growth and supports the epidemiological evidence of an increased risk of cancer among marijuana smokers.

In a recent comprehensive review of the existing literature base, Carriot & Sasco (2000) reported that users under the age of 40 years of age were more susceptible to squamous-cell carcinoma of the upper aerodigestive tract, particularly of the tongue and larynx, and possibly the lung. Others tumors being suspected are non-lymphoblastic acute leukemia and astrocytoma. In head and neck cancer carcinogenicity was observed for regular (*i.e.* more than once a day for years) cannabis smokers. Moreover, cannabis increases the risk of head and neck cancer in a dose-response manner for frequency and duration of use. THC seems to have a specific carcinogenic effect different from that of the pyrolysis products produced by (nicotine) cigarette smoking.

(3) The State of Current Scientific Knowledge Regarding the Drug or Other Substance

In general, the petitioner argues that the chemistry, toxicology and pharmacology of marijuana has been subjected to extensive study and peer review, and have been well characterized in the scientific literature. In addition, the discovery of the cannabinoid receptor has shed new light on the effects of marijuana and its mechanism of action.

The literature cited by the petitioner (Tashkin *et al.,* 1987, 1988, 1990, 1991, 1993; Barbers *et al.,* 1991; Sherman *et al.,* 1991a, 1991b; Wu *et al.,* 1992) provide data about the effects of marijuana smoke on the lungs, which, by the petitioner's own admission, is inherently unhealthy. Data show that smoking marijuana is associated with more tar than cigarettes and holding your breath (a common practice of marijuana smokers) increases carbon monoxide concentration. His assertion that Schedule I policy makes promoting safer marijuana smoking habits impossible has no basis in law (exact citations are found in petition).

Pulmonary effects of smoked marijuana include bronchodilation after acute exposure. Chronic bronchitis and pharyngitis are associated with repeated pulmonary illness. With chronic marijuana smoking, large airway obstruction and cellular inflammatory abnormalities appear in bronchial epithelium (Adams and Martin, 1996). Chronic marijuana use is associated with the same types of health problems as cigarette smoking: increased frequency of bronchitis, emphysema and asthma. The ability of alveolar macrophages to inactivate bacteria in the lung is impaired. Local irritation and narrowing of airways also contribute to problems in these patients.

Work by Perez-Reyes *et al.* (1991) and Agurell *et al.* (1989) provides data about the pharmacokinetics of THC from smoked marijuana.

When marijuana is smoked, THC in the form of an aerosol in the inhaled smoked is absorbed within seconds and delivered to the brain rapidly and efficiently. Peak venous blood levels 75–150 ng/ml usually occur by the end of smoking a cigarette and level of THC

in the arterial system is probably much higher (Agurell *et al.*, 1986).

Toxicity by definition is the ability of an agent to produce injury or cause harm (morbidity/mortality). It is not clear that the effects of marijuana use are ''well-established,'' but what is known about the psychoactive effects, lung effects, endocrine effects *etc.* would suggest that smoking marijuana is not benign.

The cardiovascular effects of smoked or oral marijuana have not presented any health problems for healthy and relatively young users. However, marijuana smoking by older patients, particularly those with some degree of coronary artery disease, is likely to pose greater risks because of the resulting increased cardiac work, increased catecholamines, carboxyhemoglobin and postural hypotension (Benzowitz and Martin, 1996; Hollister, 1988).

The endocrine system effects include moderate depression of spermatogenesis and sperm motility and decrease in plasma testosterone on males. Prolactin, FSH, LH, and GH levels are decreased in females (Mendelson and Mello, 1984). Relatively little study has been done on human female endocrine or reproductive function.

THC and other cannabinoids in marijuana have immunosuppressant properties producing impaired cell-mediated and humoral immune system responses. THC and other cannabinoids suppress antibody formation, cytokine production, leukocyte migration and killer-cell activity (Adams and Martin, 1996).

Marijuana may cause membrane perturbations in cells. At the marijuana conference in July, 1995 sponsored by NIH, NIDA and DHHS, Dr. Cabral stated that THC effects body functions by accumulating in fatty tissue. While a receptor-based mechanism of action has been determined, localized and characterized it is not clear that this necessarily negates membrane (high fatty acids) effects.

Mechanisms for marijuana's psychoactive effects were thought to be through interactions of the lipid component of cell membranes. The discovery of the cannabinoid receptor has changed that thinking and it is now believed that most of the effects of marijuana are mediated through cannabinoid receptors. Receptors are located in brain areas concerned with memory, cognition and motor coordination. An endogenous ligand, anandamide, has been identified but not studied in humans (Thomas *et al.* 1996). A specific THC antagonist, SR141716A, produces intense withdrawal signs and behaviors in rodents that have been exposed to THC for even a relatively short period of time (Adams and Martin, 1996). Clinical pharmacology of the antagonist has not been studied in humans.

Most of what is known about human pharmacology of smoked marijuana comes from experiments with plant material containing about 2 percent THC or less. Very few controlled studies have been done with elderly, inexperienced or unhealthy users and data suggest that adverse effects may differ from healthy volunteers (Hollister 1986, 1988).

Most of what is written about the pharmacological effects of marijuana is inferred from experiments on pure THC. The amount of Cannabidiol and other cannabinoids in smoked marijuana could modify the effects of THC.

Tolerance to marijuana's psychoactive effect probably results from down regulation of cannabinoid receptors which is a form of desensitization of neuronal cells. In general, tolerance to marijuana's effects is often associated with an increased dependence liability. Data indicate that people escalate the amount of marijuana they smoke and continue to use marijuana despite negative consequences. These are classic signs of developing dependence.

After repeated smoked or oral marijuana doses, marked tolerance is rapidly acquired to many of marijuana's effects: cardiovascular, autoimmune and many subjective effects. After exposure is stopped, tolerance is lost with similar rapidity (Jones *et al.*, 1981)

Withdrawal symptoms and signs appearing within hours after cessation of repeated marijuana use have been reported in clinical settings (Duffy and Milan, 1996; Mendelson *et al.,* 1984). Typical symptoms and signs were restlessness, insomnia, irritability, salivation, diarrhea, increased body temperature and sleep disturbances (Jones *et al.*, 1981).

Data on the immune system indicates that marijuana does effect the body's ability to resist microbes including bacteria, viruses and fungi and decreases the body's antitumor activity. THC effects macrophages, T-lymphocytes and B-lymphocyts. A THC receptor has been found in the spleen. These effects may be receptor mediated. In a person with compromised immune function marijuana could pose a health risk.

Acute effects of transient anxiety, panic, feelings of depression and other dysphoric moods have been reported by 17 percent of regular marijuana users in a large study (Tart, 1971). Whether marijuana can produce lasting mood disorders or schizophrenia is less clear (IOM, 1982). Chronic marijuana use can be associated with behavior characterized by apathy and loss of motivation along with impaired educational performance (Pope and Yurgelun-Todd, 1996).

DEA has found that since HHS's last medical and scientific evaluation on marijuana (1986), there have been a significant number of new findings relating to THC:

1. Cannabinoid receptors have been identified in the brain and spleen;
2. The CNS cannabinoid receptor has been cloned;
3. An endogenous arachidonic acid derivative ligand (anandamide) has been identified;
4. A high density of cannabinoid receptors have been located in the cerebral cortex, hippocampus, striatum and cerebellum; and
5. An antagonist to the cannabinoid receptor has been developed

In addition, a significant body of literature has been amassed regarding the effects of marijuana.

For example:

1. Studies on the acute and chronic effects of marijuana on the endocrine system;
2. Effect of marijuana on learning and memory;
3. Effect of marijuana on pregnant females and their offspring development;
4. Effect on the immune system;
5. Effect on the lungs; and
6. Effects of chronic use with regard to tolerance, dependence and ''amotivational syndrome.''

While many of the petitioner's arguments are based on new research findings, the interpretation of those findings requires clarification.

As was pointed out by the NIH expert committee on the medical utility of marijuana, marijuana is not a single drug. It is a variable and complex mixture of plant parts with a varying mix of biologically active material. Characterizing the clinical pharmacology is difficult especially when the plant is smoked or eaten. Some of the inconsistency or uncertainty in scientific reports describing the clinical pharmacology of marijuana results from the inherently variable potency of the plant material. Inadequate control over drug dose together with the use of research subjects with variable experience in using marijuana contributes to the uncertainty about what marijuana does or does not do.

There are studies in the scientific literature that have evaluated dose-related subjective and reinforcing effects of Cannabis sativa in humans. These

studies have assessed the subjective and reinforcing effects of cannabis cigarettes containing different potencies of THC and/or which have manipulated the THC dose by varying the volume of THC smoke inhaled (Azorlosa *et al.,* 1992; Lukas *et al.,* 1995; Chait *et al.,* 1988; Chait and Burke, 1994; Kelly *et al.,* 1993; Kipplinger *et al,* 1971, Manno *et al.,* 1970).

Chait *et al.* (1988) studied the discriminative stimulus effects of smoked marijuana cigarettes containing THC contents of 0%, 0.9%, 1.4%, 2.7%. Marijuana smokers were trained to discriminate smoked marijuana from placebo using 4 puff of a 2.7%-THC cigarettes. Subjective ratings of ''high'', mean peak ''high'' scores, and physiological measures (*i.e.,* heart rate) were significantly and dose-dependently increased after smoking the 0.9%, 1.4%, 2.7%. Marijuana cigarettes containing 1.4% THC completely substituted for 2.7%-THC on drug identification tasks, however, 0.9%-THC did not. The authors found that the onset of discriminative stimulus effects was within 90 seconds after smoking began (after the first two puffs). Since the 1.4%-THC cigarette substituted for 2-puffs of the 2.7%-THC cigarette, the authors estimate that an inhaled dose of THC as low as 3 mg can produce discriminable subjective effects.

Similarly, Lukas *et al.* (1995) reported that marijuana cigarettes containing either 1.26% or 2.53% THC produced significant and dose-dependent increases in level of intoxication and euphoria in male occasional marijuana smokers. Four of the six subjects that smoked the 1.26%-THC cigarette reported marijuana effects and 75% of these subjects reported euphoria. All six of the subjects that smoked 2.53% THC reported marijuana effects and euphoria. Peak levels of self-reported intoxication occurred at 15 and 30 minutes after smoking and returned to control levels by 90–105 minutes. There was no difference between latency to or duration of euphoria after smoking either the 1.26% or 2.53% THC cigarettes. The higher dose-marijuana cigarette produced a more rapid onset and longer duration of action than the lower dose marijuana cigarette (1.26% THC). Plasma THC levels peaked 5–10 minutes after smoking began; the average peak level attained after the low- and high-dose marijuana cigarette was 36 and 69 ng/ml respectively.

In order to determine marijuana dose-effects on subjective and performance measures over a wide dose range, Azorlosa *et al.* (1992) evaluated the effects of 4, 10, or 25 puffs from marijuana cigarettes containing 1.75 or 3.55% THC in seven male moderate users of marijuana. Orderly dose-response curves were produced for subjective drug effects, heart rate, and plasma concentration, as a function of THC content and number of puffs. After smoking the 1.75% THC cigarette, maximal plasma THC levels were 57 ng/ml immediately after smoking, 18.3 ng/ml 15 minutes after smoking, 10.3 ng/ml 30 minutes after smoking, and 7.7 ng/ml 45 minutes after smoking.

The study also show that subjects could smoke more of the low THC cigarette to produced effects that were similar to the high THC dose cigarette (Azorlosa *et al.,* 1992). There were nearly identical THC levels produced by 10-puff low-THC cigarette (98.6 ng/ml) and 4-puff high THC cigarette (89.4 ng/ml). Similarly, the subjective effects ratings, including high, stoned, impaired, confused, clear-headed and sluggish, produced under the 10 puff low- and high-THC and 25 puff low-THC conditions did not differ significantly from each other.

As with most drugs of abuse, higher doses of marijuana are preferred over lower dose. Although not preferred, these lower doses still produce cannabimimetic effects. Twelve regular marijuana smokers participated in a study designed to determine the preference of a low potency (0.64%-THC) vs. a high potency (1.95%-THC) marijuana cigarette (Chait and Burke, 1994). The subjects first sampled the marijuana of two different potencies in one session, then chose which potency and how much to smoke. During sampling sessions, there were significant dose-dependent increases in heart rate and subjective effects, including ratings of peak ''high'', strength of drug effects, stimulated, and drug liking. During choice sessions, the higher dose marijuana was chosen over the lower dose marijuana on 87.5% of occasions. Not surprising, there was a significant positive correlation between the total number of cigarettes smoked and the ratings of subjective effects, strength of drug effect, drug ''liking'', expired air carbon monoxide, and heart rate increases. The authors state it is not necessary valid to assume that the preference observed in the present study for the high-potency marijuana was due to greater CNS effects from its higher THC content. The present study found that the low- and high-potency marijuana cigarettes also differ on several sensory dimensions; the high-potency THC was found to ''fresher'' and ''hotter''. Other studies found that marijuana cigarettes containing different THC contents varied in sensory dimensions (cf., Chait *et al.,* 1988; Nemeth-Coslett *et al.,* 1986).

As described above in Factors 1 and 2, there are data to show that the effects of THC are dose-dependent and several studies have found that low-potency THC is behaviorally active and can produce cannabimimetic-like subjective and physiological effects. Preclinical and clinical experimental data demonstrate that marijuana and Δ^9-THC have similar abuse liabilities (*i.e.,* drug discrimination, self-administration, subjective effects). Both preclinical and clinical studies show that discontinuation of either marijuana and Δ^9-THC administration produces a mild withdrawal syndrome. Most of what is known about human pharmacology of smoked marijuana comes from experiments with plant material containing about 2–3% percent THC or less, in cigarette form provided by NIDA (cf., NIDA, 1996). Very few controlled studies have been done with elderly, inexperienced or unhealthy users and data suggests that adverse effects may differ from healthy volunteers (Hollister 1986, 1988).

Cannabidiol (CBD) does not have psychotomimetic properties and does not appear to produce a subjective ''high'' in human subjects (Musty, 1984). This does not mean that CBD does not have CNS effects or that it does not contribute to the subjective high produced by the cannabinoids. CBD has been clearly shown to have anti-convulsant effects as demonstrated by several techniques such as electroshock-induced seizures, kindled seizures, pentylenetetrazole-induced seizures (Carlini *et al.,* 1973; Izquierdo & Tannhauser, 1973). The suggestion that CBD does not have abuse liability is based in part on the findings that CBD does not produce THC-like discriminative stimulus effects in animals (Ford, Balster, Dewey, Rosecrans, & Harris, 1984; but see below). However, these tests were conducted with CBD administered alone and at only one or two time-points (however, see Jarbe below). The normal route of administration of THC and CBD in humans is by smoking. This mode of administration provides a variable proportion of cannabinoid ratios to the individual subject. As stated above, the chemistry of marijuana is not just the chemistry of Δ^9-THC , but at a minimum, a combination of cannabinoids. According to Turner (1980) kinetic interactions have been reported to occur among the cannabinoids since the early 1970s. Control studies with varying ratios of cannabinoid administrations and

complete time-effect functions have still not been conducted.

Domino, Domino, & Domino (1984) have shown that the rate-of-change of the subjective high after marijuana administration does not follow the rate-of-change of plasma or brain THC levels. While plasma THC function show a sharp ascending limb and exponential decline after administration, the subjective ''high'' peaks after the peak in THC and shows a protracted slow decline. The proportional ratios between the cannabinoids and their metabolites in inhaled marijuana, acting as entourage substances, may have emergent properties that cannot be ascribed to any one component of the complex stimulus administered in the smoke (Gauvin & Baird, 1999). These cannabinoid ratios may play a critical role in the initiation, maintenance, and relapse of marijuana smoking.

CBD has been clearly shown to have anxiolytic (Guimães *et al,* 1990, 1994; Musty, 1984; Onaivi, Green, & Martin, 1990; Zuardi *et al.,* 1982) and antipsychotic (Zuardi *et al.,* 1995; Zuardi, Antunes Rodrigues, & Cunha, 1991) effects in both animal and man. In the sense that many studies which have examined the subjective profiles of marijuana have demonstrated an ''anxiety'' component to THC and marijuana use, it should not be surprising that CBD's anxiolytic effects block some of these discriminative properties. However, it should not be concluded from these results that CBD's anxiolytic properties do not have or cannot acquire reinforcing efficacy. It has been suggested that the affective baseline of the drug abuser plays a critical role in the stimulus properties of drugs (Gauvin, Harland, & Holloway, 1989). The anxiolytic properties of CBD may serve to diminish the anxiety states associated with many psychopathological states, thus effectively functioning as a ''negative reinforcer''. As such, CBD may function to increase the likelihood of its administration by its ability to remove the negative affective states in anxious patients. A number of authors have summarized the process by which marijuana smokers ''learn to get high'' (cf. Jones, 1971, 1980; Cappell & Pliner, 1974). Karniol *et al.,* (1974) have clearly demonstrated that the co-administration of CBD with THC actually blocks the anxiety induced by Δ^9-THC, leaving the subjects less tense and potentiating the reinforcing effects of the THC as demonstrated by the subjects verbal reports of enjoying the experience even more. Very few experienced marijuana smokers report symptoms of anxiety (cf Jones, 1971, 1980; Petersen, 1980). The relief of the anxiety and/or psychotomimetic properties of THC by the co-administration of CBD may effectively function as a ''negative reinforcer'', increasing the likelihood of continued abuse.

Other studies have reported that cannabidiol has cannabinoid properties, including anticonvulsant effects in animal and human models (Consroe *et al.,* 1981; Carlini *et al.,* 1981; Doyle and Spence, 1995), hypnotic effects (Monti *et al.,* 1977), and rate-decreasing effects on operant behavior (Hiltunen *et al.,* 1988). Experiments with cannabidiol in combination with THC have found that certain behavioral responses induced by THC (*i.e.,* operant, schedule-controlled responding) were attenuated by cannabidiol (Borgen and Davis, 1974; Brady and Balster, 1980; Consroe *et al.,* 1977; Dalton *et al.,* 1976; Karniol and Carlini, 1973; Karniol *et al.,* 1974; Welburn *et al.,* 1976; Zuardi and Karniol, 1983; Zuardi *et al.,* 1981, 1982; Hiltunen *et al.,* 1988). However, other affects produced by THC are augmented or prolonged by the combined administration of CBD and THC or marijuana extract (Chesher and Jackson, 1974; Hine *et al.,* 1975a,b; Fernandes *et al.,* 1974; Karniol and Carlini, 1973; Musty and Sands, 1978; Zuardi and Karniol, 1983; Zuardi *et al.,* 1984). Still other studies did not report any behavioral interaction between the CBD and THC (Bird *et al.,* 1980; Browne and Weissman, 1981; Hollister and Gillespie, 1975; Järbe and Henricksson, 1974; Järbe *et al.,* 1977; Mechoulam *et al.,* 1970; Sanders *et al.,* 1979; Ten Ham and DeLong, 1975).

A study to characterize the interaction between CBD and THC was conducted using preclinical drug discrimination procedures. Rats and pigeons trained to discriminate the presence or absence of THC, and tested with CBD administered alone and in combinations with THC (Hiltunen and Järbe, 1986). Specifically, in rats trained to discriminate 3.0 mg/kg, i.p. THC, CBD (30.0 mg/kg) was administered alone and in combination with THC (0.3 and 1.0 mg/kg, i.p.). In pigeons trained to discriminate 0.56 mg/kg, i.m. THC, CBD (17.5 mg/kg) was administered alone and in combination with THC (0.1, 0.3, and 0.56 mg/kg, i.m.). CBD prolonged the discriminative stimulus effects of THC in rats, but did not change the time-effect curve for THC in pigeons. In pigeons, the administration of CBD did not produce any differential effect under a fixed ratio schedule of reinforcement (Hiltunen and Järbe, 1986).

These data suggest that CBD may somehow augment or prolong the actions of THC in rats and had no effect in pigeons. In the present study, the CBD/THC ratios ranged from 30:1 to 100:1 in rats and enhanced the stimulus effects of THC. However, similar CBD/THC ratios in pigeons (31:1, 58:1 and 175:1) did not result in any changes to THC's discriminative stimulus or response rate effects (Hiltunen and Järbe, 1986).

In conclusion, although cannabidiol does contribute to the other effects of cannabis, it appears to lack cannabimimetic properties. In addition, there does not appear to be a scientific consensus that cannabidiol pharmacologically antagonizes, in a classic sense, the effects of THC. Certain functional blockades have been demonstrated. As presented in the scientific literature cited above, the ability of cannabidiol to modify the effects of THC may be specific to only some effects of THC. Most importantly, CBD appears to potentiate the euphorigenic and reinforcing effects of THC which suggests that the interaction between THC and CBD is synergistic and may actually contribute to the abuse of marijuana.

(4) Its History and Current Pattern of Abuse

The federal databases documenting the actual abuse of marijuana are distributed and maintained by the HHS, therefore, we acknowledge and concur with HHS's review of this factor analysis.

(5) The Scope, Duration, and Significance of Abuse

The basis of the petition to remove marijuana from Schedules I and II is not based on data required by 21 U.S.C. 811 (c) (*i.e.,* the scope, duration, and significance of use of the substances).

The petitioner seems to assume that the concept, use of an illegal substance is abuse of that substance, is a concept which is universally held to the exclusion of any other definition of abuse of a substance. While this concept is valid in general terms because marijuana is not a legitimately marketed product therefore it has no legitimate use, holding that all adhere to this definition of abuse denigrates the intellectual capacity of all researchers who investigate the topic. The petitioner neglects to recognize the efforts of the DHHS and many groups which expend a great deal of time and money in research efforts directed toward developing and implementing drug-abuse prevention programs. The petitioner also rejects the notion that there are individuals who abuse marijuana even though the National Household Survey, to which the

petitioner refers, would indicate that is the case.

It has not been established that marijuana is effective in treating any medical condition. (NIH Workshop on the Medical Utility of Marijuana, 1997) At this time, there is no body of knowledge to which a physician can turn to learn which medical condition in which patient will be ameliorated at which dosage schedule of smoked marijuana nor can he/she determine in which patient the benefits will exceed the risks associated with such treatment. The petitioner, therefore, is advocating that individuals become their own physicians, a notion that even primitive man found unsatisfactory.

There is nothing absolute in the placement of a substance into a particular CSA schedule. The placement of a substance in a CSA schedule is the government's mechanism for seeing that the availability of certain psychoactive substances is limited to the industrial, scientific and medical needs which are accepted as being legitimate. The placement of a substance into Schedule I does not preclude research of that substance, nor does it preclude development of a marketable product. The National Institute on Drug Abuse, an element of the Department of Health and Human Services, convened a conference in 1995 and with NIDA's parent organization, the National Institutes of Health, assembled an ad hoc group of experts in 1997 to address issues related to the use, abuse, and medical utility of marijuana. With regard to the medical utility of marijuana, the experts concluded that the scientific process should be allowed to evaluate the potential therapeutic effects of marijuana for certain disorders, dissociated from the societal debate over the potential harmful effects of nonmedical marijuana use. All decisions on the ultimate usefulness of a medical intervention are based on a benefit/risk calculation, and marijuana should be no exception to this generally accepted principle.

The cause and effect relationship which the petitioner poses is neither substantiated nor relevant. Estimates are useful when attempting to allocate resources but they are not necessary for effective eradication of marijuana. Each year, millions of plants are destroyed before their product reaches the market. In addition, federal law enforcement activities result in the seizure of another million or more pounds of product annually.

As reviewed by Gledhill, Lee, Strote, & Wechsler (2000), rates of illicit drug use, especially marijuana, have risen uniformly among the youth in the United States in the past decade and remained steady at the end of the 1990s despite efforts to reduce prevalence. Between 1991 and 1997, rates of past 30-day marijuana use had more than doubled among U.S. 10th grade secondary school students and more than tripled among seniors, after a decade of decline. Between 1997 and 1999, rates of marijuana use among secondary school students declined for the first time in the 1990s mainly among the older students (16–17 yrs old).

Disturbing are the findings that marijuana use is steadily increasing among 8th, 10th and 12th graders at all prevalence levels. According to the 1996 survey results from the Monitoring the Future Study, 45% of seniors and 35% of 10th graders claimed to have used marijuana at least once. Among eighth graders, annual prevalence rates more nearly tripled 1992 to 1996. Accompanying the increased use of marijuana among High School seniors is a decreasing perceived risk or harm of marijuana use (Johnston *et al.,* 1996). In reality, the harm associated with the abuse of marijuana is increasing; the marijuana emergency room and treatment admission rates continue to increase in recent years.

Gledhill-Hoyt, Lee, Strote, & Wechsler (2000) examined rates and patterns of marijuana use among different types of students and colleges in 1999, and changes in use since 1993. 15,403 students in 1993, 14,724 students in 1997, and 14,138 students in 1999 were assessed. The prevalence of past 30-day and annual marijuana use increased in nearly all student demographic subgroups, and at all types of colleges. Nine out of 10 students (91%) who used marijuana in the past 30 days had used other illicit drugs, smoked cigarettes, and/or engaged in binge drinking. Twenty-nine percent of past 30-day marijuana users first used marijuana and 34% began to use marijuana regularly at or after the age of 18, when most were in college.

Coffey, Lynskey, Wolfe, & Patton (2000) examined predictors of cannabis use initiation, continuity and progression to daily use in adolescents. Over 2,000 students were examined. Peer cannabis use, daily smoking, alcohol use, antisocial behavior and high rates of school-level cannabis use were associated with middle-school cannabis use and independently predicted high-school uptake. Cannabis use persisted into high-school use in 80% of all middle-school users. Middle-school use independently predicted incidents in high-school daily use in males, while high-dose alcohol use and antisocial behavior predicted incidence of daily use in high school females. The authors also found that cigarette smoking was an important predictor of both initiation and persisting cannabis use.

Farrelly *et al.,* (2001) reviewed the NHSDA from 1990 through 1996 and compared those statistics with State law enforcement policies and prices that affect marijuana use in the general public. These authors found evidence that both higher fines for marijuana possession and increased probability of arrest decreased the probability that a young adult will use marijuana. These new data refute the petitioner's suggestion that legal control of marijuana does not have a dampening effect on its use.

(6) What, if any, Risks are There to Public Health

There are human data demonstrating that marijuana and Δ^9-THC produce an increase in heart rate, an increase in systolic blood pressure while supine, and decreases in blood pressure while standing (cf., Jaffe, 1993). The increase in heart rate is dose-dependent and its onset and duration correlate with levels of Δ^9-THC in the blood.

When DEA evaluates a drug for control or rescheduling, the question of whether the substance creates dangers to the public health, in addition to, or because of, its abuse potential must be considered. A drug substances' risk to the public health manifests itself in many ways. Abuse of a substance may affect the physical and/or psychological functioning of an individual abuser. In addition, it may have disruptive effects on the abuser's family, friends, work environment, and society in general. Abuse of certain substances leads to a number of antisocial behaviors, including violent behavior, endangering others, criminal activity, and driving while intoxicated. Data examined under this specific factor of the CSA ranges from preclinical toxicity to postmarketing adverse reactions in humans. DEA reviews data from many sources, including forensic laboratory analyses, crime laboratories, medical examiners, poison control centers, substance abuse treatment centers, and the scientific and medical literature.

Adverse effects associated with marijuana and THC as determined by clinical trials, FDA adverse drug effects and World Health Organization data, are described elsewhere (cf., Chait and Zacny, 1988; Chait and Zacny, 1992; Cone *et al.,* 1988; and Pertwee, 1991). A recent press release from the Substance Abuse and Mental Health Service Administration reported that adolescents, age 12 to 17, who use

marijuana weekly are nine times more likely than non-users to experiment with illegal drugs or alcohol; six times more likely to run away from home; five times more likely to steal; nearly four times more likely to engage in violence; and three times more likely to have thoughts about committing suicide. It was also reported that adolescents also associated social withdrawal, physical complaints, anxiety, and depression, attention problems, and thoughts of suicide with past-year marijuana use (SAMHSA, 1999). Budney, Novy, & Hughes (1999) have recently examined the withdrawal symptomology in chronic marijuana users seeking treatment for their dependence. The majority of the subjects (85%) reported that they had experienced symptoms of at least moderate severity and 47% experienced greater than four symptoms rated as severe. The most reported mood symptoms associated with the withdrawal state were irritability, nervousness, depression, and anger. Some of the behavioral characteristics of the marijuana withdrawal syndrome were craving, restlessness, sleep disruptions, strange dreams, changes in appetite, and violent outbursts. These data clearly support the validity and clinical significance of a marijuana withdrawal syndrome in man.

Toxic Effects of Marijuana and THC

Although a median lethal dose (LD_{50}) of THC has not been established in humans, it has been found in laboratory animals (Phillips *et al.,* 1971). In mice, the LD_{50} for THC was 481.9, 454.9 and 28.6 mg/kg after oral, intraperitoneal, and intravenous routes of administration. In rats, the LD_{50} for THC (extracted from marijuana) was 666.0, 372.9 and 42.5 mg/kg after oral, intraperitoneal, and intravenous routes of administration. Another study examined the toxicity of THC in rats, dogs and monkeys (Thompson *et al.,* 1972). Similarly this study found that in rats, the LD_{50} for THC was 1140.0, 400.0 and 20.0 mg/kg after oral, intraperitoneal, and intravenous routes of administration. There was no LD_{50} attained in monkeys and dogs by the oral route. Over 3000 mg/kg of THC was administered without lethality to dogs and monkeys. A dose of about 1000 mg/kg was the lowest dose that caused death in any animal. Behavioral changes in the survivors included sedation, huddled postures, muscle tremors, hypersensitivity to sound and immobility.

The cause of death in the rats and mice after oral THC was profound depression leading to dyspnea, prostration, weight loss, loss of righting reflex, ataxia, and severe decreases in body temperature leading to cessation of respiration from 10 to 40 hours after a single oral dose (Thompson *et al.,* 1972). No consistent pathologic changes were observed in any organs. The cause of death in dogs or monkeys (when it rarely occurred) did not appear to be via the same mechanism as in the rats.

In humans, the estimated lethal dose of intravenous dronabinol [(−)-Δ^9-THC] is 30 mg/kg (2100 mg/70 kg). In antiemetic studies, significant CNS symptoms were observed following oral doses of 0.4 mg/kg (28 mg/70 kg) (PDR, 1997). Signs and symptoms of mild dronabinol intoxication include drowsiness, euphoria, heightened sensory awareness, altered time perception, reddened conjunctiva, dry mouth and tachycardia. Following moderate dronabinol intoxication patients may experience memory impairment, depersonalization, mood alterations, urinary retention, and reduced bowel motility. Signs and symptoms of severe dronabinol intoxication include decreased motor coordination, lethargy, slurred speech, and postural hypotension. Dronabinol may produce panic reactions in apprehensive patients or seizures in those with an existing seizure disorder (PDR, 1997).

Thus, large doses of THC ingested by mouth were not often associated with toxicity in dogs, nonhuman primates and humans. However, it did produce fatalities in rodents as a result of profound CNS depression. Thus, the evidence from studies in laboratory animals and human case reports indicates that the lethal dose of THC is quite large. The adverse effects associated with THC use are generally extensions of the CNS effects of the drug and are similar to those reported after administration of marijuana (cf., Chait and Zacny, 1988; Chait and Zacny, 1992; Cone *et al.,* 1988; and Pertwee, 1991).

Health and Safety Risks of Δ^9-THC Use

The recent Institute of Medicine report on the scientific basis for the medicinal use of cannabinoid products stated the following:

> Not surprisingly, most users of other illicit drugs have used marijuana first. In fact, most drug users begin with alcohol and nicotine before marijuana—usually before they are of legal age. In the sense that marijuana use typically precedes rather than follows initiation of other illicit drug use, it is indeed a ''gateway'' drug (Institute of Medicine Report 1999, p. ES.7).

Golub and Johnson (1994) examined the developmental pathway followed by a sample of persons who became serious drug abusers. Of the 837 persons sampled 84% had onset to more serious drugs by the time of the interviews. Most of the sample reported having used marijuana (91%). Two-thirds of the drug abusers reported having used marijuana prior to onset to more serious drugs and an additional 19% reported having onset to marijuana and more serious drugs in the same year. These data strongly suggest that marijuana does plan an important role on the pathway to more serious drugs use. Further, the proportion who onset to marijuana before or in the same year as more serious drugs was reported to have increased substantially with time from a low of 78% for persons born from 1928 to 1952 to 95% for the most recent birth cohort of the study (1968–1973). These findings further suggest that marijuana's role as a gateway to more serious substance sue has become more pronounced over time.

Ferguson & Horwood (2000) have examined the relationship between cannabis use in adolescence and the onset of other illicit drug use. Data were gathered over the course of a 21 year longitudinal study of a birth cohort of 1,265 children. By the age of 21, just over a quarter of this cohort reported using various forms of illicit drugs on at least one occasion. In agreement with the predictions of a ''stage-theory'' of the ''gateway hypothesis'' there was strong evidence of a temporal sequence in which the use of cannabis preceded the onset of the use of other illicit drugs. Of those reporting the use of illicit drugs, all but three (99%) had used cannabis prior to the use of other illicit drugs. However, the converse was not true and the majority (63%) of those using cannabis did not progress to the use of other forms of illicit drugs. In addition, to these findings there was a strong dose-response relationship between the extent of cannabis use and the onset of illicit drug use. The analysis suggested that those using cannabis in any given year on at least 50 occasions had hazards of using other illicit drugs that were over 140 times higher than those who did not use in the year. Furthermore, hazards of the onset of other illicit drug use increased steadily with increasing cannabis use. The very strong gradient in risk reflected the facts that: (1) Among non-users of cannabis the use of other forms of illicit drugs was almost non-existent and (2) among regular users of cannabis the use of other illicit drugs was common. To address the issue of ''confounding factors'', the associations between cannabis use and the onset of illicit drug use were adjusted for a series of

prospectively measured confounding factors that included measures of social disadvantage, family functioning, parental adjustment, individual characteristics, attitudes to drug use and early adolescent behavior. After adjustments for these factors, there was still evidence of strong dose-response relationships between the extent of cannabis use in a given year and the onset of illicit drug use—the hazards of the onset of illicit drug use was 100 times those of non-users.

Critics of the ''gateway theory'' point to the presence of other confounding factors and processes that encourage both cannabis use and other forms of illicit drug use. Despite these factors, the Ferguson & Horwood (2000) study provide a compelling set of results that support the hypothesis that cannabis use may encourage other forms of illicit drug use, including the following:

1. Temporal sequence: There was clear evidence that the use of cannabis almost invariably preceded the onset of other forms of illicit drug use.
2. Dose-Response: There was clear evidence of a very strong and consistent dose-response relationship in which increasing cannabis use was associated with increasing risks of the onset of illicit drug use.
3. Resilience to control for confounding: Even following control for a range of prospectively measured social, family and individual factors, strong and consistent associations remained between cannabis use and the onset of other forms of illicit drug use. And,
4. Specificity of associations: The association could not be explained as reflecting a more general process of transition to adolescent deviant behavior since even after control for contemporaneously assessed measures of juvenile offending, alcohol use, cigarette smoking, unemployment and related measures, strong and consistent relationships between cannabis use and the onset of other forms of illicit drugs remained.

A suggested view of the ''gateway hypothesis'' states that the use of cannabis may be associated with increasing risks of other forms of illicit drug use, with this relationship being mediated by affiliations with deviant peers and other non-observed processes that may encourage those who use cannabis (and particularly heavy users) to experiment with, and use, other illicit drugs.

While marijuana is clearly not the only gateway to the use of other illicit drugs it is one of the three most typical drugs in the adolescent's armamentarium. The increased avenues to imported and ''home-grown'' marijuana which contain behaviorally-active doses of THC and CBD pose a serious threat to the health and well-being of this dimension of society.

Taylor *et al.* (2000) evaluated the relationship between cannabis dependence and respiratory symptoms and lung function in young adults, 21 years of age, while controlling for the effects of cigarette smoking. The researchers found significant respiratory symptoms and changes in spirometry occur in cannabis-dependent individuals at age 21 years, even though the cannabis smoking history is of relatively short duration. The likelihood of reporting a broad range of respiratory symptoms was significantly increased in those who were either cannabis-dependent or smoked tobacco or both compared to non-smokers. The symptoms most frequently and significantly associated with cannabis dependence were early morning sputum production (144% greater prevalence than non-smokers). Overall, respiratory symptoms in study members who met strict criteria for cannabis dependence were comparable to those of tobacco smokers consuming 1–10 cigarettes daily. In subjects who were both tobacco users and were cannabis-dependent, some effects seem to be additive, notably early morning sputum production, which occurred 8 times more frequently than non-smokers.

One of the greatest concerns to society regarding Δ^9-THC is the behavioral toxicity produced by the drug. Δ^9-THC intoxication is associated with impairments in memory, motor coordination, cognition, judgement, motivation, sensation, perception and mood (cf., Jaffe, 1993). The consequences produced by Δ^9-THC-induced behavioral impairments can greatly impact the individual and society in general. These impairments result in occupational, household, or airplane, train, truck, bus or automobile accidents, given that individuals may be attending school, working, or operating a motor vehicle under the influence of the drug. In the most general sense, impaired driving can be seen as a failure to exercise the expected degree of prudence or control necessary to ensure road safety. The operations of a motor vehicle are clearly a skilled performance that requires controlled and flexible use of a person's intellectual and perceptual resources. Cannabis interferes with resource allocations in both cognitive and attentional tasks.

In 1999, Ehrenreich *et al.,* examined the detrimental effects of chronic interference by cannabis with the endogenous cannabinoid systems during peripubertal development in humans. As an index of cannabinoid action, visual scanning and other attentional factors were examined in 99 individuals who exclusively used cannabis. Early-onset cannabis use (onset before the age of 16) showed significant impairments in attention in adulthood. These persistent attentional deficits may interact with the activities of daily living, such as operating an automobile.

Kurzthaler *et al.*, (1999) examined the effects of cannabis on a cognitive test battery and driving performance skills. The demonstrated significant impairments in the verbal memory and the trail making tests in this study reflect parallel compromises in associative control that is acknowledged as a cognitive process inherent in memory function immediately after smoking cannabis. Applied to the question of driving ability, the authors suggest that the missing functions would signify that a driver under acute cannabis influences would not be able to use acquired knowledge from earlier experiences adequately to ensure road safety.

Recently, the National Highway Traffic Safety Administration (NHTSA; 1998, 1999, 2000) conducted a study with the Institute for Human Psychopharmacology at Maastricht University in The Netherlands. Low dose and high dose THC administered alone, and with alcohol were examined in two on-road driving situations: (1) The Road Tracking Test, measuring a driver's ability to maintain a constant speed of 62 mph and a steady lateral position between the boundaries of the right traffic lane; and (2) the Car Following Test, measuring a drivers' reaction times and ability to maintain distance between vehicles while driving 164 ft. behind a vehicle that executed a series of alternating accelerations and decelerations. Both levels of THC alone, and alcohol alone, significantly impaired performances on BOTH road tests compared with baseline. Alcohol and the high dose of THC produced 36% decrements in reaction time; because the test vehicles were traveling at 59 mph, the delayed reaction times meant that the vehicle traveled, on average, an additional 139 feet beyond the point where the subjects began to decelerate. Even the lower dose of THC by itself retarded reaction times by 0.9 seconds. The NHTSA concluded that even in low to moderate doses, marijuana impairs driving performance.

In a related analysis, Yesavage, Leirer, Denari, & Hollister (1985) examined the acute and delayed effects of smoking one marijuana cigarette containing 1.9% THC (19 mg of THC) on aircraft pilot performance. Ten private pilot licensed subjects were trained in a flight simulator prior to marijuana exposure. Flight simulator performance was

measured by the number of aileron (lateral control), elevator (vertical control) and throttle changes; the size of these control changes; the distance off the center of the runway on landing; and the average lateral and vertical deviation from an ideal glideslope and center line over the final mile of the approach. Compared to baseline performance, significant differences occurred in all variables at 1 and 4 hours after smoking, except for the numbers of throttle and elevator changes at 4 hours. Most importantly, at 24 hours after a single marijuana cigarette, there were significant impairments in the number and size of aileron (lateral control) changes, size of elevator changes, distance off-center on landing, and vertical and lateral deviations on approach to landing. Interestingly, despite these performance deficits, the pilots reported no significant subjective awareness of their impairments at 24 hours. It is noteworthy that a fatal crash in which a pilot had a positive THC screen involved similar landing misjudgments.

In addition to causing unsafe conditions, marijuana use results in decreased performance and lost productivity in the workplace, including injuries, absenteeism, and increased health care costs. A NIDA report on drugs in the workplace summarized the prevalence of marijuana use in the workplace and its impact on society. This report found that in 1989, one in nine working people (11%) reported current use of marijuana (Gust and Walsh, 1989). Recent DAWN data and other surveys indicate that marijuana use is increasing, especially among younger and working age individuals.

Bray, Zarkin, Ringwalt, & Qi (2000) estimated the impact of age of dropout on the relationship between marijuana use and high school dropouts using four longitudinal surveys from students in the Southeastern U.S. public school system. Their results suggested that marijuana initiation was positively related to high school dropout. Although the magnitude and the significance of the relationship varied with age of dropout and the other substances used, the overall effect represented an odds-ratio of approximately 2.3. These data suggest that an individual is approximately 2.3 times more likely to drop out of school than an individual who has not initiated marijuana use.

When DEA evaluates a drug for control or rescheduling, whether the substance creates dangers to the public health, in addition to or because of its abuse potential, must be considered. The risk to the public health of a substance may manifest itself in many ways. Abuse of a substance may affect the physical and/or psychological functioning of an individual abuser, it may have disruptive effects on the abuser's family, friends, work environment, and society in general. Abuse of certain substances leads to a number of antisocial behaviors, including violent behavior, endangering others, criminal activity, and driving while intoxicated. Data examined under this factor ranges from preclinical toxicity to postmarketing adverse reactions in humans. DEA reviews data from many sources, including forensic laboratory analyses, crime laboratories, medical examiners, poison control centers, substance abuse treatment centers, and the scientific and medical literature.

In its official report titled ''Marijuana and Medicine: Assessing the Science Base'', the Institute of Medicine highlighted a number of risks to the public health as a result of cannabis consumption:

(1) Cognitive impairments associated with acutely administered marijuana limit the activities that people would be able to do safely or productively. For example, no one under the influence of marijuana or THC should drive a vehicle or operate potentially dangerous equipment (Page 107).

(2) The most compelling concerns regarding marijuana smoking in HIV/AIDS patients are the possible effects of marijuana on immunity. Reports of opportunistic fungal and bacterial pneumonia in AIDS patients who used marijuana suggest that marijuana smoking either suppresses the immune system or exposes patients to an added burden of pathogens. In summary, patients with pre-existing immune deficits due to AIDS should be expected to be vulnerable to serious harm caused by smoking marijuana. The relative contribution of marijuana smoke versus THC or other cannabinoids is not known. (Page 116–117)

(3) DNA alterations are known to be early events in the development of cancer, and have been observed in the lymphocytes of pregnant marijuana smokers and in those of their newborns. This is an important study because the investigators were careful to exclude tobacco smokers; a problem in previous studies that cited mutagenic effects of marijuana smoke. (Page 118–119)

(4) * * * factors influence the safety of marijuana or cannabinoid drugs for medical use: the delivery system, the use of plant material, and the side effects of cannabinoid drugs. (1) Smoking marijuana is clearly harmful, especially in people with chronic conditions, and is not an ideal drug delivery system. (2) Plants are of uncertain composition, which renders their effects equally uncertain, so they constitute an undesirable medication. (Page 127)

(7) Its Psychic or Physiological Dependence Liability

The ''dopaminergic hypothesis of drug abuse'' is not the only explanation for the neurochemical actions of drugs. The nucleus accumbens/ventral striatum areas of the brain, typically referred to as simply the Nucleus Accumbens (NAc), represents a critical site for mediating the rewarding or hedonic properties of several classes of abused drugs, including alcohol, opioids, and psychomotor stimulants (Gardner & Vorel, 1998; Koob, 1992; Koob *et al.,* 1998; Wise, 1996; Wise & Bozarth, 1987). It is generally appreciated that all of these drugs augment extracellular dopamine levels in the NAc and that this action contributes to their rewarding properties. However, recent evidence also suggests that many drugs of abuse have dopamine-independent interactions with Nac neuronal activity (Carlezon & Wise, 1996; Chieng & Williams, 1998; Koob, 1992; Martin *et al.,* 1997; Yuan *et al.,* 1992). Recent studies conducted at the Cellular Neurobiology Branch of the NIDA by Hoffman & Lupica (2001) concluded that THC modulates NAc glutamatergic functioning of dopamine. These authors suggested that increases in Nac dopamine levels may be a useful neurochemical index of drug reward but do not fully account for the complex processing of fast synaptic activity by this neuromodulator in the Nac. Moreover, because both glutamatergic and GABAergic inputs to medium spiny neurons are directly inhibited by dopamine, as well as by drugs of abuse. It is likely that these effects contribute to the abuse liability of marijuana.

In addition, the petitioner's global statements about the role of dopamine, the reinforcing effects of marijuana and other drugs, and the predictive validity of animal self-administration studies with marijuana and abuse potential in humans are not supported by the scientific literature. For example:

(1) There are drugs that do not function through dopaminergic systems that are self-administered by animals and humans (*i.e.,* barbiturates, benzodiazepines, PCP).

(2) There are drugs that are readily self-administered by animals that are not abused by man (antihistamines)

(3) There are drugs that are abused by humans that are not readily self-administered by animals (hallucinogens and hallucinogenic phenethylamines, nicotine, caffeine).

(4) There are drugs that have no effect on dopamine that are self-administered

by animals and not abused by humans (*i.e.,* antihistamines).

Physical Dependence in Animals

Abrupt withdrawal from Δ⁹-THC can produce a mild spontaneous withdrawal syndrome in animals, including increased motor activity and grooming in rats, decreased seizure threshold in mice and increased aggressiveness, irritability and altered operant performance in rhesus monkeys (cf., Pertwee, 1991). The failure to observe profound withdrawal signs following abrupt discontinuation of Δ⁹-THC may be due to (1) its long half-life in plasma and (2) slowly waning levels of Δ⁹-THC and its metabolites that continue to permit receptor adaptation.

Recently the discovery of a cannabinoid receptor antagonist demonstrates that a profound precipitated withdrawal syndrome can be produced in Δ⁹-THC tolerant animals after twice daily injections (Tsou *et al.,* 1995) or continuous infusion (Aceto *et al.,* 1995, 1996). In rats continuously infused with low doses Δ⁹-THC for four days, the cannabinoid antagonist precipitated a behavioral withdrawal syndrome, including scratching, face rubbing, licking, wet dog shakes, arched back and ptosis (Aceto *et al.,* 1996). This chronic low dose regimen consisted of 0.5, 1, 2, 4 mg/kg/day Δ⁹-THC on days 1 through 4; 5 and 25-fold higher Δ⁹-THC doses were used for the medium and high dose regimens, respectively. The precipitated withdrawal syndrome was dose-dependently more severe in the medium and high THC dose groups.

Physical Dependence in Humans

Signs of withdrawal have been demonstrated after studies with Δ⁹-THC. Although the intensity of the withdrawal syndrome is related to the daily dose and frequency of administration, in general, the signs of Δ⁹-THC withdrawal have been relatively mild (cf., Pertwee, 1991). This withdrawal syndrome has been compared to that of a short-term, low dose treatment with an opioid or ethanol, and includes changes in mood, sleep, heart rate body temperature, and appetite. Other signs such as irritability, restlessness, tremor mild nausea, hot flashes and sweating have also been noted (cf., Jones, 1983).

A withdrawal syndrome was reported after the discontinuation of oral THC in volunteers receiving dronabinol dosages of 210 mg/day for 12 to 16 consecutive days (PDR, 1997). This was 42-times the recommended dose of 2.5 mg, b.i.d. Within 12 hours after discontinuation, these volunteers manifested withdrawal symptoms such as irritability, insomnia, and restlessness. By approximately 24 hours after THC discontinuation, there was an intensification of withdrawal symptoms to include ''hot flashes'', sweating, rhinorrhea, loose stools, hiccoughs, and anorexia. These withdrawal symptoms gradually dissipated over the next 48 hours. EEG changes consistent with the effects of drug withdrawal (hyperexcitation) were recorded in patients after abrupt challenge. Patients also complained of disturbed sleep for several weeks after discontinuation of high doses of dronabinol. The intensity of the cannabinoid withdrawal syndrome is related by the chronic dose and by the frequency of chronic administration. There is also evidence that the cannabinoid withdrawal symptoms can be reversed by the administration of marijuana and Δ⁹-THC, or by treatment with a barbiturate (hexobarbital) or ethanol (Pertwee, 1991).

An acute withdrawal syndrome or ''hangover'' has been reported by Chait, Fischman, & Schuster (1985) developing approximately 9 hours after smoking a 1 g marijuana cigarette containing 2.9% THC. Five of twelve subjects reported themselves as ''dopey and hung over'' the morning after smoking the single cigarette. In a 10 second and 30 second time-production task significant marijuana hangover effects were found. The effect on the time production task is of interest since the effect obtained the morning after smoking marijuana was opposite to that observed acutely after smoking marijuana. These data may suggest an opponent compensatory rebound which may underlie the development of tolerance over periods of chronic marijuana exposure. Scores on the benzedrine-group (BG) scale, a stimulant scale of the Addiction Research Center Inventory (ARCI) consisting mainly of terms relating to intellectual efficiency and energy, were significantly higher the morning after marijuana smoking, as well. Chait, Fischman, & Schuster also reported increases on the amphetamine (A) scale of the ARCI, a measure of the dose-related effects of d-amphetamine. Cousens & DiMascio (1973) have previously reported a similar ''hangover'' and ''speed of thought alterations'' in subjects the morning after they had received a 30 mg oral dose of Δ⁹-THC. Like the ''hangover'' associated with high dose ethyl alcohol consumption, the hangover from marijuana may be qualitatively identical to, and differ only on an intensity dimension from, the withdrawal syndrome produced from chronic consumption (cf. Gauvin, Cheng, Holloway, 1993).

As described above, Haney *et al.* have recently described abstinence symptoms of an acute withdrawal syndrome following high (30 mg q.i.d.) and low (20 mg q.i.d) dose administrations of oral THC (Haney *et al.,* 1999a) and following 5 puffs of high (3.1%) and low (1.8%) THC-containing smoked marijuana cigarettes (Haney et al., 1999b). Both of these studies have delineated a withdrawal syndrome from concentrations of THC significantly lower than those reported in any other previous study and, for the first time, clearly identified a marijuana withdrawal syndrome detected at low levels of THC exposure that do not produce tolerance. These data suggest that dependence on THC may in fact be an important consequence of repeated, daily exposure to cannabinoids and that daily marijuana use may be maintained, at least in part, by the alleviation of abstinence symptoms.

As stated above, Budney, Novy, & Hughes (1999) have recently examined the withdrawal symptomology in chronic marijuana users seeking treatment for their dependence. The majority of the subjects (85%) reported that they had experienced symptoms of at least moderate severity and 47% experienced greater than four symptoms rated as severe. The most reported mood symptoms associated with the withdrawal state were irritability, nervousness, depression, and anger. Some of the behavioral characteristics of the marijuana withdrawal syndrome were craving, restlessness, sleep disruptions, strange dreams, changes in appetite, and violent outbursts. These data clearly support the validity and clinical significance of a marijuana withdrawal syndrome in man. Large-scale population studies have also reported significant rates of cannabis dependence (Kessler *et al.,* 1994; Farrell *et al.,* 1998), particularly in prison and homeless populations. Similar reports of cannabis dependence in withdrawal in other populations have been previously discussed (above; Crowley *et al.* (1998); Kouri & Pope (2000)).

Psychological Dependence in Humans

In addition to the physical dependence produced by abrupt withdrawal from Δ⁹-THC, psychological dependence on Δ⁹-THC can also be demonstrated. Case reports and clinical studies show that frequency of Δ⁹-THC use (most often as marijuana) escalates over time, there is evidence that individuals increase the number, doses, and potency of marijuana cigarettes. Data have clearly shown that tolerance

to the stimulus effects of the drug develops which could lead to drug seeking behavior (Pertwee, 1991; Aceto *et al.,* 1996; Kelly *et al.,* 1993, 1994; Balster and Prescott, 1992; Mendelson *et al.,* 1976; Mendelson and Mello, 1985; Mello, 1989). Several studies have reported that patterns of marijuana smoking and increased quantity of marijuana smoked were related to social context and drug availability (Kelly *et al.,* 1994; Mendelson and Mello, 1985; Mello, 1989). There have been, however, other studies which have demonstrated that the magnitude of many of the behavioral effects produced by Δ^9-THC and other synthetic cannabinoids lessens with repeated exposure while also demonstrating that tolerance did not develop to the euphorigenic activity, or the ''high'' from smoked marijuana (Dewey, 1986; Perez-Reyes *et al.,* 1991). Recent electrophysiological data from animals suggests that the response of VTA dopamine neurons do not diminish during repeated exposure to cannabinoids, and that this may underlie the lack of tolerance to the euphoric effects of marijuana even with chronic use (Wu & French, 2000).

The problems of psychological dependence associated with marijuana (THC) abuse are apparent from DAWN reports and survey data from the National Household Survey on Drug Abuse and the Monitoring the Future study. These databases show that the incidence of chronic daily marijuana use and adverse events associated with its use are increasing, especially among the young. At the same time, perception of risk has decreased and availability is widespread (cf., NIDA, 1996). These factors contribute to perpetuating the continued use of the marijuana.

(8) Whether The Substance Is an Immediate Precursor of a Substance Already Controlled Under This Subchapter.

According to the legal definition, marijuana (Cannabis sativa L.) is not an immediate precursor of a scheduled controlled substance. However, cannabidiol is a precursor for delta-9-tetrahydrocannabinol, a Schedule I substance under the CSA.

References

Aceto MD, Scates SM, Lowe JA, & Martin BR (1995). Cannabinoid precipitated withdrawal by the selective cannabinoid receptor antagonist, SR 141716A. Eur J Pharmacol 282:R1–R2.

Aceto MD, Scates SM, Lowe JA, & Martin BR (1996). Dependence on Δ^9-tetrahydrocannabinol: studies on precipitated and abrupt withdrawal. J Pharmacol Exper Therap 278:1290–1295.

Adams IB & Martin BR (1996). Cannabis: Pharmacology and toxicology in animals and humans. Addiction 91:1585–1614.

Agurell S, Gillespie H, Halldin M, Hollister LE, Johansson E, Lindgren JE, Ohlsson A, Szirmai M, & Widman M (1984). A review of recent studies on the pharmacokinetics and metabolism of delta-1-tetrahydrocannabinol, cannabidiol and cannabinol in man. In: Harvey DJ (Ed), Marijuana '84. Proceedings of the Oxford Symposium on Cannabis. IRL Press Ltd:Oxford, England, pp. 49–62.

Agurell S, Halldin M, Lindgren J E et al. (1986). Pharmacokinetics and metabolism of delta-1-tetrahydrocannabinoid and other cannabinoids with emphasis on man. Pharmacol Rev 38:21–43.

Agurell S, Leander K (1971). Stability, transfer and absorption of cannabinoid constituents of Cannabis (Hashish) during smoking. Acta Pharm Succica 8:391–402.

Azorlosa J, Heishman S, Stitzer M (1992). Marijuana smoking: effect of varying delta-9-tetrahydrocannabinol content and number of puffs. J Pharmacol Exp Ther 261:114–122.

Baker PB, Gough TA, Taylor BJ (1982). The physical and chemical features of Cannabis plants grown in the United Kingdom of Great Britain and Northern Ireland from seeds of known origin. Bull Narc 34:27–36.

Baker PB, Gough TA, Taylor BJ (1983). The physical and chemical features of Cannabis plants grown in the United Kingdom of Great Britain and Northern Ireland from seeds of know origin—Part II: second generation studies. Bull Narc 35:51–62.

Balster RL & Prescott WR (1992). Δ9-tetrahydrocannabinol discrimination in rats as a model for cannabis intoxication. Neurosci Biobehav Rev 16:55–62.

Barnett G, Chiang C–WN, Perez-Reyes M, Owens SM (1982). Kinetic study of smoking marijuana. J Pharmacokin Biopharm 10:495–505.

Barrett RL, Wiley JL, Balster RL & Martin BR (1995). Pharmacological specificity of Δ9-tetrahydrocannabinol discrimination in rats. Psychopharmacology 118:419–424.

Beal JA, & Martin BM (1995). The clinical management of wasting and malnutrition in HIV/AIDS. AIDS Patient Care April: 66–74.

Becker HS (1967). History, culture and subjective experience: an exploration of the social bases of drug-induced experiences. J Health Soc Behav 8:163–176.

Benowitz NL, & Jones RT (1981). Cardiovascular and metobolic considerations in prolonged cannabinoid administration in man. J Clin Pharmacol 21:214S–223S.

Bird KD, Boleyn T, Chesher GB, Jackson DM, Starmer GA, & Teo RKC (1980). Intercannabinoid and cannabidiol-ethanol interactions and their effects on human performance. Psychopharmacology 71:181–188.

Bornheim LM, Kim KY, Li J, Perotti BYT, Benet LZ (1995). Effect of cannabidiol pretreatment on the kinetics of tetrahydrocannabinol metabolites in mouse brain. Drug Metab Dispos 23:825–831.

Borgen LA, & Davis WM (1974). CBD interaction with Δ9-tetrahydrocannabinol. Res Commun Chem Pathol Pharmacol 7:663–670.

Bouquet RJ (1951). Cannabis. Bull Narc 3:14–30.

Brady JV, Hienz RD, & Ator NA (1990). Stimulus functions of drugs and the assessment of abuse liability. Drug Develop Res 20:231–249.

Brady KT, & Balster RL (1980) the effects of Δ9-tetrahydrocannabinol alone and in combination with cannabidiol on fixed-interval performance in rhesus monkeys. Psychopharmacology 72:21–26.

Braut-Boucher F, Paris M, Cosson L (1977). Mise en évidence de deux types chimiques chez le Cannabis sativa originaire d'Afrique du sud. Phytochemistry 16:1445–1448.

Braut-Boucher F (1978). Etude ecophysiologique et chimique due cannabis sativa L. cultive en Phytotron. Mise en évidence d'un type chimique nouveau chez un Chanvre originaire d'Afrique due Sud. Doctoral thesis. University of Paris XI.

Bray JW, Zarkin GA, Ringwalt C, Qi J (2000). The relationship between marijuana initiation and dropping out of high school. Health Econ 9:9–18.

Braut-Boucher F, & Petiard V (1981). Sur la mise en culture in vitro de tissue de differents types chimiques de Cannabis sativa L. C R Acad Sci (Paris) 292:833–838.

Browne RG, & Weissman A (1981). Discriminative stimulus properties of Δ9-tetrahydrocannabinol: Mechanistic studies. J Clin Pharmacol 21:227S–234S.

Budney AJ, Novy PL, Hughes JR (1999). Marijuana withdrawal among adults seeking treatment for marijuana dependence. Addiction 94:1311–1321.

Caldwell DF, Myers SA, Domino EF, & Merriam PE (1969a). Auditory and visual threshold effects of marihuana in man. Percept Motor Skills 29:755–759.

Caldwell DF, Myers SA, Domino EF, & Merriam PE (1969b). Auditory and visual threshold effects of marihuana in man:Addendum. Percept Motor Skills 29:922.

Cappell H, & Pliner P (1974). Cannabis intoxication: the role of pharmacological and psychological variables. In: Miller LL (Ed), Marijuana: Effects on human behavior. Academic Press:New York, pp. 233–264.

Carlezon WAJ, Wise RA (1996). Rewarding actions of phencyclidine and related drugs in nucleus accumbens shell and frontal cortex. J Neurosci 16:3112–3122.

Carlini EA, & Cunha JA (1981). Hypnotic and antiepileptic effects of cannabidiol. J Clin Pharmacol 32:417–427.

Carlini EA, Karniol IG, Renault PF, Schuster CR (1974). Effects of marijuana in laboratory animals and in man. Br J Pharmacol 50:299–309.

Carlini EA, Leite JR, Tannhauser M, Berardi

AC (1973). Letter: Cannabidiol and cannabis sativa extract protect mice and rats against convulsive agents. J Pharm Pharmacol 25:664–665.

Carney JM, Uwaydah IM, & Balster RL (1977). Evaluation of a suspension system for intravenous self-administration studies of water-insoluble compounds in the rhesus monkey. Pharmacol Biochem Behav 7:357–364.

Carriot F, Sasco AJ (2000). Cannabis and cancer. Rev Epidemiol Sante Publique 48:473–483.

Chait LD, Burke KA (1994). Preference for ''high'' versus low-potency marijuana. Pharmacol Biochem Behav 49:643–647.

Chait LD, Fischman MW & Schuster CR (1985). ''Hangover'' effects the morning after marijuana smoking. Drug Alcohol Depend 15:229–238.

Chait LD, & Zacny JP (1992). Reinforcing and subjective effects of oral Δ9-THC and smoked marijuana in humans. Psychopharmacology 107:255–262.

Chait LD, & Pierri J (1992). Effects of smoked marijuana on human performance. In: Murphy L, & Bartke A (Eds). Marijuana/ Cannabinoids. Neurobiology and Neurophysiology. CRC Press, Boca Raton, FL; pp. 387–423.

Chait LD, Evans SM, Grant KA, Kamien JB, Johanson CE, & Schuster CR (1988). Discriminative stimulus and subjective effects of smoked marijuana in humans. Psychopharmacology 94:206–212.

Chen J, Paredes W, Li J, Smith D, Lowinson J, & Gardner EI (1994). Psychopharmacology 102:156–162.

Chesher GB, & Jackson DM (1974). Anticonvulsant effets of cannabinoids in mice: drug interactions within cannabinoids and cannabinoid interactions with phenytoin. Psychopharmacologia (Berl) 37:255–264.

Chieng B, Williams JT (1998). Increase opioid inhibition of GABA release in nucleus accumbens during morphine withdrawal. J Neurosci 18:7033–7039.

Clark LD, & Nakashima EC (1968). Experimental studies with marihuana. Am J Psychiat 125:135–140.

Cocchetto DM, Owens SM, Perez-Reyes M, DiGuiseppi S, Miller LL (1981). Relationship between delta-9-tetrahydrocannabinol concentration and pharmacologic effects in man. Psychopharmacology (Berl) 75:158–164.

Coffey C, Lynskey M, Wolfe R, Patton GC (2000). Initiation and progression of cannabis use in a population-based Australian adolescent longitudinal study. Addiction 95:1679–1690.

Community Epidemiology Work Group. (1995). Epidemiological trends in Drug Abuse, December 1994: Volume 1: Highlights and Executive Summary. National Institute on Drug Abuse, NIH Publication No. 95–3988, pp. 54–56.

Compton DR, Rice KC, DeCosta BR, Razdan RK, Melvin LS, Johnson MR, & Martin BR (1993). Cannabinoid structure-activity relationships: correlation of receptor binding and in vivo activities. J Pharmacol Exper Ther 265:218–226.

Cone EJ, Johnson RE, Paul BD, Mell LD, & Mitchell J (1988). Marijuana-laced brownies: Behavioral effects, physiological effects and urinalysis in humans following ingestion. J Anal Toxicol 12:169–175.

Consroe P, Martin P, & Eisenstein D (1977). Anticonvulsant drug antagonism of Δ9-tetrahydrocannabinol seizures in rabbits. Res Commun Chem Pathol Pharmacol 16:1–13.

Consroe P, Martin P, & Singh V (1981). Antiepileptic potential of cannabidiol analogues. J Clin Pharmacol 21:428S–436S.

Cousens K, DiMascio A (1973). (-)Δ9 THC as an hypnotic: An experimental study of three dose levels. Psychopharmacologia (Berl.) 33:355–364.

Crancer JM, Dille JM, Delay JC, Wallace JE, Haykin MD (1969). Comparisons of the effects of marihuana and alcohol on simulated driving performance. Science 164:851–854.

Crowley TJ, Macdonald MJ, Whitmore EA, Mikulich SK (1998). Cannabis dependence, withdrawal, and reinforcing effects among adolescents with conduct symptoms and substance use disorders. Drug Alcohol Depend 50:27–37.

Dalton WS, Martz R, Kenberger L, Rodda BE, & Forney RB (1976). Influence of cannabidiol on delta-9-tetrahydrocannabinol effects. Clin Pharmacol Therap 19:300–309.

Darley CF, Tinklenbreg WT, Roth WT, Hollister LE, & Atkinson RC (1973a). Influence of marihuana on storage and retrieval processes in memory. Mem Cognit 1:196–200.

Darley CF, Tinklenbreg WT, Hollister LE, & Atkinson RC (1973b). Marihuana and retrieval from short term memory. Psychopharmacologia (Berl.) 29:231–233.

deMeijer EPM (1993). Hemp variations as pulp source researched in the Netherlands. Government-funded hemp (Cannabis sativa L.) investigation evaluates stem quality, yield, comparison to woodfibers. Pulp & Paper 67:41–43.

deMeijer EPM, van der Kamp HJ, & van Eeuwijk VA (1992). Characterisation of cannabis accessions with regard to cannabinoid content in relation to other plant characters. Euphytica 62:187–200.

Deneau GA, & Kaymakcalan S. (1971). Physiological and psychological dependence to Δ9-tetrahydrocannabinol (THC) in rhesus monkeys. Pharmacologist 13:246.

Devine ML, Dow GJ, Greenberg BR, Holsten DW, Icaza L, Jue PY, Meyers FH, O'Brien E, Roberts CM, Rocchio GL, Stanton W, & Wesson DL (1987). Adverse reactions to Δ9-tetrahydrocannabinol given as an antiemetic in a multicenter study. Clin Pharmacol 6:319–322.

Dewey WL (1986). Cannabinoid pharmacology. Pharmacol Rev 38: 151–178.

deWit H, & Griffiths RR (1991). Testing the abuse liability of anxiolytic and hypnotic drugs in humans. Drug Alcohol Depend 28:83–111.

deWit H, Bodker B, Ambre J (1992). Rate of increase of plasma drug level influences subjective response in humans. Psychopharmacology 107:352–358.

DiMarzo V, Melis M, Gessa GL (1998). Endocannabinoids: endogenous cannabinoid receptor ligands with neuromodulatory actions. TINS 21:521–528.

Domino LE, Domino SE, Domino EF (1984). Relation of plasma delta-9-THC concentrations to subjective ''high'' in marijuana users: A review and reanalysis. In: S Agurell, WL Dewey, Willette RE (Eds) The Cannabinoids: chemical, pharmacologic, and therapeutic aspects. Orlando, FL: Academic Press, pp 245–261.

Domino EF, Rennick P, & Pearl JH (1976). Short-term neuropsychopharmacological effects of marihuana smoking in experienced male users. In: Braude MC & Szara S (Eds) The Pharmacology of Marihuana. Raven Press: New York, pp 393–412.

Doorenbos NJ, Fetterman PS, Quimby MW, Turner CE (1971). Cultivation extraction and analysis of Cannabis sativa L.. Ann NY Acad Sci 191:3–15.

Doyle E, & Spence AA (1995). Cannabis as a medicine. Br J Anaesth 74:359–361.

Drew G, & Miller L (1974). Cannabis: Neural mechanisms and behavior—a theoretical review. Pharmacol Rev 38:151–178.

Duffy A, & Milin R (1996). Withdrawal syndrome in adolescent chronic cannabis users. J Am Acad Child Adolesc Psychiatry 35:1618–1621.

Ehrenreich H, Rinn T, Kunert HJ, Moeller MR, Poser W, Schilling L, Gigerenzer G, Hoehe MR (1999). Specific attentional dysfunction in adults following early start of cannabis use. Pyschopharmacology (Berl) 142:295–301.

Fairbairn JW, Hindmarch I, Simic S, Tylden E (1974). Cannabinoid content of some English reefers. Nature 249: 276–278.

Fairbairn JW, & Liebmann JA (1974). The cannabinoid content of cannabis sativa L.. grown in England. J Pharmac Pharmacol 26:413–419.

Fairbairn JW, Liebmann JA, & Simic S (1971). The tetrahydrocannabinol content of cannabis leaf. J Pharmac Pharmacol 23:558–559.

Farré M, & Camí J (1991) Pharmacokinetics and abuse liability. Br J Addict 86:1601–1606.

Farrell M, Howes S, Taylor C, Lewis G, Jenkins R, Bebbington P, Jarvis M, Brugha T, Gill B, Meltzer H (1998). Substance misuse and psychiatric comorbidity: an overview of the OPCS national psychiatric morbidity survey. Addictive Behaviors 23:909–918.

Farrelly MC, Bray JW, Zarkin GA, Wendling BW (2001). The joint demand for cigarettes and marijuana: evidence from the National Household Surveys on Drug Abuse. J Health Econ 20:51–68.

Fernandes M, Schabarak A, Coper H, & Hill R (1974). Modificarion of the Δ9-THC-actions by cannabinol and cannabidiol in the rats. Psychopharmacologia (Berl.) 38:329–338.

Fetterman PS, Doorenbos NJ, Keith ES, Quimby MW (1971). A simple gas liquid chromatography procedure for determination of cannabinoidic acids in

Cannabis sativa L. Experientia 27:988–989.
Fetterman PS, Keith ES, Waller CW, Guerrero O, Doorenbos NJ, Quimby MW (1970). Mississippi grown Cannabis sativa L.. A preliminary observation on the chemical definition of phenotype and variations in the content versus age, sex, and plant park. J Pharm Sci 60:1246–1249.
Ferguson DM, Horwood LJ (2000). Does cannabis use encourage other forms of illicit drug use? Addiction 95:505–520.
Foltin RW, Fischman MW, Brady JV, Bernstein DJ, Capriotti RM, Nellis MJ, Kelly TH (1990). Motivational effects of smoked marijuana: behavioral contingencies and low-probability activities. J Exp Anal Behav 53:5–19.
Ford RD, Balster RL, Dewey WL, Beckner JS (1977). Delta-9-THC and 11-OH-delta-9-THC: behavioral effects and relationship to plasma and brain levels. Life Sci 20:1993–2003.
Gardner EL (1992). Cannabinoid interactions with brain reward systems—The Neurobiological basis of cannabinoid abuse. In: Murphy L, & Bartke A (Eds), Marijuana/Cannabinoids: Neurobiology and Neurophysiology. CRC Press, Boca Raton, FL; pp. 275–335.
Gardner EL, & Lowinson JH (1991). Marijuana's interaction with brain reward systems: Update 1991. Pharmacol Biochem Behav 40:571–580.
Gardner EL, Paredes W, Smith D, Donner A, Milling C, Cohen D, & Morrison D (1988). Facilitation of brain stimulation reward by delta-9-tetrahydrocannabinol. Psychopharmacology 96:142–144.
Gardner EL, Vorel SR (1998). Cannabinoid transmission and reward-related events. Neurobiol Dis 5:502–533.
Gauvin DV & Baird TJ (1999). The discriminative stimulus properties of compound drug stimuli: a focus on attention. Pharmacology, Biochemistry and Behavior.
Gauvin DV, Cheng EY & Holloway FA (1993). Biobehavioral correlates of alcohol hangover. In: Galanter, M. (Ed.) Recent Developments in Alcoholism: Ten Years of Progress NY: Plenum Press, pp. 281–304.
Gauvin DV, Harland RD, & Holloway FA (1989). Drug discrimination procedures: A method to analyze adaptation level of affective states. Drug Develop Res 16:183–194.
Gledhill-Hoyt J, Lee H, Strote J, Wechsler H (2000). Increased use of marijuana and other illicit drugs at US colleges in the 1990s: results of three national surveys. Addiction 95:1655–1667.
Golub A, Johnson BD (1994). The shifting importance of alcohol and marijuana as gateway substances among serious drug abusers. Journal on the Studies of Alcohol 55:607–614.
Goudie AJ (1987). Aversive stimulus properties of drugs: The conditioned taste aversion paradigm. In: Greenshaw AJ & Dourish CT (Eds) Experimental Psychopharmacology. Humana Press: Clifton, NJ, pp. 341–391.
Guimães FS, Chiarett TM, Graeff FG, & Zuardi AW (1990). Antianxiety effect of cannabidiol in the elevated plus-maze. Psychopharmacology 100:558–559.
Guimães FS, DeAguiar JC, Mechoulam R, Breuer A (1994). Anxiolytic effect of cannabidiol derivatives in the elevated plus-maze. Gen Pharmac 25:161–164.
Gust SW, & Walsh JM (1989). Drugs in the Workplace: Research and Evaluation Data. NIDA Monograph No. 91. US Government Printing Office: Washington, DC.
Hamilton HC (1912). The pharmacopoeia requirements for Cannabis sativa. J Am Pharm Assoc 1:200–203.
Hamilton HC (1915). Cannabis sativa: Is the medicinal value found only in the Indian grown drug. J Am Pharm Assoc 4:448–451.
Hanus L, Subová D (1989). The amount of main cannabinoid substances in hemp, cultivated for industrial fibre production and their changes in the course of one vegetation period. Acta Univ Palacki Olomuc, Fac Med 122:11–23.
Hanus L, Yoshida T, Kreji (1975). Production of Δ9-tetrahydrocannabinol from hemp cultivated in climatic conditions of Czechoslovakia. Acta Univ Palacki Olomuc, Fac Med 74:173–180.
Haney M, Ward AS, Comer SD, Foltin RW, Fischman MW (1999a). Abstinence symptoms following oral THC administration to humans. Psychopharmacology 141:385–394.
Haney M, Ward AS, Comer SD, Foltin RW, Fischman MW (1999b). Abstinence symptoms following smoked marijuana in humans. Psychopharmacology 141:395–404.
Harris RT, Waters W, & McLendon D (1974). Evaluation of the reinforcing capability of Δ9-tetrahydrocannabinol in rhesus monkeys. Psychopharmacologia 37:23.
Harris D, Jones RT, Shank R, Nath R, Fernandez E, Goldstein K, Mendelson J (2000). Self-reported marijuana effects and characteristics of 100 San Francisco medical marijuana club members. J Addict Dis 19:89–103.
Heishman SJ, Huestis MA, Henningfield JE, Cone EJ (1990). Acute and residual effects of marijuana: profiles of plasma THC levels, physiological, subjective, and performance measures. Pharmacology Biochemistry & Behavior 37:561–565.
Henningfield JE (1984). Behavioral pharmacology of cigarette smoking. In: Thompson T, Dews PB & Barrett JE (Eds), Advances in Behavioral Pharmacology, Volume 4, Academic Press: Orlando, FL, pp 131–210.
Hiltunen AJ, & Järbe TUC (1986). Interactions between Δ9-tetrahydrocannabinol and cannabidiol as evaluated by drug discrimination procedures in pigeons. Neuropharmacol 25:133–142.
Hiltunen AJ, Järbe TUC, & Wängdahl K (1988). Cannabinol and cannabidiol in combination: temperature, open-field activity, and vocalization. Pharmacol Biochem Behav 30:675–682.
Hines B, Torrelio M, & Gershon S (1975a). Interactions between cannabinol and cannabidiol during abstinence in morphine-dependent rats. Res Comm Chem Pathol Pharmacol 12:185–188.
Hine B, Torrelio M, & Gershon S. (1975b). Differential effects of cannabidiol and Δ9-THC during abstinence in morphine-dependent rats. Life Sci 17:185–188.
Ho BT, Estevez VS, Englert LF (1973). The uptake and metabolic fate of cannabinoids in rat brains. J Pharm Pharmacol 25:488–490.
Hoffman AF, Lupica CR (2001). Direct actions of cannabinoids on synaptic transmission in the Nucleus Accumbens: A comparison with opioids. J Physiol 85:72–83.
Hollister LE (1974). Structure activity relationship in man of cannabis constituents and homologs and metabolites of Δ9-tetrahydrocannabinol. Pharmacology 11:3–11.
Hollister LE (1988). Cannabis—1988.(Literature Review). Acta Psychiatr Scand 78:108–118.
Hollister LE (1986). Health aspects of cannabis. Pharmacol Rev 38:1–20.
Hollister LE, & Gellespie BA (1975). Interactions in man of delta-9-tetrahydrocannabinol. II. Cannabinol and cannabidiol. Clin Pharmacol Therap 18:80–83.
Howlett AC (1987). Cannabinoid inhibition of adenylate cyclase: relative activities of marihuana constituents and metabolites. Neuropharmacology 26:507–512.
Howlett AC, Evans DM, & Houston DB (1992). The cannabinoid receptor. In: Murphy L & Bartke A (Eds) Marijuana/Cannabinoids: Neurobiology and Neurophysiology. Boca Raton: CRC Press, pp 38–72.
Huffman JW, Dai D, Martin BR, & Compton DR (1994). Design, synthesis and pharmacology of cannabimimetic indoles. BioMed Chem Lett 4:563–566.
Institute of Medicine (1982). Division of Health Sciences Policy. Marijuana and Health: Report of a study by committee of the Institute of Medicine, Washington, D.C. National Academy Press.
Institute of Medicine (1999). Marijuana and medicine: Assessing the science base. Washington, D.C.: National Academy Press.
Isbell H, Gorodetzky CW, Jasinski D, Claussen U, VonSpulak F, & Korte F (1967). Effects of (-)-Δ9-tetrahydrocannabinol in man. Psychopharmacologia 11:184–188.
Izquierdo I, Tannhauser M (1973). Letter: The effect of cannabidiol on maximal electroshock seizures in rats. J Pharm Pharmacol 25:916–917.
Järbe TU, Hiltunen AJ, & Mechoulam R (1989). Subjectively experienced cannabis effects in animals. Drug Develop Res 16:385–393.
Järbe TU, & Hendricksson BG (1974). Discriminative response control produced by hashish, tetrahydrocannabinols (Δ8-THC and Δ9-THC) and other drugs. Psychopharmacologia (Berl.) 40:1–16.
Järbe TU, Hendricksson BG, & Ohlin GC (1977). Δ9-THC as a discriminative cue in pigeon: effects of Δ8-THC, CBD, and CBN. Arch Internat Pharmacodyn Ther 228:68–72.

Järbe TU, & Mathis DA (1992). Dissociative and discriminative stimulus functions of cannabinoids/cannabimimetics. In: Murphy L & Bartke A (Eds), Marijuana/ Cannabinoids: Neurobiology and Neurophysiology. CRC Press, Boca Raton, FL, pp. 425–458.

Johnston LD, O'Malley PM, & Bachman JG (1996). National Survey Results on Drug Abuse from the Monitoring the Future Study, 1975–1995. Volume 1: Secondary School Students. U.S. Government Printing Office: Washington, DC.

Jones RT (1971). Marijuana-induced ''high'': influence of expectation, setting and previous drug experience. Pharmacol Rev 23:359–369.

Jones RT (1980). Human effects: an overview. In: Petersen RC (Ed) Marijuana research findings: 1980. NIDA Res Mono 31. U.S. Govt Printing Office: Washington DC, pp 54–79.

Jones RT, Benowitz NL, & Herning RI (1981). Clinical relevance of cannabis tolerance and dependence. J Clin Pharmacol 21:143S–152S.

Jones RT, Pertwee RG (1972). A metabolic interaction in vivo between cannabidio and delta-1-tetrahydrocannabinol. Br J Pharmacol 45:375–377.

Kamien JB, Bickel WK, Higgins ST, & Hughes JR (1994). The effects of Δ9-tetrahydrocannabinol on repeated acquisition and performance of response sequences and on self-reports in humans. Behav Pharmacol 5:71–78.

Karniol IG, & Carlini EA (1972). The content of (-) Δ9-trans-tetrahydrocannabinol (Δ9-THC) does not explain all biological activity of some Brazilian marijuana samples. J Pharm Pharmacol 24:833–835.

Karniol IG, & Carlini EA (1973). Comparative studies in man and in laboratory animals on 8-and 9-trans-tetrahydrocannabinol. Pharmacology 9:115–126.

Karniol IG, & Carlini EA (1973). Pharmacological interaction between cannabidiol and Δ9-tetrahydrocannabinol. Psychopharmacologia (Berl) 33:53–70.

Karniol IG, Shirakawa I, Kasinski N, Pfefferman A, & Carlini EA (1974). Cannabidiol interferes with the effects of Δ9-tetrahydrocannabinol in man. Eur J Pharmacol 28:172–178.

Kaymakcalan S (1973).Tolerance and dependence on cannabis. Bull Narc 25:39–47.

Kelly P, & Jones RT (1992). Metabolism of tetrahydrocannabinol in frequent and infrequent marijuana users. J Anal Toxicol 16:328–335.

Kelly TH, Foltin RW, Emurian CS, Fischman MW (1997). Are choice and self-administration of marijuana related to delta-9-THC content? Exp Clin Psychopharmacol 5:74–82.

Kelly TH, Foltin RW, & Fischman MW (1993). Effects of smoked marijuana on heart rate, drug ratings and task performance by humans. Behav Pharmacol 4:167–178.

Kelly TH, Foltin RW, Mayr MT, & Fischman MW (1994). Effects of Δ9-tetrahydrocannabinol and social context on marijuana self-administration by humans. Pharmacol Biochem Behav 49:763–768.

Kessler R, McGonagle K, Zhao S, Nelson, CB, Hughes M, Eshleman S, Wittchen H–U, Kendler KS (1994). Lifetime and 12 month prevalence of DSM–III–R psychiatric disorders in the United States: results from the National Comorbidity Survey. Arch Gen Psychiatry 51:8–19.

Kiplinger GF, Manno JE, Rodda BE, Fornery RB, Haine SE, East R, Richards AB (1971). Dose-response analysis of the effects of tetrahydrocannabinol in man. Clin Pharmacol Ther 12:650–657.

Koob GF (1992). Neural mechanisms of drug reinforcement. Ann NY Acad Sci 654:171–191.

Koob GF, Roberts AJ, Schulteis G, Parsons LH, Heyser CJ, Hyytia P, Merlo-Pich E, Weiss F (1998). Neurocircuitry targets in ethanol reward and dependence. Alcohol Clin Exp Res 22:3–9.

Khouri EM, Pope HG, Lukas SE (1999). Changes in aggressive behavior during withdrawal from long-term marijuana use. Psychopharmacology 143:302–308.

Kouri EM, Pope HG (2000) Abstinence symptoms during withdrawal from chronic marijuana use. Exper Clin Psychopharmacol 8: 483–492.

Kurzthaler I, Hummer M, Miller C, Sperner-Unterweger B, Gunther V, Wechdorn H, Battista H–J, Fleischhacker WW (1999). Effect of cannabis use on cognitive functions and driving ability. J Clin Psychiatry 60:395–399.

Lemberger L, Crabtree R, Rowe HM (1972). 11-hydroxy-9-tetrahydrocannabinol: pharmcology, disposition, and metabolism of a major metabolite of marihuana in man. Science 177:62–64.

Lemberger L, & Rubin A. (1975). The physiologic disposition of marijuana in man. Life Sci 17:1637–1642.

Lepore M, Vorel SR, Lowinson J, Gardner EL (1995). Conditioned place preference induced by Δ9-tetrahydrocannabinol: Comparison with cocaine, morphine and food reward. Life Sci 56:2073–2080.

Lichtman A, & Martin BR (1996). Δ9-tetrahydrocannabinol impairs spatial memory through a cannabinoid receptor mechanism. Psychopharmacology 126:125–131.

Little PJ, Compton DR, Johnson MR, Melvin LS, & Martin BR (1988). Pharmacology and stereoselectivity of structurally novel cannabinoids in mice. J Pharmacol Exper Ther 247:1046.

Lukas SE, Mendelson JH, Benedikt R (1995). Electroencephalographic correlates of marihuana-induced euphoria. Drug Alcohol Depend 37:131–140.

Machula IA, Dudkin SM, & Barkov NK (1992). Characterization of mechanisms mediating the effects of Δ9-tetrahydrocannabinol on behavior. In: Murphy L & Bartke A (Eds), Marijuana/ Cannabinoids. Neurobiology and Neurophysiology. CRC Press, Boca Raton, FL; pp. 525–538.

Manno JE, Kiplinger GF, Scholz N, Forney RB, Haine SE (1971). The influence of alcohol and marihuana on motor and mental performance. Clin Pharmacol Ther 12:202–211.

Manno JE, Kiplinger GF, Haine SE, Bennett IF, Forney RB (1970). Comparative effects of smoking marihuana on placebo on human motor and mental performance. Clin Pharmacol Ther 11:808–815.

Martin BR, Balster RL, Razdan RK, Harris LS, & Dewey WL (1981). Behavioral comparisons of stereoisomers of tetrahydrocannabinols. Life Sci 29:565.

Martin BR, Compton DR, Prescott WR, Barrett RL, & Razdan RK (1995). Pharmacological evaluation of dimethylheptyl analogs of Δ9-THC: reassessment of the putative three-point cannabinoid-receptor interaction. Drug Alcohol Depend 37:231–240.

Martin BR, Hall W (1997, 1998). The health effects of cannabis: key issues of policy relevance. Bulletin on Narcotics XLIX & L (1&2):85–116.

Martin G, Nie Z, Siggens GR (1997). Mu-Opioid receptors modulate NMDA receptor-mediated responses in nucleus accumbens neurons J Neurosci 17:11–22.

Mechoulam R (1973). Marijuana: Chemistry, pharmacology, metabolism, and clinical effects. NY: Academic Press.

Mechoulam R (1998). Endocannabinoids. Eur J Pharmacol 359:1–18.

Mechoulum R, Shani A, Edery HM, & Grunfield Y (1970). Chemical basis for hashish activity. Science 169:611–612.

Mello NK (1989). Drug self-administration procedures: Alcohol and marijuana. In: Fischman MW, & Mello NR (Eds). Testing for Abuse Liability of Drugs in Humans. US Government Printing Office:, Washington, DC; pp.147–170.

Mello NK, & Mendelson JH (1985). Operant acquisition of marijuana by women. J Pharmacol Exper Therap 235:162–171.

Mendelson JH, & Mello NK (1984). Reinforcing properties of oral Δ^9-tetrahydrocannabinol, smoked marijuana and nabilone: Influence of previous marijuana use. Psychopharmacology 83:351–356.

Mendelson JH, & Mello NK (1984). Effects of marijuana on neuroendocrine hormones in human males and females. In Braude, M.C. and Ludford, J.P., (Eds). Marijuana Effects on the Endocrine and Reproductive Systems. National Institute on Drug Abuse Monograph 44. DHHS Pub No. (ADM) 84–1278. U.S. Printing Office: Washington, DC.

Mendelson JH, Rossi AM, & Meyer RE (1974). The Use of Marijuana: A Psychological and Physiological Inquiry. Plenum Press: New York.

Microgram. 30: 1, 1997.

Miller LL, Cocchetto DM, & Perez-Reyes M (1983). Relationship between several pharmacokinetic parameters and psychometric indices of subjective effects of Δ9-tetrahydrocannabinol in man. Eur J Pharmacol 25:633–637.

Monti JM (1977). Hypnotic-like effects of cannabidiol in the rat. Psychopharmacology 55:263–265.

Musty RE (1984). Possible anxiolytic effects of cannabidiol. In: Agurell S, Dewey WL, Willette RE (Eds) The cannabinoids: chemical, pharmacologic, and

therapeutic aspects. NY: Academic Press, pp. 795–815.
Musty RE, & Sands R (1978). Effects of marijuana extract distillate and cannabidiol on variable interval performance as a function of food deprivation. Pharmacology 16:199–205.
Musty RE, Reggio P, & Consroe P (1995). A review of recent advances in cannabinoid research and the 1994 International Symposium on Cannabis and the Cannabinoids. Life Sci 56:1933–1940.
Nakamura EM, da Silva EA, Concilio GM, Wilkinson DA, & Masur J (1991). Reversible effects of acute and long-term administration of Δtetrahydrocannabinol (THC) on memory in the rat. Drug Alcohol Depend 28:167–175.
National Highway Traffic Safety Administration (2000a). Marijuana and alcohol combined severely impede driving performance. Ann Emerg Med 35:398–399.
National Highway Traffic Safety Administration (2000b). NHTSA Technical Report #225.
National Highway Traffic Safety Administration (1999). NHTSA Technical Report #201.
National Highway Traffic Safety Administration (1998). NHTSA Technical Report #185.
National Institute in Drug Abuse (1996). Conference Highlights. National Conference on Marijuana Use: Prevention, Treatment, and Research. July 19–20, 1995. Sponsored by National Institute in Drug Abuse, National Institutes of Health, NIH Publication No, 96:96–4106.
NCADI: 1996 DAWN Survey.
Nelson K, Walsh D, Deeter P, & Sheehan F (1994). A Phase II study of delta-9-tetrahydrocannabinol for appetite stimulation in cancer-associated anorexia. J Palliat Care 10:14–18.
Nemeth-Coslett R, Henningfield JE, O'Keefe MK, & Griffiths RR (1986). Effects of marijuana smoking on suvjective ratings of tobacco smothing. Pharmacol Biochem Behav 25:569–665.
Nilsson I, Agurell S, Nilsson JLG, Widman M, Leander K (1973). Two cannabidiol metabolites formed by rat liver. J Pharm Pharmacol 25: 486–487.
Onaivi ES, Green MR, Martin BR (1990). Pharmacological characterization of cannabinoids in the elevated plus maze. J Pharmacol Exp Ther 253: 1002–1009.
Paris M, Nahas GG (1984). Botany: the unstabilized species. In: Nahas GG (Ed.) Marihuana in science and medicine. NY: Raven Press, pp 3–36.
Paris M, Boucher F, & Cosson L (1975). Importance des composé à chaine propylique dans le Cannabis originaire d'Afrique du Sud. Plantes Med Phytother 9:136–139.
Parker LA, & Gillies T (1995). THC-induced place and taste aversions in Lewis and Sprague-Dawley rats. Behav Neurosci 109:71–78.
Patton WDM, & Pertwee RG. (1973). The actions of cannabis in man. In: Mechoulam R (Ed), Marijuana: chemistry, pharmacology, metabolism, and clinical effects. Academic Press: New York, pp 287–333.
Perez-Reyes M, Simmons J, Brine D, Kimmel GL, Davis KH, Wall ME (1976). Rate of penetration of delta-9-tetrahydrocannabinol and 11-hydroxy-delta-9-tetrahydrocannabinol to the brain of mice. In: Nahas G, Paton WDM, Idänpään-Heikkilä JE (Eds), Marihuana: chemistry, biochemistry, and cellular effects. Springer-Verlag: New York, pp 179–185.
Perez-Reyes M, Timmons MC, Davis KH, & Wall EM (1973). A comparison of the pharmacological activity in man of intravenously administered delta-9-tetrahydrocannabinol, cannabinol, and cannabidiol. Experientia 29:1368–1369.
Perez-Reyes M, White WR, McDonald SA, Hicks RE, Jeffcoat AR, Cook CE (1991). The pharmacologic effects of daily marijuana smoking in humans. Phamacol Biochem Behav 40: 691–694.
Perio A, Rinaldi-Carmona M, Maruani J, Barth F, LeFur G, & Soubrié P (1996). Central mediation of the cannabinoid cue: activity of a selective CB_1 antagonist, SR 141716A. Behav Pharmacol 7:65–71.
Pertwee RG (1991) Tolerance to and dependence on psychotropic cannabinoids. In: The Biological Bases of Drug Tolerance and Dependence. Academic press: New York; pp. 231–263.
Phillips RN, Turk RF, & Forney RB (1971). Acute toxicity of delta-9-tetrahydrocannabinol in rats and mice. Proc Soc Exper Biol Med 136:260.
Physicians Desk Reference, 51st edition. (1997). Medical Economics Company, Inc., Monvale, New Jersey, pp. 2353–2355.
Pickens R, Thompson T, & Muchow DC (1973). Cannabis and phencyclidine self-administered by animals. In:Goldfarb L, & Hoffmeister F (Eds) Psychic Dependence (Bayer-Symposium IV). Springer-Verlag, Berlin; pp. 78.
Pope HG, & Yurgelun-Todd D (1996). The residual cognitive effects of heavy marijuana use in college students. JAMA 275:521–527.
Pradhan SN (1984). Pharmacology of some synthetic tetrahydrocannabinols. Neurosci Biobehav Rev 8:369–385.
Preston KL, Walsh SL, & Sannerud CA (1997). Indirect measures related to drug reinforcement. In: Johnson BA, & Roache J (Eds), Drug Addiction and its Treatment: Nexus of Neuroscience and Behavior. Raven Press:New York; pp 91–114.
Razdan RK (1986). Structrue-activity relationships in cannabinoids. Pharmacol Rev 38:75.
Razdan RK, & Howes JF (1983). Drugs related to tetrahydrocannabinol. Med Res Rev 3:119–146.
Report to the Director, National Institutes of Health, by the Ad Hoc Group of Experts, (1997). Workshop on the Medical Utility of Marijuana, National Institutes of Health, Bethesda, MD February 19–20, 1997, available on the NIH Homepage http://www.nih.gov/news/medmarijuana/medicalmarijuana.html Date: July 25, 1997.
Sanders J, Jackson DM, & Starmer GA (1979). Interactions among the cannabinoids in the antagonism of the abdominal constriction response in the mouse. Psychopharmacology 61:281–285.
Sarafian TA, Marques-Magallanes JA, Shau H, Tashkin D, Roth MD (1999). Oxidative stress produced by marijuana smoke: an adverse effect enhanced by cannabinoids. Am J Respir Cell Mol Biol 20: 1286–1293.
Substance Abuse and Mental Health Services Administration (1999). Federal study links wide range of behavior problems to marijuana use by teens. A SAMHSA report: adolescent self-reported behaviors and their association with marijuana use. http://www.samhsa.gov/press/980922fs.htm.
Takahashi RN, & Singer G (1979). Self-administration of Δ9-tetrahydrocannabinol by rats. Pharmacol Biochem Behav 11:737.
Tanda G, Munzar P, Goldberg SR (2000). Self-administration behavior maintained by the psychoactive ingredient of marijuana in squirrel monkeys. Nature Neurosci 3: 1073–1074.
Tart CT (1971). On Being Stoned: A Psychological Study of Marijuana Intoxication. Science and Behavior Books: Palo Alto, CA.
Taylor DR, Poulton R, Moffitt TE, Ramankutty P, Sears MR (2000). The respiratory effects of cannabis dependence in young adults. Addiction 95:1669–1677.
Ten Ham M, & DeJong Y (1975). Absence of interaction between Δ9-tetrahydrocannabinol Δ9-THC) and cannabidiol in aggression, muscle control, and body temperature experiments in mice. Psychopharmacologia (Berl) 41:169–174.
Thomas BF, Adams IB, Mascarella SW, Martin BR, & Razdan RK (1996). Structure -activity analysis of anandamide analogs: Relationship to a cannabinoid pharmacophore. J Med Chem 39:471–479.
Thompson GW, et al. (1970–1972). Determine toxicity of delta-8 and delta-9-tetrahydrocannabinol and marijuana extract. Mason Research Institute, Worcester, Massachusetts Reports I–XIX to the National Institutes of Mental Health. Contract No. HSM 42–70–95 (June 1970–June 1971) and No. HSM 42–71–79 (June 1971–January 1972).
Tsou K, Patrick SL, & Walker JM (1995). Physical withdrawal in rats tolerant to Δ9-tetrahydrocannabinol precipitated by a cannabinoid receptor antagonist. Eur J Pharmacol 280:R13–R15.
Turner CE (1980). Chemistry and metabolism. In: Petersen RC (Ed) Marijuana research findings: 1980. NIDA Res Mono 31. U.S. Gov't Printing Office: Washington DC, pp 81–97.
Turner CE (1980). Marijuana research and problems: an overview. Pharmac Internat May: 93–96.
Turner CE, ElSohly MA, & Boeren EG (1980a). Constituents of cannabis sativa

L. XVII. A review of the natural constituents. J Nat Prod 43:169–234.
Turner CE, Elsohly MA, Boeren EG (1980b). Constituents of Cannabis sativa. XV. Botanical and chemical profile of Indian variant. Planta Med 37:217–225.
Turner CE, Elsohly MA, Lewis GS, Lopez-Santibanez I, Carranza J (1982). Constituents of Cannabis sative L., XX: the cannabinoid content of Mexican variants grown in Mexico and in Mississippi, United States of America. Bull Narc 34:45–59.
Turner JC, Hemphill JK, Mahlberg PG (1980). Trichomes and cannabinoid content of developing leaves and bracts of Cannabis sativa L., Cannabacceae. Am J Bot 67:1397–1406.
U.S. Department of Justice. Drug Enforcement Administration (1994). Cannabis Investigations Section. 1993 Domestic cannabis Eradication/Suppression Program. Washington, DC.
U.N. Division of Narcotic Drugs (1974). The chemistry of cannabis and its components. MNAR/9/1974–GE, 74–11502.
U.N. International Narcotics Control Board (1994). Psychotropic Substances, Statistics for 1993. United Nations Publication, Vienna, Austria, pp. 39–42.
U.S. Department of Health and Human Services (1995). National Household Survey on Drug Abuse. Main Findings, 1993, U.S. Government Printing Office, Washington, DC 1995.
U.S. Department of Health and Human Services (1995). National Household Survey on Drug Abuse. Population Estimates 1994, U.S. Government Printing Office, Washington, DC.
Vachon L, Sulkowski A, & Rich E. (1974). Marihuana effects on learning, attention and time estimation. Psychopharmacology 39:1–11.
Wall ME, Perez-Reyes M (1981). The metabolism of delta-9-tetrahydrocannabinol and related cannabinoids in man. J Clin Pharmacol 21:178S–189S.
Welburn PJ, Starmer GA, Chesher GB, & Jackson DM (1976). Effets of cannbinoids on the abdominal constriction response in mice: within cannbinoid interactions. Psychopharmacologia (Berl.) 46:83–85.
Weil AT, & Zinberg NE (1969). Acute effects of marihuana on speech. Nature 222:434–437.
Weil AT, Zinberg NE, & Nelsen JM (1968). Clinical and psychological effects of marihuana in man. Science 162:1231–1242.
Wiley JL, Barrett RL, Balster RL, & Martin BR (1993a). Tolerance to the discriminative stimulus effects of Δ^9-tetrahydrocannabinol. Behav Pharmacol 4:581–585.
Wiley JL, Barrett RL, Britt DT, Balster RL, & Martin BR (1993b). Discriminative stimulus effects of Δ^9-tetrahydrocannabinol and $\Delta^{9\text{-}11}$-tetrahydrocannabinol in rats and rhesus monkeys. Neuropharmacology 32:359–365.
Wiley JL, Huffman JW, Balster RL, & Martin BR (1995a). Pharmacological specificity of the discriminative stimulus effects of Δ9-tetrahydrocannabinol in rhesus monkeys. Drug Alcohol Depend 40:81–86.
Wiley JL, Lowe JA, Balster RL, & Martin BR (1995b). Antagonism of the discriminative stimulus effects of Δ^9-tetrahydrocannabinol in rats and rhesus monkeys. J Pharmacol Exper Therap 275:1–6.
Wise RA (1996). Neurobiology of addiction. Curr Opin Neurobiol 6:243–251.
Wise RA, Bozarth MA (1987). A psychomotor stimulant theory of addiction. Psychol Rev 94:469–492.
Wu X, French ED (2000). Effects of chronic Δ^9-tetrahydrocannabinol on rat midbrain dopamine neurons: an electrophysiological assessment. Neruopharmacology 39:391–398.
Yesavage A, Leirer VO, Denari M, Hollister LE (1985). Carry-over effects of marijuana intoxication on aircraft pilot performance: A preliminary report. Am J Psychiatry 142:1325–1329.
Yuan XR, Madamba S, Siggens GR (1992). Opioid peptides reduce synaptic transmission in the nucleus accumbens. Neurosci Lett 134:223–228.
Zacny JP, Chait LD (1989). Breathhold duration and response to marijuana smoke. Pharmacol Biochem Behav 33:481–484.
Zacny JP, Chait LD (1991). Response to marijuana as a function of potency and breathhold duration. Psychopharmacology 103:223–226.
Zhang Z–F, Morgenstern H, Spitz MR, Tashkin DP, Yu G–P, Marshall R, Hsu TC, Schantz SP (1999). Marijuana use and increased risk of squamous cell carcinoma of the head and neck. Cancer Epidemiol Biomarkers & Prevent 8:1071–1078.
Zuardi AW, Antunes Rodriguez J, & Cunha JM (1991). Effects of cannabidiol in animal models predictive of antipsychotic activity. Psychopharmacology 104:260–264.
Zuardi AW, & Karniol IG (1983). Effect on variable-interval performance in rats of ''9-tetrahydrocannabinol and cannabidiol, separately and in combination. Brazil J Med Biol Res 16:141–146.
Zuardi AW, Finkelfarb E, Bueno OFA, Musty RE, & Karniol IG (1981). Characteristics of the stimulus produced by the mixture of cannabidiol with Δ9-tetrahydrocannabinol. Arch Internat Pharmacodynam Ther 249:137–146.
Zuardi AW, Morais SL, Guimarães FS, Mechoulam R (1995). Antipsychotic effect of cannabidiol. J Clin Psychiatry 56:485–486.
Zuardi AW, Shirakawa I, Finkelfarb E, & Karniol IG (1982). Action of cannabidiol on the anxiety and other effects produced by Δ9-THC in normal subjects. Psychopharmacology 76:245–250.
Zuardi AW, Teixeira NA, & Karniol IG (1984). Pharmacological inter action of the effects of Δ9-trans-tetrahydrocannabinol and cannabidiol on serum corticisterone levels in the rat. Arch Internat Pharmacodyn Ther 269:12–19.

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Assistant Section Chief, Environmental Enforcement Section, Environment and Natural Resources Division.

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DEPARTMENT OF JUSTICE

Notice of Lodging of Consent Decree Under the Clean Water Act

Notice is hereby given that on December 31, 2008, a proposed consent decree (the ''Decree'') in *United States and State of Oregon* v. *Pacific Northern Environmental Corp., dba Dedicated Fuels, Inc.,* Civil Action No. 3:08–cv–01513–HU, was lodged with the United States District Court for the District of Oregon.

In this action the United States and State of Oregon sought civil penalties for Pacific Northern Environmental Corp.'s (''PNE'') violation of the Clean Water Act's spill prohibition. PNE owns and operates a heating oil business located in North Bend, Oregon, as well as several gas stations in the area. On July 8, 2006, a tanker truck owned and operated by Dedicated carrying several hundred barrels of diesel fuel overturned while traveling on Highway 38, near Milepost 17, just east of Scottsburg, Oregon. Approximately 197 barrels of diesel fuel spilled. Diesel fuel that did not ignite in the ensuing fire migrated to the Umpqua River. PNE's discharge to the Umpqua River violated the Clean Water Act and Oregon law. Under the consent decree, PNE will pay the United States and the State of Oregon civil penalties of $74,272 and $20,000, respectively. Additionally, PNE agrees to perform a supplemental environmental project (''SEP''), the cost of which shall be not less than $47,640.

The Department of Justice will receive for a period of thirty (30) days from the date of this publication comments relating to the consent decree. Comments should be addressed to the Assistant Attorney General, Environment and Natural Resources Division, and either e-mailed to *pubcomment-ees.enrd@usdoj.gov* or mailed to P.O. Box 7611, U.S. Department of Justice, Washington, DC 20044–7611, and should refer to *United States and State of Oregon* v. *Pacific Environmental Corp., dba Dedicated Fuels, Inc.,* Civil Action No. 3:08–cv–01513–HU, D.J. Ref. 90–5–1–1–09175.

The consent decree may be examined at the Office of the United States Attorney, Mark O. Hatfield U.S. Courthouse, 1000 SW. Third Avenue, Suite 600, Portland, OR, 97204, and at U.S. EPA Region 10, 1200 Sixth Avenue, Seattle, WA, 98101. During the public comment period, the consent decree may also be examined on the following Department of Justice Web site: *http://www.usdoj.gov/enrd/Consent_Decrees.html.* A copy of the consent decree may also be obtained by mail from the Consent Decree Library, P.O. Box 7611, U.S. Department of Justice, Washington, DC 20044–7611, or by faxing or e-mailing a request to Tonia Fleetwood (*tonia.fleetwood@usdoj.gov*), fax no. (202) 514–0097, phone confirmation number (202) 514–1547. In requesting a copy from the Consent Decree Library, please enclose a check in the amount of $5.75 (25 cents per page reproduction cost) payable to the U.S. Treasury or, if by e-mail or fax, forward a check in that amount to the Consent Decree Library at the stated address.

Robert E. Maher, Jr.,

Assistant Section Chief, Environmental Enforcement Section.

[FR Doc. E9–579 Filed 1–13–09; 8:45 am]

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DEPARTMENT OF JUSTICE

Notice of Lodging Proposed Consent Decree

In accordance with Departmental Policy, 28 CFR 50.7, notice is hereby given that a proposed Consent Decree in *United States* v. *Savoy Senior Housing Corp., et al.*, No. 6:06–cv–31 (W.D. Va.), was lodged with the United States District Court for the Western District of Virginia, Lynchburg Division, on January 7, 2009.

The proposed Consent Decree concerns a complaint filed by the United States against Savoy Senior Housing Corporation, Savoy Liberty Village, LLC, SDB Construction, Inc., Jacob A. Frydman, Best G.C., Inc. (a/k/a Best Grading), and Acres of Virginia, Inc., for alleged violations of Section 301(a) of the Clean Water Act (CWA), 33 U.S.C. 1311(a). The proposed Consent Decree resolves all allegations against the defendants for discharging dredged or fill material, and/or controlling and directing such discharges, into waters of the United States at a 140-acre property located in Campbell County, Virginia, without a permit issued by the United States Army Corps of Engineers. The proposed Consent Decree also resolves all allegations against the defendants for discharging sediment in stormwater, and/or controlling and directing such discharges, into waters of the United States on or from the same property, both without a CWA permit and in violation of such a permit once it was obtained.

The proposed Consent Decree requires Savoy Senior Housing Corporation, Savoy Liberty Village, LLC, SDB Construction, Inc., Best G.C., Inc., and Acres of Virginia, Inc., to pay to the United States a civil penalty. The proposed Consent Decree also requires these defendants to restore certain areas on and adjacent to the 140-acre site, and also to fund off-site mitigation through the purchase of credits from stream and wetland restoration banks in the region.

The Department of Justice will accept written comments relating to the proposed Consent Decree for thirty (30) days from the date of publication of this Notice. Please address comments to Kenneth C. Amaditz, Trial Attorney, Environmental Defense Section, P.O. Box 23986, Washington, DC 20026–3986, and refer to *United States* v. *Savoy Senior Housing Corp., et al.*, DJ # 90–5–1–1–17868.

The proposed Consent Decree may be examined at the Clerk's Office, United States District Court for the Western District of Virginia in Lynchburg, Virginia. In addition, the proposed Consent Decree may be viewed at *http://www.usdoj.gov/enrd/Consent_Decrees.html.*

Russell M. Young,

Assistant Chief, Environmental Defense Section, Environment & Natural Resources Division.

[FR Doc. E9–605 Filed 1–13–09; 8:45 am]

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DEPARMENT OF JUSTICE

Drug Enforcement Administration

[Docket No. 05–16]

Lyle E. Craker; Denial of Application

On December 10, 2004, the Deputy Assistant Administrator, Office of Diversion Control, issued an Order to Show Cause to Lyle E. Craker, Ph.D. (Respondent), of Amherst, Massachusetts. The Show Cause Order proposed the denial of Respondent's pending application for a registration as a bulk manufacturer of marijuana on two grounds. Show Cause Order at 1.

First, the Show Cause Order alleged that Respondent's ''registration would not be consistent with the public interest as that term is used in 21 U.S.C. 823(a).'' Show Cause Order at 1. Second, the Show Cause Order alleged that the Respondent's registration would be inconsistent ''with the United States'

obligations under the Single Convention on Narcotic Drugs (Single Convention), March 30, 1961, 18 U.S.T. 1407.'' *Id.*

With respect to both of these contentions, noting that Respondent sought registration ''to supply analytical, pre-clinical and clinical researchers with marijuana,'' the Show Cause Order emphasized that the ''National Institute on Drug Abuse (NIDA), a component [of] the National Institutes of Health (NIH)'' and ''the United States Department of Health and Human Services [HHS], oversees the cultivation, production and distribution of research-grade marijuana on behalf of the United States Government.'' *Id.* at 2.

With respect to the contention that Respondent's proposed registration is inconsistent with the public interest, the Show Cause Order stated that, under 21 U.S.C. 823(a), ''DEA must limit the number of producers of research-grade marijuana to that which can provide an adequate and uninterrupted supply under adequately competitive conditions.'' *Id.* at 4. The Show Cause Order then stated: ''For the past 36 years, the University of Mississippi has provided such supply under the foregoing criteria, and there is no indication that this registrant will fail to do so throughout the duration of its current registration. While the University of Massachusetts is free to compete with the University of Mississippi to obtain the next NIDA contract to produce research-grade marijuana, there is no basis under Section 823(a) to add an additional producer.'' *Id.*

With respect to the contention of Respondent's sponsor, the Multidisciplinary Association for Psychedelic Studies (MAPS), that marijuana provided by NIDA to researchers was both qualitatively and quantitatively inadequate, the Show Cause Order alleged that marijuana provided by NIDA was ''of sufficient quantity and quality to meet'' the needs of ''legitimate and authorized research[ers].'' *Id.* at 3.

The Show Cause Order also noted MAPS's contentions that ''NIDA is limited to supplying marijuana for research purposes and cannot supply marijuana on a prescription basis,'' that ''this limitation effectively prohibits a sponsor * * * from expending the necessary large amounts of funds to conduct drug development studies resulting in [a] marijuana prescription product,'' and that granting Respondent a registration would resolve this problem. *Id.* In response to these contentions, the Show Cause Order alleged that to obtain approval for the marketing of a new drug under the Food, Drug, and Cosmetic Act (FDCA), the safety and effectiveness of the drug must be demonstrated through three phases of clinical trials, and that clinical trials involving marijuana had not progressed beyond the first phase (phase 1). *Id.* at 2–4.

The Show Cause Order further noted that the policy of HHS for approving the distribution of marijuana to researchers ''has not unduly limited clinical research with marijuana.'' *Id.* at 5. More specifically, the Show Cause Order alleged that ''[s]ince the year 2000, there have been or are eleven approved clinical trials utilizing smoked marijuana,'' and that approved ''marijuana researchers administer marijuana to almost 500 human subjects.'' *Id.* The Show Cause Order also alleged that since 2000, there were ''four approved pre-clinical trials in laboratory and animal modes.'' *Id.* at 5. Relatedly, the Show Cause Order also asserted that ''DEA has no statutory authority to overturn HHS' policy.'' *Id.*

With respect to the contention that Respondent's registration would be inconsistent with the United States' obligations under the Single Convention, the Show Cause Order again referenced that HHS, through NIDA, oversees the cultivation, production and distribution of research-grade marijuana on behalf of the United States Government and alleged that ''[i]n accordance with the Single Convention, the Federal Government [is required] to limit marijuana available for clinical research to [this] source.'' *Id.* at 4.

Respondent timely requested a hearing. The matter was assigned to Administrative Law Judge (ALJ) Mary Ellen Bittner, who conducted a hearing on August 22–26 and December 12–14 and 16, 2005. At the hearing, the parties put on testimonial evidence and introduced documentary evidence. Following the hearing, the parties submitted briefs containing their proposed findings of fact, conclusions of law, and argument.

On February 12, 2007, the ALJ issued her recommended decision. Therein, the ALJ rejected the Government's contention that the Single Convention precluded Respondent's registration. In so holding, the ALJ acknowledged that the Convention requires that its signatories maintain a ''government monopoly on importing, exporting, wholesale trading, and maintaining stocks.'' ALJ at 82. The ALJ reasoned, however, that ''[i]t also appears, although it is not entirely clear, that the marijuana grown by the National Center [1] or by any other registrant for utilization in research would qualify as either 'medicinal' * * * or as 'special stocks' within the meaning of'' the Convention. *Id.* at 82 (citing Single Convention, art. 1, para. (1)(o) & (x)).

The ALJ then turned to whether Respondent had established that his registration would be consistent with the public interest when considering the six enumerated factors of 21 U.S.C. 823(a). With respect to the first factor, 21 U.S.C. 823(a)(1), the ALJ first recited the relevant text of this provision, which requires DEA to consider maintenance of effective controls against diversion by limiting the manufacturing of schedule I or II controlled substances ''to a number of establishments which can produce an adequate and uninterrupted supply of these substances under adequately competitive conditions for legitimate medical, scientific, research, and industrial purposes.'' ALJ at 82 (quoting § 823(a)(1)). Noting that there is precedent for the agency to interpret this provision in two distinct ways regarding the issue of adequacy of competition (either by considering or not considering the issue),[2] the ALJ stated that she would evaluate the issue in both ways. *Id.* at 83.

Under the first approach of interpreting 21 U.S.C. 823(a)(1) to allow DEA to disregard the issue of adequacy of competition as long as the agency finds that the applicant for registration would provide effective controls against diversion, the ALJ concluded that ''there is no evidence or contention that either Respondent or anyone working with him would be likely to divert the marijuana from the growing or drying or storage areas.'' *Id.*

The ALJ next rejected the Government's contention that there was a risk of diversion because Mr. Rick Doblin, the Director of MAPS, would determine who was to receive the marijuana. In so holding, the ALJ reasoned that Mr. Doblin would not have physical possession of the marijuana and that Respondent would only send marijuana to researchers with DEA registrations and the requisite approval of HHS. ALJ at 84. The ALJ thus concluded that ''the research project has procedures in place to adequately protect against diversion of the marijuana'' and that ''there is minimal risk of diversion.'' *Id.*

[1] The National Center is an entity of the University of Mississippi which currently holds the contract with NIDA for growing marijuana to supply United States researchers.

[2] The meaning of 21 U.S.C. 823(a)(1) and the competition issue are discussed in detail in part C of the discussion section of this final order.

Under the second approach of interpreting 21 U.S.C. 823(a)(1) to require DEA to consider whether competition is inadequate, the ALJ first turned to whether the supply of marijuana currently available to researchers through HHS is adequate. In this regard, the ALJ found that while ''there have been some problems with the marijuana that the National Center produces, * * * a preponderance of the evidence establishes that the quality is generally adequate.'' *Id.* The ALJ further found, however, that ''NIDA's system for evaluating requests for marijuana for research has resulted in some researchers who hold DEA registrations and requisite approval from [HHS] being unable to conduct their research because NIDA has refused to provide them with marijuana.'' *Id.* The ALJ thus concluded ''that the existing supply of marijuana is not adequate.'' *Id.* The ALJ also concluded that competition is inadequate within the meaning of 21 U.S.C. 823(a)(1). *Id.* [3] The ALJ thus held that the first public interest factor, 21 U.S.C. 823(a)(1), supported granting Respondent's application.

Under the second public interest factor, 21 U.S.C. 823(a)(2), the ALJ found that there was ''neither evidence nor contention that Respondent has not complied with applicable laws'' and thus concluded that this factor supported the granting of Respondent's application. *See id.*

Under the third public interest factor, 21 U.S.C. 823(a)(3), as to whether granting Respondent's application would promote technical advances in the art of manufacturing controlled substances, the ALJ found that Respondent has ''considerable experience in cultivating medicinal plants, which might promote technical advances in the cultivation of marijuana or developing new medications from it.'' ALJ at 85–86. The ALJ nonetheless found that ''there is not sufficient evidence in the record on which to base a finding as to whether granting Respondent's registration would promote technical advances.'' *Id.* at 86.

Under the fourth public interest factor, 21 U.S.C. 823(a)(4), the ALJ found that it was ''undisputed that Respondent has never been convicted of any violation of any law pertaining to controlled substances'' and therefore this factor weighed in favor of granting the application. *Id.*

Under the fifth public interest factor, 21 U.S.C. 823(a)(5), the ALJ considered Respondent's ''past experience in manufacturing controlled substances and the existence of effective controls against diversion.'' *Id.* The ALJ acknowledged that ''Respondent has no experience in manufacturing controlled substances.'' *Id.* Noting that Respondent ''does have experience in growing medicinal plants'' and that ''the risk of diversion is minimal,'' the ALJ concluded that this factor supported granted the application. *Id.*

Finally, under the sixth public interest factor, 21 U.S.C. 823(a)(6), in analyzing such other factors as are relevant to and consistent with public health and safety, the ALJ rejected the Government's contention that granting the application would ''circumvent[]'' HHS's policy with respect to the provision of marijuana to researchers. *Id.* Reasoning that ''the NIH Guidance by its own terms applies to marijuana that [HHS] makes available, [and] not [to] marijuana that might be available from some other legitimate source[,]'' the ALJ concluded that ''the NIH Guidance is not a factor in determining whether Respondent's application should be granted.'' *Id.* The ALJ thus concluded that granting Respondent's application ''would be in the public interest,'' and recommended that I grant his application. *Id.* at 87.

The Government excepted to the ALJ's decision on numerous grounds, and Respondent filed a response to the Government's exceptions. Thereafter, the record was forwarded to me for final agency action.

Having considered the record as a whole, I hereby issue this Decision and Final Order. For reasons explained more fully below, I reject the ALJ's legal conclusion ''that the Single Convention does not preclude registering Respondent.'' *Id.* at 82. Moreover, I reject the ALJ's finding that the proposed registration is consistent with the public interest when considering the six factors enumerated in 21 U.S.C. 823(a). *Id.* at 82–86. I therefore reject the ALJ's recommendation that the application be granted. *See id.* at 87.

Findings

Under Federal Law, marijuana and tetrahydrocannabinols (THC) are schedule I controlled substances. 21 U.S.C. 812(c), Schedule I(c)(10) & (17). Congress placed marijuana and THC in schedule I because the substances have ''a high potential for abuse,'' ''no current accepted medical use in treatment in the United States,'' and ''a lack of accepted safety for use * * * under medical supervision.'' 21 U.S.C. 812(b)(1). *See also* 66 FR 20038 (2001) (denying petition to reschedule marijuana from schedule I), *petition for review dismissed*, *Gettman* v. *DEA*, 290 F.3d 430 (D.C. Cir. 2002).[4]

Marijuana is cultivated from the cannabis plant, which is recognized as ''a very adaptive plant [whose] characteristics are even more variable than most plants.'' GX 25, at 7. Marijuana, which consists primarily of the dried flowering tops and leaves of the cannabis plant,[5] ''is a variable and complex mixture of biologically active compounds.'' *Id.* As of 2001, 483 different chemical constituents had been identified in marijuana, including approximately 66 cannabinoids.[6] 66 FR at 20041; Tr. 1142, 1147. ''THC[7] is the main psychoactive cannabinoid in marijuana''; the plant, however, also contains ''[v]arying proportions of other cannabinoids, mainly cannabidiol (CBD) and cannabinol (CBN),'' which ''sometimes [exist] in quantities that might modify the pharmacology of THC or cause effects of their own.'' *Id.* at 7–8.

[3] In so finding, the ALJ rejected the Government's contention that because the NIDA contract is open to competitive bidding, adequate competition exists. According to the ALJ, ''[t]he question is not * * * whether the NIDA process addresses that agency's needs, but whether marijuana is made available to all researchers who have a legitimate need for it in their research. As discussed above, I answer that question in the negative.'' *Id.* at 85.

As further support for her conclusion, the ALJ reasoned that ''the NIDA contract requires the contractor to analyze'' marijuana seized by law enforcement agencies, and that ''a qualified cultivator may not be able to fulfill'' this requirement.''*Id.*

[4] As related in the Notice, the FDA recommended that marijuana be maintained in schedule I of the CSA. The FDA based its finding on, *inter alia,* the extensive evidence that marijuana has a history and pattern of abuse, that it is ''[t]he most frequently used illicit drug,'' and that it ''has a high potential for abuse.'' 66 FR at 20047 & 20051. The FDA also found that ''[t]here are not FDA-approved medical products,'' ''marijuana does not have a currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions,'' and ''that, even under medical supervision, marijuana has not been shown to have an acceptable level of safety.'' 66 FR at 20052.

[5] The legal definition of marijuana, as set forth in the CSA, 21 U.S.C. 802(16), is as follows: The term ''marihuana'' means all parts of the plant Cannabis sativa L., whether growing or not; the seeds thereof; the resin extracted from any part of such plant; and every compound, manufacture, salt, derivative, mixture, or preparation of such plant, its seeds or resin. Such term does not include the mature stalks of such plant, fiber produced from such stalks, oil or cake made from the seeds of such plant, any other compound, manufacture, salt, derivative, mixture, or preparation of such mature stalks (except the resin extracted therefrom), fiber, oil, or cake, or the sterilized seed of such plant which is incapable of germination.

[6] Cannabinoids are chemical compounds that are unique to the cannabis plant (not found in any other plant). Tr. 1140–41.

[7] While there are numerous isomers of THC (all of which fall within the listing of ''Tetrahydrocannabinols'' in schedule I of the CSA and many of which are found in the cannabis plant), delta-9-THC is the isomer that is recognized as the primary psychoactive component in marijuana and, for this reason the term ''THC'' is often used to refer to delta-9-THC. *See* 66 FR at 20045; Tr. 1146–47.

The National Center and NIDA's Drug Supply Program

Since 1968, the National Center for Natural Products Research (National Center), a division of the University of Mississippi, has held a contract with the Federal Government to grow marijuana for research purposes and held the requisite registrations under the Controlled Substances Act (CSA), as well as the federal law that preceded the CSA, authorizing the University to conduct such activity.[8] Tr. 1152–53, 1350–51. *See also* 21 CFR 1301.13. The contract, which is open for competitive bidding at periodic intervals, *see* GX 15, is administered by NIDA, a component of NIH (which is part of HHS), pursuant to its Drug Supply Program. RX 1, at 231. Since 1999, the term of the contract has been five years. *See* GXs 13 & 15; Tr. 1156.

Under the NIDA contract, the National Center ''[g]row[s], harvest[s], store[s], ship[s] and analyze[s] cannabis of different varieties, as required.'' GX 13, at 6. The contract requires that the National Center ''shall serve as NIDA's cannabis drug repository,'' as well as ''develop and produce standardized marijuana cigarettes within a range of specified THC content, and placebos for use in pre-clinical and clinical research programs,'' and maintain minimum stocks of both bulk marijuana and marijuana cigarettes of various THC contents, and store them in a DEA approved facility. *Id.* at 6–7.

Marijuana potency is primarily based on the concentration (percentage by weight) of THC in the plant material. Tr. 1148–49. As of August 25, 2005, the National Center held on behalf of NIDA approximately 1055 kilograms (kg) of marijuana with THC contents ranging up to 12.26 percent. *See* RX 53. This inventory includes six batches of marijuana with THC contents ranging from 9.02 to 9.89 percent,[9] one batch (of nearly 19 kg) with a THC content of 10 percent, nearly 25 kg with a THC content of 11.34 percent, and approximately 27 kg with a THC content of 12.26 percent.[10] *See id.* In his testimony, Mahmoud ElSohly, Ph.D., who is the Principal Investigator under the NIDA contract, and who has overseen the National Center's work with marijuana since 1980, stated that the Center is capable of producing marijuana with a THC content of 20 percent or more.[11] Tr. 1130–31, 1152, 1203, 1254–55.

The contract also requires the National Center to ''ship to research investigators as authorized by the [NIDA] Project Officer upon receipt of a shipment order.'' GX 13, at 7. While the NIDA ''Project Officer may pre-authorize any normal recurring requests that the contractor will then fill once it has received'' various assurances,[12] the contract further states that ''[a]ll other requests should be submitted to the NIDA Project Officer for approval.'' *Id.* at 8. Moreover, ''[i]f there is a reason to question a particular request, the Contractor shall inform the NIDA Project Officer who will make a final decision on providing the material and quantity requested.'' *Id.* As these provisions make clear, the National Center has no authority to distribute any of the marijuana it produces pursuant to the NIDA contract without NIDA's approval.[13]

In 1997, the White House Office of National Drug Control Policy asked the Institute of Medicine (IOM), a component of the National Academy of Sciences, to conduct a review of the scientific evidence regarding the potential health benefits and risks of marijuana and its constituent cannabinoids. RX 1, at 7. In 1999, the IOM published its report. The IOM found, among other things, that ''[d]efined substances, such as purified cannabinoid compounds, are preferable to plant products, which are of variable and uncertain composition. Use of defined cannabinoids permits a more precise evaluation of their effects, whether in combination or alone.'' RX 1, at 22. With respect to this issue, the IOM reached the following conclusion: ''Scientific data indicate the potential therapeutic value of cannabinoid drugs, primarily THC, for pain relief, control of nausea and vomiting, and appetite stimulation; smoked marijuana, however, is a crude THC delivery system that also delivers harmful substances.'' Id. The report further stated:

> The therapeutic effects of cannabinoids are most well established for THC, which is the primary psychoactive ingredient of marijuana. But it does not follow from this that smoking marijuana is good medicine.
>
> Although marijuana smoke delivers THC and other cannabinoids to the body, it also delivers harmful substances, including most of those found in tobacco smoke. In addition, plants contain a variable mixture of biologically active compounds and cannot be expected to provide a precisely defined drug effect. For those reasons there is little future in smoked marijuana as a medically approved medication. If there is any future in cannabinoid drugs, it lies with agents of more certain, not less certain, composition.'' [14]

[8] Initially, the National Center obtained a researcher's registration; it now also holds a manufacturer's registration.

[9] These batches range from approximately 12 to 15 kg in size.

[10] As of the date of the hearing, more than 920,000 marijuana cigarettes of various THC concentrations including placebo had been manufactured pursuant to the NIDA contracts between 1974 and 2003. GX 27.

[11] 11 As Dr. ElSohly explained, he has grown numerous strains of marijuana from seeds that have been obtained from a variety of countries and has used them to do ''genetic selection to have genetic material of high potency.'' Tr. 1255.

[12] These include that the researcher have the appropriate DEA registration and FDA/IND approvals, provide assurance that the marijuana ''will not be resold'' and ''will be used only for research or patient purposes,'' that the use of the marijuana will adhere to the appropriate Safety Standards for research,'' and that the researcher agree ''to comply with all Federal, State and Local Safety requirements for use of the materials.'' *See* GX 13, at 8.

[13] Independent of its contract with NIDA, the National Center holds an additional registration to manufacture marijuana and THC. GXs 75 & 78. The National Center was granted this registration under the terms of a Memorandum of Agreement (MOA) entered into with DEA in 1999. GX 78. As set forth in the MOA, the purpose of the registration was ''to allow the Center to develop a new product formulation for effecting delivery of [THC] in a pharmaceutically acceptable dosage form suppository * * * and to provide crude THC extract to a DEA-registered manufacturer of THC for further purification.'' *Id.* at 2. The MOA further stated that, under the terms thereof, the Center would ''manufacture marijuana for the purpose of extracting THC therefrom.'' *Id.* Subsequently, the Center submitted a new application for a registration to bulk manufacture marijuana and THC ''to prepare marihuana extract for further purification into bulk active [THC] for use in launching FDA-approved pharmaceutical products.'' 70 FR 47232 (2005). DEA has not yet issued a final order as to this application. (DEA publishes in the **Federal Register** all final orders on applications for registration to bulk manufacture schedule I and II controlled substances.)

The MOA further provided that ''[i]n accordance with articles 23 and 28 of the Single Convention on Narcotic Drugs * * * private trade in 'cannabis' is strictly prohibited. Therefore, the Center shall not distribute any quantity of marijuana to any person other than an authorized DEA employee.'' GX 78, at 2. Continuing, the MOA explained that ''[t]he Single Convention does not prohibit private trade in 'cannabis preparations,'" and noted that this term, ''within the meaning of the Single Convention, is a mixture, solid or liquid containing cannabis, cannabis resin, or extracts or tinctures of cannabis.'' *Id.* Because ''[t]he THC that the Center will extract from marijuana [is] considered such a 'cannabis preparation[,]' * * * the Center may, in accordance with the Single Convention, distribute the crude THC extract to private entities'' provided the Center otherwise complies with the CSA and DEA regulations. *Id.* at 2–3. The MOA also set forth a detailed series of controls to maintain accountability of the marijuana from acquisition of the seeds through the extraction of THC from the harvested material. *Id.* at 3–7.

[14] To similar effect, an ad hoc group of experts, who were selected by NIH and convened in 1997 as part of a workshop to assess the potential medical uses of marijuana, issued a report to the Director of NIH, which noted:

> As with any smoked drug (e.g., nicotine or cocaine), characterizing the pharmacokinetics of THC and other cannabinoids from smoked marijuana is a challenge. A person's smoking behavior during an experiment is difficult for a researcher to control. People differ. Smoking behavior is not easily quantified. An experienced marijuana smoker can titrate and regulate doses to obtain the desired acute psychological effects and

Id. at 195–96. *See also* GX 53 (letter from Alice P. Mead, GW Pharmaceuticals, P.L.C., to Christine V. Beato, Acting Asst. Sec. for Health, HHS (Apr. 12, 2005)) (''[H]erbal cannabis should comprise only the starting material from which a *bona fide* medical product is ultimately derived. * * * [S]tandardizing herbal starting material represents only the first of many steps necessary to create a modern medicine that is safe and effective for use in specific medical conditions. * * * [A] final medical product * * * must also be delivered in a dosage form that is consistent in composition and that allows the patient to obtain an identifiable and reliable amount of medication.'') (emphasis in original).

Accordingly, the IOM recommended that clinical trials using cannabinoid drugs should be conducted with ''the goal of developing rapid-onset, reliable, and safe delivery systems.'' *Id.* at 197. The IOM also advised that clinical trials involving smoked marijuana ''should involve only short-term marijuana use (less than six months), should be conducted in patients with conditions for which there is a reasonable expectation of efficacy, should be approved by institutional review boards, and should collect data about efficacy.'' *Id.*

Also in 1999, due in part to an increased interest in marijuana research and taking into account the IOM report, HHS decided to change the procedures by which it would supply marijuana to researchers. Tr. 1632–33; GX 24. The new procedures were announced in a document released by NIH on May 21, 1999. GX 24, at 1. In the announcement, ''HHS recognize[d] the need for objective evaluations of the potential merits of cannabinoids for medical uses[,]'' and that ''[i]f a positive benefit is found, * * * the need to stimulate development of alternative, safer dosage forms.'' *Id.* at 2. Toward this end, NIH explained that the new procedures were designed to increase the availability of marijuana for research purposes by, among other things, making such marijuana ''available on a cost-reimbursable basis.'' *Id.* This new procedure allowed researchers who were privately funded to obtain marijuana from HHS by reimbursing the NIDA contractor for the cost of the marijuana. Tr. 1633; *see also* GX 31, at 3. This was a departure from the prior practice (pre-1999), whereby HHS only made marijuana available to persons who received NIH funding. *Id.* The new procedures implemented by HHS in 1999 remain in effect today. Tr. 1629.

HHS further stated in 1999 that it intended through the new procedures ''to make available a sufficient amount of research-grade marijuana to support those studies that are the most likely to yield usable, essential data.'' GX 24, at 2. With respect to those researchers who do not have NIH funding, HHS explained that ''the scientific merits of each protocol will be evaluated through a Public Health Service interdisciplinary review process [which] will take into consideration a number of factors, including the scientific quality of the proposed study, the quality of the organization's peer-review process, and the objective of the proposed research.'' *Id.*

HHS then identified the criteria it would apply in evaluating requests for marijuana:

> The extent to which the protocol incorporates the elements of good clinical and laboratory research;
>
> The extent to which the protocol describes an adequate and well-controlled clinical study to evaluate the safety and effectiveness of marijuana and its constituent cannabinoids in the treatment of a serious or life threatening condition;
>
> The extent to which the protocol describes an adequate and well-controlled clinical study to evaluate the safety and effectiveness of marijuana and its constituent cannabinoids for a use for which there are no alternative therapies;
>
> The extent to which the protocol describes a biopharmaceutical study designed to support the development of a dosage form alternative to smoking; [and]
>
> The extent to which the protocol describes high-quality research designed to address basic, unanswered scientific questions about the effects of marijuana and its constituent cannabinoids or about the safety or toxicity of smoked marijuana.

Id. at 3.

HHS further noted that ''[a] clinical study involving marijuana should include certain core elements,'' and that ''[a] study that incorporates the [1997] NIH Workshop recommendations will be expected to yield useful data and therefore, will be more likely to receive marijuana under the HHS program.'' *Id.*

Finally, HHS explained that the ''proposed protocols must be determined to be acceptable under FDA's standards for authorizing the clinical study of investigational new drugs.'' *Id.* Relatedly, HHS stated that ''although FDA's review of Phase 1 submissions will focus on assessing the safety of Phase 1 investigations, FDA's review of Phases 2 & 3 submissions will also include an assessment of the scientific quality of the clinical investigations and the likelihood that the investigations will yield data capable of meeting statutory standards for marketing approval.'' *Id.* HHS further made clear that if a protocol is approved, ''NIDA will provide the researcher with authorization to reference NIDA's marijuana Drug Master File.'' *Id.* at 4.

At the administrative hearing in this case, Steven Gust, Ph.D., Special Assistant to the Director of NIDA, explained that, in addition to seeking to facilitate research into the possible medical utility of marijuana, the new procedures implemented by HHS in 1999 were intended ''to make the process more standardized, and to * * * provide some expertise that did not really exist at NIDA in terms of reviewing applications that involved * * * the use of marijuana * * * for treatment of diseases.'' Tr. 1632–33. Accordingly, HHS ''established a separate peer review process that * * * moved the review into the Public Health Service [a component of HHS] * * * where additional expertise from other NIH Institutes and other Federal agencies'' could be utilized in reviewing the scientific merit of the applications. *Id.* at 1633–34. Dr. Gust further explained that the members of the review committee are drawn from the various specialty institutes of NIH, and the Substance Abuse and Mental Health Services Administration (SAMHSA). *Id.* at 1692; 1713–15.[15] Dr. Gust also testified that the ''scientific bar has been set very low, [so] that any project that has scientific merit is approved,'' and that ''anything that gets approved gets NIDA marijuana.'' *Id.* at 1700–01. As of April 2004, HHS had approved at least seventeen pre-clinical or clinical studies of marijuana, which were sponsored by the California Center for Medical Cannabis Research (CMCR).[16] GX 31, at

to avoid overdose and/or minimize undesired effects. Each puff delivers a discrete dose of THC to the body. Puff and inhalation volume changes with phase of smoking, tending to be highest at the beginning and lowest at the end of smoking a cigarette. * * * During smoking, as the cigarette length shortens, the concentration of THC in the remaining marijuana increases; thus, each successive puff contains an increasing concentration of THC.

One consequence of this complicated process is that an experienced marijuana smoker can regulate almost on a puff-by-puff basis the dose of THC delivered to lungs and thence to brain. A less experienced smoker is more likely to overdose or underdose. Thus a marijuana researcher attempting to control or specify dose in a pharmacologic experiment with smoked marijuana has only partial control over the drug dose actually delivered.

See GX 25, at 9–10 (Workshop on the Medical Utility of Marijuana).

[15] Dr. Gust initially testified that someone from FDA sits on the committee but later stated that he was not exactly sure if this was so. Tr. 1712.

[16] The California research studies were conducted pursuant to a law enacted by California in 1999 known as the Marijuana Research Act of 1999. Cal.

Continued

3. According to one witness who testified on behalf of Respondent, all of the CMCR-sponsored researchers who applied to NIDA for marijuana did in fact receive marijuana from NIDA. Tr. 694–95.

Respondent's Application and Contentions

Respondent is a Professor in the Department of Plant, Soil and Insect Sciences at the University of Massachusetts Amherst. Tr. 13. On June 28, 2001, Respondent submitted an application to bulk manufacture the schedule I controlled substances marijuana and tetrahydrocannabinols.[17] GXs 1 & 3; 21 CFR 1308.11(d). Respondent's application is sponsored by the Multidisciplinary Associations for Psychedelic Studies (MAPS). GX 3, at 1.

Because Respondent seeks a registration to manufacture a schedule I controlled substance, DEA required that he complete a questionnaire.[18] In response to the question regarding the purpose for which he sought registration, Respondent stated that ''[t]he plant material will be grown for federally-approved uses only, including analytical, pre-clinical, and clinical research,'' and that ''no material is intended for illegal use or for medical marijuana patients whose use may be legal under state, but not federal law.'' GX 3, at 1.[19]

Respondent added that ''[t]he production costs * * * would be underwritten by a grant'' from MAPS. *Id.* According to Respondent, ''MAPS is seeking to develop the marijuana plant into an FDA-approved prescription medicine,'' and that ''[t]he growth of plants at [UMASS] is a necessary step for supplying quality marijuana for use in MAPS' drug development process.'' *Id.* Respondent also advised that ''MAPS will sponsor research at other institutions using smoked marijuana and marijuana delivered through a vaporizer device that heats, but does not burn the plant material, thus reducing the products of combustion normally found in smoked marijuana.'' *Id.*

Respondent further stated that his ''[c]ustomers would include both MAPS-sponsored research and research sponsored by other organizations.'' *Id.* at 3. Relatedly, Respondent explained that ''[r]esearchers conducting MAPS sponsored research would receive supplies of the plant material free, while other researchers would either receive the marijuana free or through a donation to MAPS.'' *Id.* at 1. *See also* Tr. 225 (''I may very well be approached by other people with approved studies who need a source also.'').

At the hearing, Mr. Rick Doblin, the President of MAPS,[20] also testified regarding the purpose of Respondent's application. Mr. Doblin, who admitted that he engages in recreational use of marijuana on a weekly basis, explained that ''[t]he reason we need a supply from Dr. Craker is that we are engaged in trying to make marijuana into an FDA-approved prescription medicine, and * * * we need to establish a drug master file for a particular product, and * * * we need to conduct research with that product, and have that product available to us for potential marketing should we get FDA approval.'' Tr. 603, 718–19. Mr. Doblin testified as to his ''belie[f] that smoked marijuana or vaporized marijuana in plant form will successfully compete with marijuana extracts on price.'' *Id.* at 605. He also testified as to his belief that the ''efficacy and safety'' of vaporized plant-form marijuana ''will be similar'' to drugs containing cannabinoid extracts and that ''the efficacy will be similar and safety slightly different with smoked'' marijuana than with drugs containing cannabinoid extracts. *Id.*

Mr. Doblin further testified that he ''disagree[d]'' with the Institute of Medicine's conclusion that defined and purified cannabinoid compounds ''are preferable to plant products, which are of variable and uncertain composition.'' *Id.* at 654. Mr. Doblin also testified that ''what we're trying to do is get the Public Health Service and NIDA out of the picture; they're only in the picture just for marijuana only because they have a monopoly. And that is what is so obstructing the system.'' *Id.* at 666.

Finally, Mr. Doblin testified that MAPS would only need between $5 to $10 million ''to make marijuana into a medicine'' through the various stages of the FDA new drug approval (NDA) process.[21] *Id.* at 701; *see also id.* at 703. In his testimony, Mr. Doblin did not, however, identify a single instance in which an entity (whether for-profit or nonprofit) had taken a drug—let alone a botanical substance with known safety issues, *See, e.g.*, GX 43, at 9—through the multi-faceted NDA process for a similar cost.[22] Moreover, while Mr.

Health & Safety Code § 11362.9. This state law established the ''California Marijuana Research Program'' to develop and conduct studies on the potential medical utility of marijuana. *Id.* (The program is also referred to as the ''Center for Medicinal Cannabis Research'' (CMCR). Tr. 396.) The state legislature appropriated a total of $9 million for the marijuana research studies. Tr. 397. The state law was enacted following the passage of Proposition 215, a ballot initiative otherwise known as the Compassionate Use Act of 1996. Tr. 395–96; *see also United States* v. *Oakland Cannabis Buyers' Cooperative* (''*OCBC*''), 532 U.S. 483, 486 (2001).

[17] On his application for registration (GX 1), Respondent incorrectly checked the box for ''dosage form'' manufacturing when, in fact (based on the activity in which he proposes to engage), he is seeking to become registered as a ''bulk'' manufacturer. In written questions DEA submitted to Respondent as a follow-up to the application, DEA properly characterized the activity as ''bulk manufacture,'' and Respondent, in his written answers to these questions, gave no indication that he disagreed. *See* GX 3. Also, in his testimony at the hearing, Respondent acknowledged that his plan was to send marijuana ''in bulk'' to others, who would roll it into cigarettes. Tr. at 243. Respondent also testified that MAPS President Rick Doblin ''assisted in the response to the *bulk* manufacturer's questions.'' Tr. 352 (emphasis added). Cf. 32 CFR 1300.02(b)(32) (defining ''drug product'' as ''an active ingredient in dosage form that has been approved or otherwise may be lawfully marketed under the Food, Drug, and Cosmetic Act for distribution in the United States''); 21 CFR 1301.72(a) & 1304.22(a) (listing ''bulk materials awaiting further processing'' separately from ''finished products'').

[18] As set forth in 21 CFR 1301.15: ''The Administrator may require an applicant to submit such documents or written statements of fact relevant to the application as he/she deems necessary to determine whether the application should be granted.''

[19] Respondent further testified that it was his intention to simply send bulk marijuana to researchers who would then roll their own cigarettes. Tr. at 243.

[20] When asked during the hearing about the title of his organization (Multidisciplinary Association for Psychedelic Studies) and, in particular the term ''Psychedelic,'' Mr. Doblin explained, in part, ''it's about tools and procedures that bring to the surface people's subconscious and unconscious and, you know, deeper emotions.'' Tr. 474.

[21] In a recent Supreme Court decision, Justice Ginsberg, in a dissenting opinion, summarized the process by which FDA approves new drugs for marketing as follows:

> The process for approving a new drug begins with preclinical laboratory and animal testing. The sponsor of the new drug then submits an investigational new drug application seeking FDA approval to test the drug on humans. *See* 21 U.S.C. 355(i); 21 CFR 312.1 *et seq.* (2007). Clinical trials generally proceed in three phases involving successively larger groups of patients: 20 to 80 subjects in phase I; no more than several hundred subjects in phase II; and several hundred to several thousand subjects in phase III. 21 CFR 312.21. After completing the clinical trials, the sponsor files a new drug application containing, *inter alia*, ''full reports of investigations'' showing whether the ''drug is safe for use and * * * effective''; the drug's composition; a description of the drug's manufacturing, processing, and packaging; and the proposed labeling for the drug. 21 U.S.C. 355(b)(1).
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> *Riegel* v. *Medtronic, Inc.*, 128 S.Ct. 999, 1018–19 n.15 (2008) (Ginsburg, J., dissenting).

[22] While Respondent produced evidence establishing that the $800–880 million costs of bringing a new drug to market includes research and development costs incurred for drugs that are not approved, as well as opportunity costs (the cost of investing in research rather than something else), *see* Tr. 161, 734–36, Respondent has not shown a single instance in which an entity has obtained FDA approval of a drug through the NDA process for the cost range which Mr. Doblin claimed would be sufficient to obtain approval of plant-form marijuana.

Moreover, the IOM Report states that the average cost of a Supplemental New Drug Application (SNDA), which is used when a company seeks to obtain FDA approval to market a drug (which has already gone through the three phases of clinical

Doblin testified that ''the mission statement [of MAPS] is to develop psychedelics and marijuana into FDA-approved medicines and then to educate the public about that'' (Tr. 478), the vagaries of his testimony prevent a clear determination of how far along in that goal he envisions MAPS to be.[23]

Correspondence Pertaining to the Application

Subsequent to Respondent's submission of his application for a DEA registration, on March 4, 2003, the Chief of DEA's Drug and Chemical Evaluation Section wrote to Respondent noting that ''it appears that the basis for your application is the purported need for a higher potency and higher 'quality' marijuana product than that currently available from the National Institute on Drug Abuse.'' GX 29, at 1. The DEA letter further explained that the Agency had ''contacted NIDA, the Department of Health and Human Services * * * and some current researchers'' and had ''determined that * * * the quality of marijuana available from NIDA is acceptable,'' that a high potency product with a THC content of 7 to 8 percent was currently ''available to bona fide research protocols,'' and that if ''[i]n the future, should federally approved research protocols require a higher potency marijuana (*i.e.* 15 percent THC), all believe that it could be supplied by NIDA.'' *Id.*

Thereafter, on June 2, 2003, Respondent wrote to DEA acknowledging that during a visit with several agency Diversion Investigators, the discussion had ''primarily focused[ed] on the need for an alternative source of plant material to that grown at the University of Mississippi under contract to the National Institute of Drug Abuse (NIDA).'' GX 30. Continuing, Respondent stated that ''[a] second source of plant material is needed to facilitate privately-funded, FDA-approved research into medical uses of marijuana, ensuring a choice of sources and an adequate supply of quality, research-grade marijuana for medicinal applications.'' *Id.* Consistent with these statements, Respondent has declined to bid on the NIDA contract. Tr. 252–53.

Respondent further asserted that while ''the primary researchers now receiving plant material may openly state to you that they are satisfied with the current source, * * * in private conversations these same researchers indicate a fear of having the current supply eliminated if they complain about the available source material.'' GX 30. As support for his contention regarding the level of researcher's satisfaction with NIDA's marijuana, Respondent attached two items: a reprint of a newspaper article and a letter from a Dr. Ethan Russo to the then-Chief of DEA's Drug and Chemical Evaluation Section. *See* GX 30a & 30b.

At the hearing, Respondent testified that at the time he filed his application, he had become concerned, based on conversations he had with ''other people,'' that the marijuana provided by the National Center ''may have been of relatively low quality, and that [it] was not readily available to run the clinical trials which some people wanted to run.'' Tr. 215. When asked to provide the names of these ''other people'' who had told him this, Respondent said he did not recall. *Id.*

Respondent's Contentions Regarding the Inadequacy of NIDA Marijuana

Respondent makes three principal claims in support of his contention that the supply of marijuana currently available through NIDA is inadequate. First, he claims that ''NIDA does not provide medical marijuana to all legitimate researchers'' and that ''NIDA has refused to provide marijuana to at least three legitimate researchers.'' Resp. Prop. Findings at 12. Second, he claims that ''the quality of the NIDA marijuana raises concerns for researchers and patients.'' *Id.* at 16. Third, he claims that ''the NIDA supply was inadequate because a pharmaceutical developer could not reasonably rely on NIDA marijuana to take marijuana through the FDA new drug approval process.'' Respondent's Response to Govt.'s Exceptions (hereafter, ''Respondent's Resp.'') at 16.

HHS's Denials of Researcher's Requests for NIDA Marijuana

Respondent's first claim is based on three incidents over a decade-long time period in which he alleges that researchers were improperly denied access to NIDA's marijuana. The first incident, which occurred in 1995, involved an application submitted by Donald Abrams, M.D., who sought

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trials and been approved for marketing) for a new indication, was $10 to 40 million. RX 1, at 214. It should be noted, however, that in taking a drug through the three phases, its sponsor will have obtained extensive data regarding the drug's safety including ''adverse effects of the drug [and] clinically significant drug/drug interactions.'' 21 CFR 314.50(d)(5)(vi).

In support of his assertion that MAPS could obtain FDA approval for only $5 to $10 million, Mr. Doblin testified that marijuana is different than other drugs that go through the FDA approval process. Mr. Doblin based this assertion on his contentions that: marijuana has been used by ''tens of millions of people'' while others drugs going though the NDA process are only used by a few thousand; there is ''an enormous body of evidence about [marijuana's] safety * * * that we don't need to replicate;'' and sufficient data to satisfy the FDA as to marijuana's safety and efficacy could be obtained by testing only 500 to 600 people. *Id.* at 737–38.

The FDA's guidance document for botanical drug products makes plain that ''[a] botanical drug product that is not generally recognized as safe and effective for its therapeutic claims is considered a new drug under § 201(p) of the [Food, Drug, and Cosmetic] Act,[]'' and that ''any person wishing to market a botanical drug product that is a new drug is required to obtain FDA approval of an NDA * * * for that product.'' GX 92A, at 7. Moreover, ''an NDA must contain substantial evidence of effectiveness derived from adequate and well-controlled clinical studies, evidence of safety, and adequate CMC [chemistry, manufacturing, and controls] information.'' *Id. See also* GX 92A, at 27–38 (specifying the information that must be provided to FDA for phase 3 clinical studies of a botanical product to meet the requirements of the FDA regulations governing the contents of INDs). Finally, with respect to the nonclinical safety assessment required to support phase 3 clinical trials, the FDA guidance states:

To support safety for expanded clinical studies or to support marketing approval of a botanical drug product, toxicity data from standard toxicology studies in animals may be needed * * *. A botanical product submitted for marketing approval as a drug will be treated like any other new drug under development. Safety data from previous clinical trials conducted in foreign countries will be considered in determining the need for nonclinical studies. However, previous human experience may be insufficient to demonstrate the safety of a botanical product, especially when it is indicated for chronic therapy. Systematic toxicological evaluations could be needed to supplement available knowledge on the general toxicity, teratogenicity, mutagenecity, and carcinogenicity of the final drug product.

Id. at 34. While Mr. Doblin asserted that MAPS would not ''need to replicate all those studies about the genetics, * * * the effect on reproduction, the effect in all sorts of bodily systems,'' Tr. 737, he did not identify any specific studies performed in other countries that establish the safety of marijuana for testing in phase 3 clinical studies. While millions of people have undoubtedly used marijuana, few have done so subject to the scientific rigor of a controlled clinical trial. Nor did Respondent produce any credible evidence establishing that the various types of animal studies which FDA usually requires to support phase 3 clinical trials would not have to be performed. GX 92A, at 35–37.

[23] As indicated above, based on the record, no clinical trials involving marijuana have advanced beyond phase 1. Moreover, each sponsor must submit to FDA his/her own IND to be authorized to conduct clinical investigation with a new drug (such as marijuana). *See* 21 CFR 312.20, 312.23. Again, given the vagaries of Mr. Doblin's testimony, it cannot be determined whether there is sufficient existing preclinical laboratory and animal studies data to support a submission of an IND for whatever proposed indications that Mr. Doblin has in mind for his envisioned FDA-approved marijuana medicine. But even assuming, *arguendo*, that MAPS could successfully submit an IND based on existing data, it would still have to proceed through extensive clinical trials (*see* 21 CFR 312.21), and then—assuming that such trials are fully successful at demonstrating the basis for safety and efficacy (which often is not the case with clinical trials)—MAPS would still have to submit and obtain approval of an NDA. All of these steps, and the uncertainties as to the outcomes of each step, further call into question Mr. Doblin's estimate of being able to obtain FDA approval of marijuana for only $5 to $10 million.

marijuana from NIDA to study its effects on persons with HIV-related wasting syndrome. RX 15, at 1. NIDA rejected Dr. Abrams's application ''based upon issues of design, scientific merit and rationale.'' [24] Dr. Abrams subsequently submitted a revised research protocol that NIDA found to be scientifically meritorious and for which NIDA supplied marijuana in 1997.[25] *See* GX 21, at 1. NIDA also supplied Dr. Abrams with marijuana for subsequent studies. *Id.;* Tr. 689. In any event, for purposes of determining the relevance of the 1995 incident in which Dr. Abrams' original protocol was rejected by NIDA, it is notable that this occurred before HHS adopted its new guidelines for the provision of marijuana for research purposes. As Dr. Gust testified, in 1995, HHS's practice was to provide marijuana only to researchers who obtained NIH funding—a practice that was abandoned by HHS in 1999 when the agency adopted its new procedures for facilitating marijuana research (allowing privately funded researchers to also obtain marijuana). Tr. 1749.

The second incident involved an application by Dr. Ethan Russo, a neurologist, who sought funding from NIDA to study the use of marijuana to treat migraine headaches beginning around 1996. Tr. 527–28. The precise dates of the events related to Dr. Russo are somewhat unclear as Respondent presented these events through the testimony of Mr. Doblin. (Dr. Russo did not testify.) *Id.* Based on Mr. Doblin's testimony, it appears that during 1996–97, NIDA twice rejected Dr. Russo's protocol for reasons which are not clearly established by the record. *Id.* at 527, 691–92. However, according to Mr. Doblin, Dr. Russo conceded that, on both of these two occasions when NIDA rejected his protocol, NIDA's bases for doing so did include ''some valid critiques.'' Tr. 692. Mr. Doblin testified that Dr. Russo subsequently attempted for a third time to obtain marijuana from NIDA, but on this third occasion he decided not to seek government funding but to seek private funding to purchase the marijuana from NIDA. *Id.* at 692. According to Mr. Doblin, this third protocol submitted by Dr. Russo was approved by both the FDA and Dr. Russo's institutional review board, but NIDA again refused to supply marijuana. *Id.* at 692–93. When asked when this last denial by NIDA occurred, Mr. Doblin testified: ''I think it was 1999.'' *Id.* at 693.

As noted above, NIH announced on May 21, 1999, HHS's new procedures for making marijuana available to researchers. Bearing in mind that Respondent had the burden of proving any proposition of fact that he asserted in the hearing, 21 CFR 1301.44(a), nothing in Mr. Doblin's testimony, or any other evidence presented by Respondent, established that HHS denied Dr. Russo's request for marijuana under the new procedures implemented by the agency in 1999. Indeed, Respondent produced no evidence showing that HHS has denied marijuana to any clinical researcher with an FDA-approved protocol subsequent to the adoption of the 1999 guidelines.

The third incident involved an application by Chemic Laboratories (Chemic), which—at the request of Mr. Doblin—sought marijuana from NIDA in 2004 [26] for a proposed study involving a device known as the ''Volcano Vaporizer'' (hereafter ''Volcano''). RX 49 & 52B. To understand the nature and purpose of this proposed study, some earlier facts that were disclosed at the hearing need to be considered. According to Mr. Doblin's testimony, prior to this incident (*i.e.*, before Chemic applied to NIDA for marijuana in 2004), Mr. Doblin had devised an elaborate arrangement whereby Chemic received marijuana to conduct an earlier study with the Volcano using marijuana obtained outside of the HHS process and without the knowledge or approval of HHS or DEA. Specifically, Mr. Doblin admitted that he encouraged persons who obtained marijuana from ''buyers' clubs'' in California as well as persons who obtained their marijuana from NIDA under HHS's ''compassionate use program'' [27] to anonymously send their marijuana to a DEA-registered drug testing laboratory so that MAPS could compare the potency of the ''buyers' clubs'' marijuana with that supplied by NIDA.[28] Tr. 668–82. Acting at the behest of Mr. Doblin, once the drug testing laboratory completed its analysis of the marijuana it received through these sources, it delivered the ''extra'' marijuana to Chemic, so that Chemic could conduct testing on the Volcano. *Id.* Chemic did conduct such testing,[29]

[24] That the above-quoted grounds were the bases upon which NIDA denied Dr. Abrams' original application is implicit from the letter that Dr. Abrams submitted to NIDA in response to the denial (RX 15). These bases are explicitly stated in NIDA's April 19, 1995, letter to Dr. Abrams, which appears on MAPS' Web site (at *http://www.maps.org/mmj/leshner.html*) and of which I take official notice. This letter from NIDA stated, among other things, the following:

Our decision here is based upon issues of design, scientific merit and rationale. We believe that your study will not adequately answer the question posed.

Although the study propose[d] seeks to make a dose-effect comparison of smoked marijuana to delta-9-tetrahydrocannabinol (THC), there is no real dosing control. The marijuana is to be taken home and there is no requirement and way to ensure that the subjects smoke all available materials on any fixed schedule. Additionally, that they are given a two-week supply of marijuana at one time further confounds the study design. Thus, we believe the dose-effect component is confounded since the study cannot correlate variability in weight gain with dosage.

We also believe the study lacks adequate sample size to make any inferences regarding the dose-effect relationship. . . . Another confounding variable not adequately controlled for in your proposed study is diet. Neither the total daily caloric intake nor the percentages of the composition of the foodstuffs is assessed.

In accordance with the Administrative Procedure Act (APA), an agency ''may take official notice of facts at any stage in a proceeding—even in the final decision.'' U.S. Dept. of Justice, *Attorney General's Manual on the Administrative Procedure Act* 80 (1947) (Wm. W. Gaunt & Sons, Inc., Reprint 1979). In accordance with the APA and DEA's regulations, Respondent is ''entitled on timely request to an opportunity to show to the contrary.'' 5 U.S.C. 556(e); *see also* 21 CFR 1316.59(e). To allow Respondent the opportunity to refute the facts of which I take official notice, Respondent may file a motion for reconsideration within fifteen days of service of this order which shall commence with the mailing of the order.

[25] Following the 1996 passage of proposition 215, NIDA contacted Dr. Abrams and asked him if he would redesign his study to determine whether marijuana usage by persons who were HIV-positive (but who did not have AIDS-wasting syndrome) increased viral load as well as the interaction of marijuana with protease inhibitors. Tr. 523–24. Dr. Abrams agreed to do so and NIDA provided him with a $1 million grant to fund the study.

[26] It appears from the record that Chemic initially applied to HHS for marijuana in 2003 but, at HHS's request, Chemic submitted a revised protocol, which HHS considered to be submitted in 2004. *See* GXs 49 & 52B.

[27] *See Kuromiya* v. *United States,* 78 F.Supp.2d 367 (E.D. Pa. 1999) (describing compassionate use program under which less than 10 persons currently receive marijuana from HHS).

[28] Because marijuana is a schedule I controlled substance, human use is limited to ''Government-approved research'' in accordance with 21 U.S.C. 823(f). *See OCBC,* 532 U.S. at 491–492 and n.5. In accordance with § 823(f) and the DEA regulations, where a schedule I controlled substance is used in research—including the HHS compassionate use program—the activities involving the substance must be limited to those authorized in the research protocol. *See* 21 CFR 1301.13(e)(1)(v), 1301.18. Research activities beyond those specified in the protocol are prohibited absent the submission and approval of a supplemental protocol. 21 CFR 1301.18(d). Respondent made no attempt to assert that any of the research protocols associated with the compassionate use program allow for the distribution of marijuana to a drug testing laboratory, as there is no basis for such an assertion. The CSA prohibits the distribution of any controlled substance except as authorized by the Act, 21 U.S.C. 841(a)(1), and the Act makes no allowance for ultimate users (including research subjects) to distribute their controlled substances to others.

[29] Chemic was not registered with DEA under 21 U.S.C. 823(f) to conduct research with marijuana and when DEA later learned that Chemic was seeking to conduct a second marijuana study (when Chemic subsequently sought to obtain marijuana directly from NIDA and sought DEA's authorization for doing so), the agency so advised Chemic that this activity required a research registration. *See* RX 49, at 2. DEA registrants are only authorized to conduct activities with controlled substances ''to

which was funded by MAPS and the California National Organization for the Reform of Marijuana Laws (CaNORML), and Chemic published its results in two reports, one of which was co-authored by CaNORML.[30] *See id.*

Thus, this ''third incident'' to which Respondent points involved an effort by MAPS to expand upon the research that Chemic had conducted on the Volcano—this time using marijuana directly obtained from NIDA rather than using marijuana obtained without the knowledge or approval of HHS or DEA. Id. Under MAPS sponsorship and oversight, Chemic so applied to NIDA in 2004. Id.; RX 52B. The protocol submitted by Chemic proposed to heat marijuana obtained from NIDA and from a Dutch ''medical marijuana'' program to three different temperature levels below its combustion temperature and to then ''compare the quality and relative percentage of available cannabinoids'' in the material obtained from each source. RX 52B, at 2–3.

By letter dated July 27, 2005, a U.S. Public Health Service (PHS) committee of scientists, which evaluated Chemic's protocol pursuant to the 1999 Guidance, rejected it on the grounds that the ''project does not add to the scientific knowledge base in a significant way.'' [31] Id. at 4. With respect to the protocol's purpose of comparing the cannibinoid content of NIDA and Dutch marijuana, the PHS committee found that ''[m]arijuana varies in THC content and [that] simply demonstrating that this device can measure those differences is of little scientific value.'' *Id.* at 3. The PHS committee also found that the protocol's other purposes (''to conduct a reliability study of the device by analyzing multiple vapor collections'' and to ''determine the 'precision, accuracy, robustness and efficacy' of the vaporizing device'') did ''not appear to be a hypothesis driven research project,'' but rather, ''analogous to a process that is used to 'validate' an analytical method.'' *Id.* The PHS committee thus concluded that the ''overall aims of the project appear to be descriptions of work that would need to be conducted as part of good standard laboratory procedure prior to a clinical study.'' *Id.*

The PHS Committee further noted that, at that time (2005), a separate, HHS-approved clinical trial involving marijuana and the Volcano was already underway. *Id.* This then-ongoing clinical trial was being conducted by Dr. Abrams and was sponsored by the CMCR, using NIDA-supplied marijuana. *Id.*; Tr. 689. Moreover, as the letter from the PHS Committee indicates, one of the documents that Dr. Abrams had previously submitted in support of his then-ongoing clinical trial was a report that Chemic itself had prepared regarding its prior study of marijuana and the Volcano.[32] GX 52B, at 3. Given that Dr. Abrams' clinical trial was ''underway and is examining the pharmacodynamics and pharmacokinetics of several different potencies of marijuana in human volunteers using the Volcano(c) device,'' the Committee concluded that ''[i]t is difficult to see what additional scientific knowledge will be provided by the current protocol, considering the prior work done by the applicant, as described in the above report, and the ongoing clinical trial at CMCR.'' *Id.*

Respondent also introduced into evidence a letter from the President of Chemic to HHS responding to several points raised by the PHS Committee in denying Chemic's application. *See* RX 55. Respondent's letter does not, however, establish that HHS impermissibly denied Chemic's application for marijuana.[33] To the contrary, the evidence supports the conclusion that HHS (acting through the PHS Committee) made its determination not to supply marijuana on this occasion based on scientific considerations, finding that Chemic's then-latest proposed study was duplicative of prior and ongoing research and not likely to provide useful data.

Respondent's Contention That NIDA's Marijuana Is of Poor Quality

Respondent also contends that ''[t]he quality of the NIDA marijuana raises concerns for researchers and patients.'' Resp. Prop. Findings at 16. In this regard, Respondent asserts that various researchers have complained that NIDA's marijuana is of inconsistent potency, that NIDA's marijuana is harsh, that NIDA's marijuana is frequently several years old and not fresh, that the available product is of low potency, and that NIDA's product includes stems and seeds. *See id.* at 16–27. Contrary to Respondent's view, the evidence does not ''demonstrate[] serious concerns about the quality of NIDA's'' marijuana products. *Id.* at 27. As explained below, Respondent's contentions are largely based on snippets from questionnaires in which the researchers generally indicated their overall satisfaction with the quality of NIDA's marijuana. As the ALJ found, ''a preponderance of the record establishes that the quality is generally adequate.'' ALJ at 84.

With respect to the contention that NIDA's marijuana is of inconsistent potency or inadequate potency, Respondent relies on comments contained on three questionnaires that were completed by researchers at DEA's request. Resp. Prop. Findings at 17–18. One of the questions asked: ''Have you ever had any difficulty obtaining marijuana from NIDA for all strengths of cigarettes to meet research requirements?'' GX 16, at 8. While Dr. Grant of the CMCR answered affirmatively and added that ''having consistency of 6% -8% [THC] content have been difficult,'' he further stated that NIDA ''ha[s] been *accommodating* by trying to produce the high % products in a timely manner.'' *Id.* at 9 (emphasis in original). In response to another question regarding the adequacy of NIDA's products, Dr. Grant noted that ''NIDA has been reliable[,]'' and ''they have been easy to work with and amenable to accommodating for the requirements of the study.'' *Id.* at 6.

It is true that Dr. Grant, in answering this question, noted the problems with the range of potency in the higher potency material. Dr. Grant explained, however, that the problems he found regarding the range of potency were attributable to the cigarettes being ''handrolled and thus difficult to prepare.'' *Id.* Moreover, Dr. Grant answered ''yes'' to the question of whether NIDA's current products were ''adequate for your research purposes

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the extent authorized by their registration and in conformity with other provisions of [the CSA].'' 21 U.S.C. 822(b).

[30] The first report, which was submitted by Chemic in 2003 to MAPS and CaNORML, is titled ''Evaluation of Volcano(r) Vaporizer for the Efficient Emission of THC, CBD, CBN and the Significant Reduction and/or Elimination of Polynuclear-Aromatic (PNA) Analytes Resultant of Pyrolisis,'' and is available on MAPS' Web site at *http://www.maps.org/mmj/vaporizerstudy4.15.03.* The second report, titled ''Cannabis Vaporizer Combines Efficient Delivery of THC with Effective Suppression of Pyrolitic Compounds,'' also appears on MAPS' Web site at *http://www.maps.org/mmj/Gieringer-vaporizer.pdf.* I take official notice of both documents. *See also http://www.maps.org/news-letters/v13n1/13111gie.pdf* (2003 MAPS news letter discussing Vaporizer studies sponsored by MAPS and NORML and the Marijuana Policy Project), of which I take official notice.

[31] HHS also noted that there were ''a number of technical concerns'' with Chemic's proposal. RX 52B, at 4.

[32] The report, titled ''Evaluation of Volcano® Vaporizer for the efficient emission of THC, CBD, CBN and the significant reduction and/or elimination of polynuclear-aromatic (PNA) analytes resultant of pyrolysis,'' appears on MAPS Web site as discussed in note 30.

[33] If Chemic had a valid basis to challenge HHS's denial of its request for marijuana, it presumably had remedies available to challenge that agency action either within HHS or in the courts. *See, e.g.*, 5 U.S.C. 702 (''A person suffering legal wrong because of agency action * * * is entitled to judicial review thereof.''). Respondent produced no evidence showing that Chemic has pursued any such remedies.

with regard to potency?'' *Id.* at 15. Also, in response to the question of whether ''these problems [have] ever compromised the study?,'' Dr. Grant indicated: ''N/A.'' *Id.* at 6.

Dr. Grant further indicated that he had ''no'' information that ''would lead [him] to believe that the future supply of marihuana required for research would be insufficient or unavailable through NIDA,'' *id.* at 8, and that he had ''no'' concerns regarding ''the availability of research-grade marijuana from NIDA'' to meet CMCR's future needs. *Id.* at 9. While Dr. Grant also indicated that it would be clinically important to evaluate a higher potency product than the 7–8 percent THC content marijuana CMCR was currently using, he also indicated that CMCR had not sought a higher potency product but had only discussed with NIDA the feasibility of such a product. *Id.* at 16.

On his questionnaire, Ronald Ellis, M.D., of the University of California, San Diego, noted that in ''[a]t least two shipments, [there] was some variability on stated THC content and the actual [content] measured.'' GX 17, at 6. Dr. Ellis further noted, however, that NIDA personnel ''have been very responsive.'' *Id.* Apparently, Dr. Ellis's clinical trial received some marijuana which was supposed to have a THC content of 8 percent, but only had a content of approximately 7 percent. *Id.* at 9. Dr. Ellis indicated, however, that the potency of NIDA's current product was adequate for research purposes. *Id.*

Respondent also relies on Dr. Donald Abrams' ''no'' answer regarding the consistency of the potency of NIDA's product. Resp. Prop. Findings at 18 (citing GX 21, at 6). Dr. Abrams further noted that ''[o]riginally approved for 3.9% THC content, midway through the 'Short-term effects * * *' protocol, NIDA informed [us] that the potency had been downgraded to 3.5%. Everything since is said to be at 3.5%.'' GX 21, at 6. Notably, the ''Short-term effects'' study occurred more than a decade ago, and Dr. Abrams did not indicate that there had been further problems with the consistency of the potency of the marijuana supplied by NIDA for several later studies he conducted.

Nor does the evidence support Respondent's contention that the marijuana available through NIDA is of insufficient potency to satisfy the needs of legitimate researchers. In his brief, Respondent relies on the statements of Drs. Grant and Abrams that it would be beneficial to evaluate the efficacy of marijuana cigarettes with a higher THC content than what was currently being supplied by NIDA. Resp. Prop. Findings at 22–23 (citing GX 16 & 21). Respondent, however, produced no evidence establishing that any researcher has obtained approval of FDA and other reviewing authorities to conduct clinical trials using higher THC content marijuana. As Dr. Abrams explained, he ''wanted to use a higher potency product but there were questions from the [scientific review board] and the funding agency [CMCR].'' GX 21, at 9.

Moreover, as Dr. ElSohly testified, the National Center has in inventory substantial quantities of bulk marijuana material with THC contents of ten to eleven percent and has some material with a THC content of fourteen percent.[34] Tr. 1203. Dr. ElSohly also testified that the National Center could produce marijuana with a THC content of up to 20 percent. *Id.* He further testified that he had informed ''some of the investigators that if they want to, they can order material of a certain potency'' and ''roll their own cigarettes.'' *Id.* at 1204–05.

Respondent also maintains that NIDA's marijuana is harsh and that some patients have complained that it was ''inferior in sensory qualities (taste, harshness) [to] the marijuana they smoke outside the laboratory,'' and that ''it was the worst marijuana they had ever sampled.'' Resp. Prop. Findings at 19–21. Yet, as the questionnaires completed by the researchers indicate, only a small percentage of study subjects have complained about the harshness of NIDA's marijuana. See GX 18, at 7 (one of ten patients complained); GX 21, at 8 (four out of fifty dropped out because of quality); GX 22, at 7 (''Out of 100 plus subjects, no more than [three] may have commented that the product was harsh.'').[35] Moreover, as one of the researchers noted, it was unclear whether the harshness was related to the actual marijuana cigarettes or the placebo material.[36] As for Respondent's further contention that some patients complained that NIDA's marijuana ''was the worst they had ever sampled,'' this evidence does not establish that the taste of the products rendered them unsuitable for their intended use.[37] Furthermore, Respondent provides no scientific basis for his suggestion that the research subjects' description of the degree of their subjective satisfaction with the experience of smoking marijuana in a research setting should be a criterion for judging the adequacy of the quality of marijuana for research purposes.[38]

Finally, Respondent contends that NIDA's marijuana is frequently ''not fresh'' and that it includes stems and seeds. Resp. Prop. Findings at 21–22; 25–27. While the record contains some evidence that older marijuana loses some if its potency, all but one of the researchers indicated that neither the lack of freshness nor the existence of plant parts (stems and seeds) had adversely impacted their research. *See* GX 16, at 13 (CMCR); GX 17, at 7 (Dr. Ellis); GX 18, at 7 (Dr. Corey-Bloom); GX 19, at 7 (Dr. Israelski);[39] GX 20, at 7 (Dr. Wallace); GX 22, at 7 (Dr. Polich); GX 28, at 7 (Prof. Lichtman); *but see* GX 21, at 7–8 (Dr. Abrams) (indicating that four

[34] Respondent also cites the questionnaire of Prof. Aron Lichtman, of the Department of Pharmacology, Virginia Commonwealth University, who conducted research in animals. Resp. Proposed Findings at 23 (citing GX 28). On his questionnaire, Prof. Lichtman indicated that he ''would [have] prefer[red] something at a higher potency, but at the time, 3–4% was the highest potency available.'' GX 28, at 9. Prof. Lichtman's questionnaire indicated, however, that his study had last obtained marijuana in 1999. Prof. Lichtman's answer is thus not probative of whether NIDA is currently capable of providing marijuana of adequate potency to support legitimate research needs.

Respondent's evidence regarding the potency of marijuana distributed by NIDA for patients in the former Compassionate Investigational New Drug program likewise dates back to 1999. See Resp. Prop. Findings at 24 (citing RX 19, at 47–48). As such, the evidence is not probative of whether NIDA is currently capable of supplying marijuana of adequate potency.

[35] Dr. ElSohly testified: ''I think you had like 50 subjects, and only three or four complained of the harshness. That's a very small percentage. You are going to get that regardless of what you administer.'' Tr. at 1589.

[36] As Dr. Cory-Bloom noted, it was unclear whether the harshness was attributable to actual marijuana cigarettes or placebo cigarettes. GX 18, at 7. Relatedly, Dr. ElSohly testified that the complaints of harshness were likely attributable to the placebo because ''all of the components have been extracted out . . . [s]o this will be just like smoking * * * grass or * * * hay or something like that or just paper that might have this harshness, and there's no soothing effect of the other components in the plant material.'' Tr. 1289–90.

[37] Respondent also cites to hearsay evidence regarding the experience of a single patient who had previously used non-NIDA marijuana (illegally obtained from California ''buyers'' clubs'') without problems but then purportedly developed bronchitis upon smoking NIDA marijuana. Resp. Prop. Findings at 21; Tr. 570. Even if I were to credit this testimony, the record as a whole establishes that NIDA's marijuana was well tolerated in the great majority of the various studies' subjects.

[38] Marijuana is known to cause, among other things, ''a distortion in the sense of time associated with deficits in short-term memory and learning,'' ''difficulty carrying on an intelligible conversation,'' anxiety, paranoia, panic, depression, dysphoria, delusions, illusions, and hallucinations. RX 1 (IOM report), at 101–102. These effects impact the determination of what, if any, weight to attach to research subjects' descriptions of their satisfaction with the marijuana they have smoked.

[39] Dr. Israelski did not recall any complaints about the ''freshness'' of NIDA's marijuana.

out of fifty patients had ''dropped out due to quality'').

Moreover, with respect to the existence of stems and seeds in NIDA's marijuana, Dr. ElSohly acknowledged that prior to 2001, there may have some stems and seeds in the marijuana it sent to the Research Triangle Institute (the contractor for the manufacture of the cigarettes). Tr. 1300–01. Dr. ElSohly further testified, however, that in 2001, the National Center acquired a special de-seeding machine which removes all the seeds and stems from the marijuana that is used to manufacture cigarettes. *Id.* at 1301. Respondent produced no evidence showing that the marijuana which the National Center has since supplied has contained stems and seeds.[40]

Respondent's Contention That NIDA's Marijuana Is Inadequate To Support The Development of Plant-Form Marijuana Into an FDA-Approved Prescription Drug

Respondent further contends that the existing supply of NIDA marijuana is inadequate because ''MAPS seeks to develop botanical marijuana as an FDA-approved prescription drug.'' Resp. Prop. Findings at 8. In support of this contention, Respondent makes two primary factual assertions. First, he claims that ''to develop a pharmaceutical product, a developer must have assured access to a reliable, dependable source of the particular formulation of the product the developer needs, both for research, and for distribution if the product is approved,'' and that ''[w]ithout such a source, there is no development.'' *Id.* at 9. Second, he claims that ''even before the Phase [1] and Phase [2] studies on a product, the developer must generally submit a Drug Master File,''[41] and that the Drug Master File (DMF) for NIDA's marijuana contains proprietary information which NIDA controls. *Id.*

As for Respondent's contentions regarding the need to submit a DMF, Respondent asserts that ''there is no procedure to force [the DMF's] owner to make a Drug Master File, or the information in it, available to a drug developer.'' Resp. Prop. Findings at 10 (citing Tr. 447–49; testimony of Dale Gieringer). While Respondent concedes that NIDA ''has allowed the researchers whom it chooses to supply with marijuana to rely on that file,'' and that FDA has approved several Phase 1 studies using NIDA marijuana and the information contained in the DMF, *id.* at 10, it contends that because NIDA's mission is to study drug abuse, it is not likely that ''NIDA would authorize MAPS to rely on the NIDA marijuana [DMF] currently on file with the FDA.'' *Id.* at 45.

The 1999 HHS Guidance makes clear, however, that if a proposed research project meets the Department's criteria for the provision of research-grade marijuana, ''NIDA will provide the researcher with authorization to reference NIDA's marijuana Drug Master File.'' GX 24, at 4. Moreover, as the FDA has explained, ''the submission of a DMF is not required by law or regulation,'' but rather, ''is submitted solely at the discretion of the holder.'' *Guideline For Master Drug Files*, at 2. The FDA regulations provide: ''FDA ordinarily neither independently reviews drug master files nor approves or disapproves submissions to a drug master file. Instead, the agency customarily reviews the information only in the context of an application under part 312 or part [314].'' 21 CFR 314.420(a). Accordingly, as the FDA Guidelines explain, while ''the information contained in [a] DMF may be used to support an Investigational New Drug Application (IND), [or] a New Drug application (NDA) * * * [a] DMF is NOT a substitute for an IND [or] NDA.'' *Guideline For Master Drug Files,* at 3.

Relatedly, David Auslander, M.D., the Government's expert witness in pharmaceutical development, testified that ''not all companies do Drug Master Files'' and that ''FDA does not necessarily require a Drug Master File to do a Phase [1] and Phase [2] study in all cases if the Drug Master File * * * comes from a producer that's different from the sponsor itself.'' Tr. 2024. Dr. Auslander also explained that a drug developer may not even have a Drug Master File at the time it applies to conduct Phase 1 or Phase 2 studies. *Id.* As Dr. Auslander further testified, the necessary information can be submitted in an IND or an NDA. *Id.* at 2024–25.

As for the contention that NIDA is not a reliable source of supply, it is undisputed that a for-profit drug developer would be unlikely to take a drug through the FDA approval process unless it was ''assured that they would have a drug supply that is unchanging and reliable.'' Tr. 117 (testimony of Irwin Martin, Ph.D.). Dr. Martin also testified that ''[o]ne of the biggest problems in drug development is the unfortunate need sometimes to repeat studies. If you have a new formulation or your drug source has changed, you many need to repeat years worth of data because you can no longer assure that the data you developed with this earlier version of [the] drug will actually be the same drug as you now have.'' *Id.* at 118. Dr. Martin further testified that while ''no reasonably business-oriented company would ever develop a product'' if it did not have a reliable and consistent supply source, he also noted that if a company had to change its supply source, a company could try to show that the new product was pharmcokinetically equivalent to the old product. Tr. 120–21; *see also* Tr. 2027.

Also on this issue, Dr. Auslander testified further on behalf of the Government that if the developer's source changed, it ''would not necessarily repeat the Phase [1] and [2] clinical studies over again, but * * * would do additional chemical studies, stability [studies] * * * to show that the quality of material from source A and the quality of material acquired from source B are equivalent.'' Tr. 2027–28. Both Respondent's and the Government's experts agreed, however, that if the developer could not establish equivalence between the two products, ''it would not be a trivial experience'' for the developer. *Id.* at 2029; *see also id.* at 121 (testimony of Dr. Martin that developer would have to start over).

Relatedly, Respondent further asserts that there is ''overwhelming'' evidence that NIDA ''would not be likely to choose to serve as the supplier to a medical marijuana pharmaceutical product developer even if it were authorized to so.'' Resp. Prop. Findings at 10. In support of this assertion, Respondent extracts two sentences from a letter in which Nora Volkow, M.D., NIDA's director, responded to Mr. Doblin's letter accusing NIDA/HHS of ''seriously obstructing'' Chemic's research involving the Volcano which MAPS was sponsoring (and whose application HHS ultimately denied).[42] *See id.* (quoting RX 13; ''It is

[40] In support of its contention that NIDA marijuana contains stems and seeds which renders the product's quality inadequate, Respondent also cites an article, ''Chronic Cannabis Use in the Compassionate Investigational New Drug Program.'' Resp. Prop. Findings at 26 (citing RX 19, at 49–50). Respondent particularly notes two photographs of marijuana that was manufactured in April 1999. *See id.* This evidence thus predates the National Center's 2001 acquisition of a de-seeding machine.

[41] I also take official notice of the FDA's *Guideline For Drug Master Files* (Sept. 1989) (available at *http://www.fda.gov/cder/guidance/dmf.htm/*).

According to this FDA guideline (at 2), ''[a] Drug Master File (DMF) is a submission to the [FDA] that may be used to provide confidential detailed information about facilities, processes, or articles used in the manufacturing, processing, packaging, and storing of one or more human drugs.''

[42] In that letter, Mr. Doblin also mentioned that DEA had indicated that it would not review Chemic's application to import ten grams of Dutch marijuana until NIDA/HHS completed its review of Chemic's protocol. RX 14. Mr. Doblin also

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not NIDA's role to set policy in this area or to contribute to the DEA licensing procedures. Moreover, it is also not NIDA's mission to study the medicinal use of marijuana or to advocate for the establishment of facilities to support this research.''). *See also* RX 14 (letter of Mr. Doblin; ''NIDA/HHS is seriously obstructing a privately-funded drug development program aimed at evaluating marijuana's potential use as an FDA-approved medication.'').

In that letter, Dr. Volkow declined to intervene explaining that:

> * * * NIDA is just one of the participants on the HHS review panel and continues, on behalf of the U.S. Government, to provide supplies of well-characterized cannabis for both NIH and non-NIH-funded research. The latter is conducted according to the procedure established in 1999 by HHS for obtaining access to marijuana for research purposes. It is not NIDA's role to set policy in this area or to contribute to the DEA licensing procedures. Moreover, it is not NIDA's mission to study the medicinal uses of marijuana or to advocate for the establishment of facilities to support this research. Therefore, I am sorry but I do not believe that we can be of help to you in resolving these concerns.

RX 13. As both this letter and the 1999 Guidance make plain, HHS—and not NIDA—is the policymaker regarding the criteria for determining who can obtain research-grade marijuana from NIDA. As NIDA does not independently control to whom it may supply marijuana for legitimate research, the letter is not indicative of whether NIDA would be a reliable source of marijuana for an entity which sought to develop plant-form marijuana into an FDA-approved prescription medicine.

Respondent also points to the 1999 Guidance document's statement that ''[t]he goal of this program must be to determine whether cannabinoid components of marijuana administered through an alternative delivery system can meet the standards enumerated under the Federal Food, Drug, and Cosmetic Act for commercial marketing of a medical product. As the IOM report stated, 'Therefore, the purpose of clinical trials of smoked marijuana would not be to develop marijuana as a licensed drug, but such trials could be a first step towards the development of rapid-onset, nonsmoked cannabinoid delivery systems.' '' [43] GX 24, at 2.

As found above, the IOM's recommendation was based on its conclusion that ''[a]lthough marijuana smoke delivers THC and other cannabinoids to the body, it also delivers harmful substances, including most of those found in tobacco smoke. In addition, plants contain a variable mixture of biologically active compounds and cannot be expected to provide a precisely defined drug effect. For those reasons there is little future in smoked marijuana as a medically approved medication.'' RX 1, at 195–96.

Moreover, the HHS Guidance does not address what the Secretary's response would be were the current clinical trials to show that the efficacy/safety profile of smoked marijuana supported FDA approval of it as a prescription medicine for particular indications or patient populations. Nor does it address what the Secretary's response would be if clinical trials were to show that the efficacy/safety of vaporized plant form marijuana for particular indications supported its approval as a prescription drug.

Dr. Gust testified that notwithstanding the stated goal of the 1999 Guidance, a researcher who ''had an IND from FDA * * * would not have a problem getting marijuana.'' Tr. 1718. Further, in response to the ALJ's question as to whether a researcher whose goal was to obtain FDA approval of plant-form marijuana would have more difficulty obtaining marijuana from HHS than a researcher who sought to produce an extract-based product, Dr. Gust testified: ''I don't believe so.'' *Id.* at 1719–20.

Dr. Gust also explained that whether plant-form marijuana should be approved as a prescription medicine is ''not a question for the'' PHS committee that reviews requests for NIDA marijuana. *Id.* at 1720. Rather, ''it's a question for the regulation and approval process that goes on through FDA.'' *Id.* Finally, while Dr. Gust acknowledged that ''HHS would strongly endorse'' the IOM's view that ''if there's going to be an approved medication, it's going to be a purified constituent of marijuana that will be delivered in a non-smokable form,'' he further testified that in his experience, there was no bias against ''the concept of approving marijuana as a medication'' at the level of PHS review. *Id.* at 1722.[44]

Respondent further asserts that ''it is not at all clear that NIDA *could* serve as a source for a pharmaceutical product.'' Resp. Prop. Findings at 11 (emphasis in original). Notwithstanding Mr. Doblin's beliefs regarding the likely safety/efficacy profiles of smoked and vaporized marijuana, *see* Tr. at 605, it is highly speculative whether clinical trials will ultimately support FDA approval of plant-form marijuana through either delivery system.[45]

As further support for this contention, Respondent references that Dr. ElSohly answered ''That's correct'' when asked the following question by Respondent's counsel: ''So if somebody wants to develop a commercial product with marijuana, they could not use the NIDA marijuana; is that fair?'' Resp. Prop. Findings at 11 (quoting Tr. 1463). It is not clear exactly what to make of Dr. ElSohly's answer to this question.[46] In

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referenced DEA's handling of Respondent's application.

[43] In discussing the content of the HHS Guidance, Respondent asserts: ''And it expressly states that 'the purpose of clinical trials of smoked marijuana would not be to develop marijuana as a licensed drug.' '' Resp. Proposed Findings at 11 (quoting GX 24, at 2). Notably, Respondent's quotation edits out the Guideline's reference to the IOM Report. The complete text of the Guidance shows, however, HHS did not come to this conclusion without evidentiary support, but rather, relied on the extensive findings of the IOM.

[44] In discussing this testimony, the ALJ noted that Dr. Gust had acknowledged that a researcher with an FDA-approved protocol might nonetheless be denied marijuana by the PHS committee under the criteria set forth in the guidance. ALJ at 51 (citing Tr. 1694). There is, of course, no evidence that any researcher with an FDA-approved protocol has been denied marijuana subsequent to the 1999 guidelines. Dr. Gust's answer was based on a hypothetical question. Accordingly, this portion of Dr. Gust's testimony provides no basis to question his credibility as to whether in his experience, HHS (and the PHS review committees) are biased against researchers who seek to obtain FDA approval for plant-form marijuana.

[45] Given that, as indicated above, marijuana has been found to contain hundreds of different chemicals, including a variable mixture of biologically active compounds that cannot be expected to provide a precisely defined drug effect, IOM has expressed the view that, ''if there is any future in cannabinoid drugs, it lies with agents of more certain, not less certain, composition.'' RX 1, at 195–96.

[46] Based on the questions that led up to the above-quoted question, it appears that, in answering ''That's correct,'' Dr. ElSohly was confirming that the marijuana he grows pursuant to the NIDA contract may not be taken by the University of Mississippi (without prior authorization from NIDA) for use in the commercial development of a THC extract product where such commercial activity was not authorized by NIDA. *See* Tr. at 1462–63. Indeed, the following subsequent exchange between Respondent's counsel and Dr. ElSohly suggests that Dr. ElSohly correctly understood that there was no prohibition on the use of NIDA marijuana for the development of commercial products:

> Q: Dr. ElSohly, if an organization like MAPS, for example, a nonprofit or pharmaceutical organization, wanted to try to develop smoked marijuana into an FDA-approved medicine, could it use the marijuana that you grow to the preclinical and clinical testing if NIDA agreed?
>
> A: I would say yes.

Tr. 1562–63. Moreover, even if Dr. ElSohly was of the mistaken view that the marijuana he grew for NIDA could never be used by anyone for commercial product development, such a misunderstanding on Dr. ElSohly's part would not be controlling for purposes of this proceeding. The record is clear that it is HHS—not Dr. ElSohly—that determines the terms of his contract, including to whom and under what circumstances he may supply marijuana; and the record is also clear that Dr. ElSohly follows the instructions he receives from NIDA as to whom to deliver the marijuana. Further, as explained above, the record reveals that HHS's policy contains no prohibition on the use of

any event, no provision of the National Center's contract with NIDA imposes any prohibition on the use of the marijuana produced under the contract for the purposes of the development of a commercial product. Indeed, the language of the contract with NIDA suggests otherwise. While Article H.13 states that ''contract funds shall not be used to support activities that promote the legalization of any drug or other substance included in schedule I'' of the CSA, it further provides that ''[t]his limitation shall not apply when the contractor makes known to the contracting officer that there is significant medical evidence of a therapeutic advantage to the use of such drug or other substance or that federally sponsored clinical trials are being conducted to determine therapeutic advantage.'' GX 13, at 20 (citing Pub. L. 108–447, § 510, 108 Stat. 2809 (2005)). Likewise, the new procedures that HHS announced in 1999 for providing marijuana for medical research contain no restriction on using NIDA-supplied marijuana for the development of commercial products. GX 24. To the contrary, by adopting a new procedure whereby privately funded researchers could obtain marijuana from NIDA at cost, HHS made it possible starting in 1999 for a commercially sponsored researcher to develop a drug product using NIDA-supplied marijuana. *See id.* at 2. Finally, Respondent cites no provision of law that prohibits NIDA from serving as a supply source for a prescription drug approval process.[47]

Evidence Regarding the Remaining Statutory Factors

There is no evidence that Respondent has not complied with applicable state or local laws. *See* Gov. Proposed Findings at 139 (discussing 21 U.S.C. 823(a)(2)). Moreover, Respondent has never been convicted of any controlled-substance related offense. Tr. 78; *see* 21 U.S.C. 823(a)(4).

As for factor five, on the questionnaire, Respondent acknowledged that he ''has no current or previous registrations and is unaware of any registration [having] previously [been] granted to the university.'' GX 3, at 3. While Respondent testified that he would meet all ''appropriate security conditions,'' he also acknowledged that ''I've never grown marijuana or any other controlled substance.'' Tr. 79. He further testified that ''We have not—I have no experience in the control against diversion.'' *Id.* Relatedly, Respondent testified that he had no personal experience in providing security for plants, *id.* at 255, and that both graduate students and technicians would be used to perform the various tasks associated with the project. *Id.* at 254 (''I usually don't go down and water the plants in the greenhouse; I usually have a technician that does that.''); *id.* at 254–55 (''They [the graduate students and technicians] would probably do the transplanting[,]'' and ''a daily check on any environmental controls we have.''). Respondent presented no evidence that any person who would be involved in the daily operation of the project would have experience in the lawful manufacture or distribution of schedule I and II controlled substances.[48]

Finally, Respondent testified that he believed that granting his application would promote technical advances in the art of manufacturing controlled substances and the development of new substances. *Id.* at 74–76. More specifically, Respondent asserted that granting his application would advance ''the understanding [of] any possible clinical use of marijuana if we were able to supply this to investigators to run trials.'' *Id.* at 75–76. Respondent also testified that ''we would learn more about how the environment affects the constituents in the plant material which would enable'' a potential manufacturer, were marijuana to become approved by the FDA as a drug, to ''know the environment it needs to be grown under to produce a clinical marijuana.'' *Id.* at 76. Respondent further opined that granting his registration would promote technical advances because part of the purpose of growing the marijuana was to allow MAPS to test its vaporizer. *Id.* at 77–78. Respondent acknowledged, however, that he would not personally be working on MAPS's vaporizer device or on any other delivery device. *Id.* at 230. He also acknowledged that he has no patents regarding the growing of any medicinal plants. *Id.* at 238.

Discussion

Pursuant to 21 U.S.C. 823(a), ''[t]he Attorney General shall register an applicant to manufacture controlled substances in schedule I or II if he determines that such registration is consistent with the public interest and with the United States obligations under international treaties, conventions, or protocols in effect on May 1, 1971.'' 21 U.S.C. 823(a). ''In determining the public interest,'' § 823(a) directs the Attorney General to consider the following factors:

(1) Maintenance of effective controls against diversion of particular controlled substances and any controlled substances in schedule I or II compounded therefrom into other than legitimate medical, scientific, research, or industrial channels, by limiting the importation and bulk manufacture of such controlled substances to a number of establishments which can produce an adequate and uninterrupted supply of these substances under adequately competitive conditions for legitimate medical, scientific, research, and industrial purposes;

(2) Compliance with applicable State and local law;

(3) Promotion of technical advances in the art of manufacturing these substances and the development of new substances;

(4) Prior conviction record of applicant under Federal and State laws relating to the manufacture, distribution, or dispensing of such substances;

(5) Past experience in the manufacture of controlled substances, and the existence in the establishment of effective controls against diversion; and

(6) Such other factors as may be relevant to and consistent with public health and safety.

Id. This Agency's regulations further provide that ''[a]t any hearing on an application to manufacture any controlled substance listed in Schedule I or II, the applicant shall have the burden of proving that the requirements for such registration pursuant to [§ 823(a)] are satisfied.'' 21 CFR 1301.44(a).

As § 823(a) makes plain, even if an applicant satisfies its burden of proof with respect to the public interest inquiry, it cannot be granted a registration unless its proposed activities are consistent with the United States' obligations under international treaties. The United States is a party to

the marijuana grown pursuant to the NIDA contract for commercial development purposes.

[47] As for Respondent's contention that the Government did not ''introduce any evidence that NIDA could or would [serve as a supply source] to support its claim that NIDA's supply is adequate to meet all legitimate medical and scientific purposes,'' Resp. Prop. Findings at 11, Respondent, and not the Government, has the burden of proof on the issue of whether supply is inadequate within the meaning of 21 U.S.C. 823(a)(1). *See* 21 CFR 1301.44(a).

[48] Respondent testified that he had performed classified work on plants for the U.S. Army and that ''there were security systems in place similar to the security systems you have in this building'' (referring to DEA Headquarters, where the hearing took place), and he answered ''Yes'' when asked by his counsel whether he recognized ''the importance of that sort of security in a situation like this registration application.'' Tr. 367. It is unclear what Respondent meant by ''the security systems you have in this building,'' since the only security to which he would have been exposed in entering DEA Headquarters to testify were the requirements of passing through a metal detector, being accompanied by a DEA employee, and wearing a visitor's badge. These DEA Headquarters security measures have nothing to do with the security measures required of DEA registrants who handle controlled substances, which are set forth in 21 CFR 1301.71 through 1301.76. Thus, this portion of Respondent's testimony was ambiguous and did not establish, for purposes of 21 U.S.C. 823(a)(5) that, if his application were granted, there would exist in his establishment effective controls against diversion.

the Single Convention. Accordingly, whether Respondent's proposed activities are consistent with this Nation's obligations under the Convention is a threshold question.

A. Whether Respondent's Proposed Registration Is Consistent With the Single Convention

The Single Convention imposes a comprehensive series of measures to control narcotic drugs and other substances including marijuana (which is referred to in the Single Convention as ''cannabis'').[49] Under the Convention, cannabis is both a Schedule I and Schedule IV [50] drug and is subject to the control measures applicable to each schedule. Single Convention, art. 2, para. 5; *see also* Secretary-General of the United Nations, *Commentary on the Single Convention on Narcotic Drugs, 1961,* 65 (1973) (hereinafter, Commentary). Moreover, under article 28, ''[i]f a Party permits the cultivation of the cannabis plant for the production of cannabis or cannabis resin, it shall apply thereto the system of controls as provided in article 23 respecting the opium poppy.'' Single Convention, art. 28, Para. 1. As the Commentary further explains:

> The system of control over all stages of the drug economy which the Single Convention provides has two basic features: limitation of narcotic supplies of each country * * * to the quantities that it needs for medical and scientific purposes, and authorization of each form of participation in the drug economy, that is, licensing of producers, manufacturers and traders. * * * In the case of the production of opium, coca leaves, cannabis and cannabis resin, this regime is supplemented by the requirement of maintaining government monopolies for the wholesale and international trade in these drugs in countries which produce them. * * *

Commentary at 263.

Amongthese controls is the requirement that ''[t]he Agency shall * * * have the exclusive right of importing, exporting, wholesale trading and maintaining stocks other than those held by manufacturers of opium alkaloids, medicinal opium or opium preparations.'' Single Convention art. 23, para. 2(e). The Convention further provides, however, that the ''Parties need not extend this exclusive right to medicinal opium and opium preparations.'' [51] *Id.*

The Commentary to article 28 thus explains that ''[a] Party permitting the cultivation of the cannabis plant for cannabis and cannabis resin must, pursuant to article 23, paragraph [2(e)(2)] in connexion with article 28, paragraph 1, grant its national cannabis agency *the exclusive right of wholesale * * * trade in these drugs.*'' Commentary at 314 (emphasis added). The Commentary further explains that the Government ''need not extend this exclusive right to extracts and tinctures of cannabis.'' *Id.*

Respondent raises several arguments as to why his registration would be consistent with the Single Convention. First, he argues that ''the Convention clearly contemplates that more than one cultivator or bulk manufacturer may be licensed by the member nation's licensing agency.'' Resp. Prop. Findings at 66. Second, he argues that because his ''crop would be medical marijuana, grown and processed to be adapted for medicinal use, it is not subject to the agency's 'exclusive right' for 'maintaining stocks.' '' *Id.* at 67.

Relatedly, Respondent argues that because DEA has granted Dr. ElSohly a registration to ''grow marijuana for private purposes'' and does not require him to ''turn[] over those stocks to any government agency,'' granting his application will likewise conform with the Single Convention. Respondent further contends that Dr. ElSohly has been able to grow marijuana outside of the NIDA contract and that ''DEA would not have issued those licenses had they violated the Single Convention.'' *Id.* at 68. Respondent also argues that the United Kingdom, which is also Party to the Convention, has allowed marijuana to be grown by a private entity (GW Pharmaceuticals) without its government taking physical possession. *Id.* Likewise, in his Response to the Government's exceptions to the ALJ's recommended decision, Respondent argues that the ALJ ''correctly held that Article 23 [para.] 2(d) does not require the government to take physical possession of [his] crop.'' Respondent's Resp. at 9.

In concluding that the ''Single Convention does not preclude registering Respondent,'' the ALJ offered three reasons. First, based on the United Kingdom's regulatory scheme, she reasoned that ''it appears * * * that the parties to the Single Convention are free to construe the term 'physical possession' as they see fit.'' ALJ 82. As for the remaining two reasons, the ALJ explained that ''[i]t also appears, although it is not entirely clear, that the marijuana grown by the National Center or by any other registrant for utilization in research would qualify as either 'medicinal' within the meaning of article 1, paragraph (1)(o), or a 'special stocks' within the meaning of article 1, paragraph (1)(x), and that therefore the government monopoly on importing, exporting, wholesale trading, and maintain stocks would not apply.'' *Id.*

Neither the ALJ's rationales nor Respondent's arguments are persuasive. As for the argument that the Single Convention does not require that the Government take physical possession, the argument provides no comfort to Respondent for two reasons. First, the argument ignores that taking possession and engaging in wholesale distribution are two separate activities under the Convention. Notably, in his briefs, Respondent does not even acknowledge the distinction. *See* Resp. Proposed Findings and Conclusion of Law at 64–70; Respondent's Resp. at 9–12.

Second, as Respondent's evidence makes clear, his purpose for seeking a registration is not simply to grow marijuana, but to distribute it outside of the HHS system. Mr. Doblin's testimony

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[49] Under the Single Convention, '' 'cannabis plant' means any plant of the genus Cannabis.'' Article 1(c). The Single Convention defines ''cannabis'' to include ''the flowering or fruiting tops of the cannabis plant (excluding the seeds and leaves when not accompanied by the tops) from which the resin has not been extracted, by whatever name they may be designated.'' Article 1(b). This definition of ''cannabis'' under the Single Convention is less inclusive than the CSA definition of ''marihuana.'' *See* 21 U.S.C. 802(16). However, this distinction in inconsequential for purposes of the matters at issue in this proceeding.

[50] The Single Convention's use of the term ''Schedule IV'' is not to be confused with the CSA's use of the same term. Under the Convention, the terms ''Schedule I, Schedule II, Schedule III and Schedule IV mean the correspondingly numbered list of drugs or preparations annexed to this Convention.'' Single Convention, art. 1, para. 1(u). As the Convention further explains, ''[t]he drugs in Schedule IV shall also be included in Schedule I and subject to all measures of control applicable to drugs in the latter Schedule'' as well as the additional measures contained in article 2, paragraph 5. *Id.* art. 2, para. 5.

Under Article 2, paragraph 5, the Convention requires that [a] Party shall adopt any special measures of control which in its opinion are necessary having regard to the particularly dangerous properties of a drug so included. *Id.* art. 2, para. 5(a). The Convention further directs that:

> A Party shall, if in its opinion the prevailing conditions in its country render it the most appropriate means of protecting the public health and welfare, prohibit the production, manufacture, export and import of, trade in, possession or use of any such drug except for amounts which may be necessary for medical and scientific research only, including clinical trials therewith to be conducted under or subject to the direct supervision and control of the Party.

Id. art. 2, para. 5(b).

[51] Article 23 of the Convention further provides that ''[a] Party that permits the cultivation of the opium poppy for the production of opium shall establish, if it has not already done so, and maintain, one or more government agencies * * * to carry out the functions required under this article.'' Single Convention art. 23, para. 1. Moreover, ''[a]ll cultivators of the opium poppy shall be required to deliver their total crops of opium to the Agency. The Agency shall purchase and take physical possession of such crops as soon as possible, but not later than four months after the end of the harvest.'' *Id.* para. 2(d).

that ''what we're trying to do is get the [PHS] and NIDA out of the picture,'' Tr. 666, makes this plain. *See also* Tr. 225 (testimony of Respondent; ''I may very well be approached by other people with approved studies who need a source also.''). Thus, Respondent's contention that the Single Convention does not prohibit multiple cultivators is beside the point, since his proposed purpose for gaining authorization to grow marijuana (so that MAPS—rather than HHS/NIDA—can control distribution of the marijuana) would defy one of the central control provisions of the Single Convention with respect to cannabis cultivation. As the Commentary to the Single Convention states:

> Countries * * * which produce * * * cannabis * * * , [i]n so far as they permit private farmers to cultivate the plants * * *, cannot establish with sufficient exactitude the quantities harvested by individual producers. If they allowed the sale of the crops to private traders, they would not be in a position to ascertain with reasonable exactitude the amounts which enter their controlled trade. The effectiveness of their control régime would thus be considerably weakened. In fact, experience has shown that permitting licensed private traders to purchase the crops results in diversion of large quantities of drugs into illicit channels. * * * [T]he acquisition of the crops and the wholesale and international trade in these agricultural products cannot be entrusted to private traders, but must be undertaken by governmental authorities in the producing countries. Article 23 * * * and article 28 * * * therefore require a government monopoly of the wholesale and international trade in the agricultural product in question in the country which authorizes its production.

Commentary at 278. Indeed, the central theme of Respondent's argument—starting with the opening sentence of his Proposed Findings and Conclusion of Law and repeated throughout the document—is that the very Government monopoly over the wholesale distribution of marijuana that the Single Convention demands is the primary evil that Respondent seeks to defeat through obtaining a DEA registration. Thus, from the outset of the analysis, Respondent's proposed registration cannot be reconciled with United States obligations under the treaty.

Respondent offers no argument that his proposed distributions would not constitute wholesale trading under the Convention. *See, e.g.*, GX 3, at 3 (''customers would include both MAPS-sponsored research and research sponsored by other organizations.''). Respondent's proposed activity in distributing to researchers does not constitute retail trading because his customers are not the ultimate users of the marijuana, but rather researchers, who would then dispense the drugs to ultimate users. *See* Commentary at 329 (A manufacturer's ''license does not in any event * * * include the retail trade in drugs.'').[52]

In construing the meaning of ''United States obligations under [the Single Convention]'' in the context of 21 U.S.C. 823(a), any reliance by the ALJ or Respondent on the United Kingdom's practice is misplaced.[53] For one, as set forth in § 823(a), Congress assigned to the Attorney General sole authority to determine whether a proposed registration under this provision is consistent with United States obligations under the Single Convention. Nowhere in the CSA does Congress call upon the Attorney General to rely on—or even consider—how other nations interpret the Single Convention as a basis for the Attorney General's determination of what are the United States obligations under the treaty.[54] Second, the Single Convention contains provisions that call upon each nation that is a party to the treaty to determine, in its own opinion, whether and how to tailor its control measures commensurate with the circumstances particularized to that country. For example, article 2, paragraph 5, of the Single Convention states the following with respect to drugs included in Schedule IV (including cannabis):

> (a) A Party shall adopt any special measures of control which in its opinion are necessary having regard to the particularly dangerous properties of a drug so included; and
>
> (b) A Party shall, if in its opinion the prevailing conditions in its country render it the most appropriate means of protecting the public health and welfare, prohibit the production, manufacture, export and import of, trade in, possession or use of any such drug except for amounts which may be necessary for medical and scientific research only, including clinical trials therewith to be conducted under or subject to the direct supervision and control of the Party.

Thus, what the United Kingdom might, in its opinion, deem to be appropriate control measures to meet its obligations under the Single Convention given the circumstances involving cannabis in Britain might be distinct from what the United States finds, in its opinion, to be the appropriate control measures to fit the circumstances involving cannabis in the United States.[55]

If the United States were to look to any outside entity for guidance on compliance with the Single Convention, that entity would be the International Narcotics Control Board (INCB), which is the United Nations organ created by the Single Convention to implement, and monitor compliance with, the Convention. *See* Single Convention, articles 5, 9–15, 19–20. In its 2005 Annual Report, the INCB reiterated: ''Articles 23 and 28 of the [Single] Convention provide for a national cannabis agency to be established in countries where the cannabis plant is cultivated licitly for the production of cannabis, even if the cannabis produced is used for research purposes only.'' [56] Similarly, the INCB issued a statement in 2008 stating, with respect to the standards under the Single Convention

[52] Under the CSA and DEA regulations, wholesale distribution and dispensing (retail distribution) are independent activities and require separate registrations. *See* 21 U.S.C. 802(11) (definition of ''distribute'' excludes dispensing); *compare* 21 U.S.C. 823(b) *with* 823(f) (separate registration required for distributor versus dispenser); *see also* 21 CFR 1301.13(e) (listing categories of registration and authorized activities). Only a practitioner (and not a manufacturer or distributor) can dispense a controlled substance to a patient. *See id.* at 1301.13(e)(1).

Moreover, the Single Convention is a drug-control regime. The precise economic arrangements between Respondent, MAPS, and any other potential customers, are therefore irrelevant in determining whether his proposed activity would constitute wholesale trading.

[53] There was a dispute between the parties as to the admissibility of the document Respondent submitted (attached to RX 26) purporting to set forth the United Kingdom's explanation of how it carried out its obligation under the Single Convention to establish a national cannabis agency. Tr. 1812. After having the parties brief the issue, the ALJ noted, in a ''Memorandum to Counsel and Ruling,'' that one of the Government's objections was that Respondent did ''not explain how exhibit 26 was issued or under what authority.'' The ALJ concluded that ''although the circumstances under which exhibit 26 came to be promulgated are not clear, it appears that the document is in effect in the United Kingdom.'' *Id.* The ALJ did not explain her basis for this conclusion. *See id.* It is unnecessary to determine whether this ruling by the ALJ was proper because, even assuming, *arguendo,* that the document accurately represented the official position of the United Kingdom and was issued by the appropriate representative of the British Government, for the reasons explained above, reliance on this document for determining how to interpret the Single Convention for purposes of 21 U.S.C. 823(a) is inappropriate.

[54] For this reason, it is unnecessary to expressly reject the interpretation contained in the document submitted by Respondent (attached to RX 26) titled ''United Kingdom National Cannabis Agency: Protocol.''

[55] In any event, there is no evidence that the British Government has allowed GW to engage in the type of activity for which Respondent seeks to become registered—the wholesale distribution of plant-form marijuana. Rather, as DEA has done with respect to the National Center and its project to supply THC extract to Mallinckrodt (GX 78), the British Government has granted GW a license to grow marijuana for the limited purpose of producing extract for a pharmaceutical product. Rx 26, Ex. A at 2.

[56] The above-quoted statement appears on page 16, in paragraph 81, of the 2005 INCB Annual Report, which is available at *http://www.incb.org/pdf/e/ar/2005/incb_report_2005_2.pdf.* I take official notice of the report.

relating to the control of cannabis, that ''[s]uch standards require, inter alia, the control of cultivation and production of cannabis by a national cannabis agency.'' [57] As explained above, it is this control of the cultivation and production of cannabis by a national agency of the United States to which Respondent is fundamentally opposed, thereby demonstrating the inconsistency between his application and the Single Convention.

The ALJ further reasoned that ''although it is not entirely clear,'' the marijuana Respondent seeks to grow would be exempt from the Government's exclusive right to engage in wholesale trading because it would qualify as either ''medicinal'' or ''special stocks.'' ALJ at 82. As explained below, the ALJ erred on both counts.

In his response to the Government's exceptions, Respondent contends that the ''[t]he Single Convention defines 'medicinal' marijuana as that 'which has undergone the process necessary to adapt it for medicinal use.' '' Respondent Resp. at 10 (quoting art I. para 1 (o)). The Single Convention, however, contains no such term.

Rather, the Convention defines only the term ''[m]edicinal opium.'' Single Convention art 1, para.1(o) (defining ''medicinal opium'' as ''opium which has undergone the processes necessary to adapt it for medicinal use.''). Accordingly, Respondent's argument rests solely on an analogy to the term ''medicinal opium.'' Respondent's reliance is misplaced as it ignores several critical distinctions between what was formerly known as ''medicinal opium'' and what it contends is ''medicinal marijuana.''

As the Commentary explains: ''The Single Convention follows earlier narcotics treaties in defining 'medicinal opium' as a special form of opium in which that drug is used in medical treatment.'' Commentary at 21–22. The Commentary goes on to state that ''medicinal opium'' is a form of opium powder to which lactose has been added ''to reduce its morphine content *to the standard* of about 10 percent prescribed for 'medicinal opium.' '' *Id.* (emphasis added).

In a footnote, the Commentary further explains that ''[t]he fifth edition of the *Pharmacopœa Helvetica* (1949) * * * defines 'medicinal opium' as opium powder reduced to a content of 9.2 to 10.2 per cent of anhydrous morphine by the addition of lactose. This pharmacopœa calls 'medicinal opium' also 'powdered opium.' '' Commentary at 22 n.8. The Commentary then notes that ''[t]he term 'medicinal opium' ha[d] been abandoned in'' in favor of the terms ''powdered opium'' and ''standardized powered opium'' in several pharmacopœas which had been published in the late 1960s. *Id.* (citing *British Pharmacopœa* 686 (1968), and *Pharmacopœa Internationalis* 403 (2d ed. 1967)). Of further note, the term is not used at all in more recent pharmacopœas.[58] *See, e.g., The United States Pharmacopeia 2008,* at 2860–61 (31st Rev. 2007); *British Pharmacopoeia 2008,* at 1599–1601 (2007).

Thus, the term ''medicinal opium'' is now obsolete. The term's obsolescence itself provides ample reason to disregard it in determining the scope of the United States' obligations with respect to marijuana. But even if the term is still relevant, Respondent ignores that the term referred to a product which had not only been extracted from the opium poppy but had also undergone several further processes (including the addition of another substance, lactose) to prepare it for use in other drugs and to obtain a specific and *standardized* content of morphine, its primary active ingredient. *See British Pharmacopoeia 2008,* at 1599 (''Raw opium is intended only as a starting material for the manufacture of galenical preparations. It is not dispensed as such.''); GX 53, at 3 (letter of GW Pharmaceuticals) (''[O]pium is a Schedule II substance, but it merely provides the starting material for a number of pharmaceutical dosage forms that are lawfully marketed in the U.S. Herbal opium is not itself used directly by patients.'').

Indeed, the inclusion of ''medicinal opium'' in the various older Pharmacopœas indicates that there were recognized standards for the substance's manufacture and composition and that the drug had an accepted medical use in humans. *See, e.g., The United States Pharmacopeia* (17th Rev. ed. 1965), at xxv (noting that federal law ''designate[s] the Pharmacopeia as establishing the standards of strength, quality, and purity of medicinal products recognized therein when sold in interstate commerce for medicinal use''); [59] *see also The United States Pharmacopeia 2008,* at v (''*USP 31* * * * contains science-based standards for drugs, biologics, dietary, and excipients used in dosage forms and products. With few exceptions, all articles for which monographs are provided in *USP 31* * * * are legally marketed in the United States or are contained in legally marketed articles.''); *British Pharmacopoeia 2008,* at 4 (''The requirements stated in the monographs of the Pharmacopoeia apply to articles that are intended for medicinal use. * * * An article intended for medicinal use that is described by means of an official title must comply with the requirements of the relevant monograph.'').

In contrast, there are no recognized standards with respect to herbal marijuana. And consistent with the recognition in almost every country that marijuana has no accepted medical use, neither marijuana, cannabis, nor THC is listed in the various pharmacopeias. *See The United States Pharmacopeia 2008,* at 1620, 2588–2589, 3366–3367; *British Pharmacopoeia 2008,* at 375–376, 1373–1374, 2111–2112; *European Pharmacopoeia,* at 777, 1495, 1997. *Cf. James Everard's Breweries* v. *Day,* 265 U.S. 545, 562 (1924) (rejecting contention that Congress arbitrarily determined that ''intoxicating malt liquors possessed no substantial and essential medicinal properties''; ''Neither beer nor any other intoxicating malt liquor is listed as a medicinal remedy in the United States Pharmacopeia. They are not generally recognized as medicinal agents. There is no consensus of opinion among physicians and medical authorities that they have any substantial value as medical agents. * * * '').

Moreover, it is beyond question that, in the United States, marijuana has no currently accepted medical use and there are no FDA-approved medical products consisting of marijuana. *See OCBC,* 532 U.S. at 491 (''for purposes of the [CSA], marijuana has 'no currently accepted medical use' at all.''); 66 FR at 20052 (as stated by the FDA, ''[t]here are no FDA-approved marijuana products.''). Thus, by any plausible application of the term ''medicinal opium'' to cannabis, as a factual matter, there is currently no such thing in the United States as ''medicinal cannabis.'' Respondent effectively concedes this point, by describing the purpose of his proposed registration as being ''to *develop* the marijuana plant into an

[57] This statement was made in an INCB press release issued on February 8, 2008, which is available at *http://www.unis.unisvienna.org/unis/pressrles/2008/usinar1023.html,* and of which I take official notice.

[58] There is also no listing of any opium-containing product in the latest edition (2008) of FDA's ''Orange Book,'' which lists each drug product currently approved for marketing under the FDCA based on a determination by the FDA that the drug is safe and effective. *See http://www.fda.gov/cder/orange/obannual.pdf.*

[59] *See also European Pharmacopoeia* 1, § 1.1 (4th ed. 2001) (General Statements) (''The active ingredients (medicinal substances), excipients (auxiliary substances), pharmaceutical preparations and other articles described in monographs are intended for human consumption and veterinary use (unless explicitly restricted to one of these uses)'').

FDA-approved prescription medicine.'' GX 3, at 1 (emphasis added).

Finally, even if all the foregoing considerations were ignored and DEA were to treat the marijuana that Respondent seeks to grow as akin to ''medicinal opium'' for purposes of the Single Convention, Respondent's proposed activity would still be inconsistent with the Convention for the following reason. As the Commentary explains: ''Opium-producing countries may thus authorize private manufacture of, and private international and domestic wholesale trade in, medicinal opium and opium preparations. *The opium other than medicinal opium needed for such manufacture must however be procured from the national opium agency.*'' Commentary at 284 (emphasis added). Thus, under the Convention, even if ''medicinal cannabis'' may be privately traded, the treaty requires that the raw material needed to produce the ''medicinal cannabis'' (i.e., the marijuana plant material) must be obtained from the national cannabis agency. This again reflects the central theme of cannabis control under the Single Convention—that the national agency must control the production and distribution of the raw marijuana material used for research or any other permissible purpose. Respondent's unwillingness to accept this principle illustrates how his proposed registration is fundamentally at odds with the treaty.

The ALJ also reasoned that the marijuana Respondent seeks to grow would qualify under the Convention as ''special stocks'' and thereby be exempt from the ''exclusive government's right to maintain stocks.'' ALJ at 82. Even Respondent acknowledges the ALJ's error on this point. *See* Respondent's Resp. at 12 (''[I]t is evident that [the ALJ] simply inadvertently referenced the wrong term from Article 1.''). The term ''special stocks'' under the Convention refers to ''drugs held in a country or territory by the Government of such country or territory for special government purposes and to meet exceptional circumstances.'' Single Convention, Art. 1, para. 1(w). Neither party is suggesting, and there is no basis to conclude, that the marijuana Respondent seeks to produce fits into this definition.[60]

While recognizing that the ALJ misread the term ''special stocks,'' Respondent argues that the marijuana he seeks to produce nonetheless qualifies as retail ''stocks,'' because it is marijuana that will be held '' 'by institutions or qualified persons in the duly authorized exercise of therapeutic or scientific functions.' '' *Id.* (quoting Single Convention, art. 1, para. 1(x)). Respondent thus contends that the marijuana he seeks to produce is exempt from the government monopoly provisions of article 23, paragraph 2, subparagraph (e).

Respondent is mistaken. The entire text of the relevant provision explains that the marijuana Respondent would maintain does not fall within the exception to the definition of ''stocks.'' What is excluded under the treaty from the definition of ''stocks'' are those drugs held ''[b]y retail pharmacists or other authorized retail distributors and by institutions or qualified persons in the duly authorized exercise of therapeutic or scientific functions.'' Single Convention, art. 1, para. 1(x)(iv). As this provision makes plain, the exemption applies only to the drugs held by those persons or entities who are authorized to dispense to ultimate users.

Respondent is not, however, a licensed pharmacist or physician and obviously cannot legally seek a practitioner's registration, which is required to dispense. *See* 21 U.S.C. 823(f). Rather, he is seeking to produce raw cannabis plant material to supply researchers. His proposed activity thus does not fall within the exemption for ''qualified persons in the duly authorized exercise of therapeutic or scientific functions'' within the meaning of the Single Convention.

Moreover, even with respect to cannabis material acquired for retail purposes that does fit within the exception of article 1, paragraph (x)(iv), the treaty still requires that such material be obtained via the national agency. As the Commentary explains with respect to opium (and therefore also with respect to cannabis, by virtue of article 28), while ''[t]he retail trade in, and other retail distribution of, opium * * * need not be in the hands of the monopoly[,] [r]etail traders or distributors must, however, acquire their opium from the'' Government. Commentary at 284. Respondent's arguments repeatedly fail to acknowledge or accept this concept that lies at the core of the Single Convention. Yet, there is no escaping that, by seeking through his application to dismantle the existing Government control over the distribution of cannabis produced by growers and turn a share of that control over to MAPS, Respondent's goal is antithetical to the treaty. For the foregoing reasons, the provision of article 1, paragraph (x)(iv) exempting certain material from the definition of ''stocks'' does not support Respondent.

As for Respondent's point that DEA has previously allowed the University of Mississippi to grow marijuana to produce ''marijuana extracts that the University then sells to pharmaceutical companies to develop products'' (Resp. Prop. Findings at 68), it is true that DEA has previously allowed such activity under a Memorandum of Agreement (MOA) that was entered into in 1999. GX 78. However, that MOA expressly states:

> In accordance with articles 23 and 28 of the Single Convention on Narcotic Drugs, 1961 (''Single Convention''), private trade in ''cannabis'' is strictly prohibited. Therefore, the Center shall not distribute any quantity of marijuana to any person other than an authorized DEA employee.
>
> The Single Convention does not prohibit private trade in ''cannabis preparations,'' however. A ''cannabis preparation,'' within the meaning of the Single Convention, is a mixture, solid or liquid containing cannabis, cannabis resin, or extracts or tinctures of cannabis. The THC that the Center will extract from marijuana would be considered such a ''cannabis preparation.'' Therefore, the Center may, in accordance with the Single Convention, distribute the crude THC extract to private entities (provided such distributions of THC by the Center comply with all requirements set forth in the CSA and DEA regulations).

Id. at 2–3 (footnote explaining treaty definition of cannabis omitted). Thus, the MOA was specifically designed to ensure that the University of Mississippi would not be distributing cannabis outside of the Government-controlled system required by the Single Convention. *See* Single Convention, art. 23, para. 1(e) (exempting ''preparations'' from government monopoly on wholesale distribution). In contrast, Respondent does *not* seek to distribute a cannabis extract or any other processed cannabis material that constitutes a ''preparation'' within the meaning of the Single Convention. Instead, Respondent seeks to grow and distribute marijuana plant material that has undergone no processing other than drying (and therefore does not come within the Single Convention definition of ''preparation'').[61]

[60] The term ''special stocks'' is operative in the Single Convention only in ways that have no bearing on this adjudication. *See* art. 19, paras. 1(d) & 2(d) (requiring parties to furnish the INCB with annual estimates of, among other things, ''[q]uantities of drugs necessary for addition to special stocks'' and amounts taken therefrom); art. 20, para. 3 (parties' statistical returns to INCB need not address those relating to special stocks); art. 21, para. 2 (explaining how to take into account special stocks for purposes of countries' limitations on manufacture and importation).

[61] The above-quoted 1999 MOA was issued with respect to the University of Mississippi's 1998

Continued

As the foregoing demonstrates, while the Single Convention does not necessarily prohibit the registration of an additional manufacturer, what it does prohibit is the wholesale distribution of plant-form marijuana by any entity other than the United States Government. Respondent is not under contract with HHS to supply it with marijuana and has made clear that the purpose of his registration is to distribute marijuana outside of the HHS system. Because it is clear that Respondent's proposed activity is not within one of the exemptions from the obligatory government monopoly imposed by the Convention, he has failed to show that his proposed activities would be consistent with the Single Convention.[62] *See* 21 U.S.C. 823(a). Accordingly, his proposed registration is precluded under Federal law.

B. Whether Respondent's Proposed Registration Is Consistent With the Public Interest

As explained in the preceding section, Respondent's registration is clearly inconsistent with the United States' obligations under the Single Convention. While this ground alone compels DEA to deny the application, as explained below, an analysis of the public interest criteria of 21 U.S.C. 823(a) leads to the conclusion that Respondent's registration is inconsistent with the public interest. This provides a separate basis—independent of the treaty consideration—on which the application must be denied.

As stated above, under § 823(a), there are six factors that must be evaluated in determining whether a proposed registration is consistent with the public interest. The public interest factors ''are considered in the disjunctive.'' *Southwood Pharmaceuticals, Inc.,* 72 FR 36487, 36497 (2007). I may rely on any one or a combination of factors and give each factor the weight I deem appropriate in determining whether to deny an application for a registration. *See Green Acre Farms, Inc.,* 72 FR 24607, 24608 (2007); *ALRA Laboratories, Inc.,* 59 FR 50620, 50621 (1994). Moreover, I am ''not required to make findings as to all of the factors.'' *Hoxie* v. *DEA,* 419 F.3d 477, 482 (6th Cir. 2005); *Morall* v. *DEA,* 412 F.3d 165, 173–74 (D.C. Cir. 2005).

1. Public Interest Factor One

The first public interest factor is the:

maintenance of effective controls against diversion of particular controlled substances and any controlled substance in schedule I or II compounded therefrom into other than legitimate medical, scientific, research, or industrial channels, *by limiting the importation and bulk manufacture of such controlled substances to a number of establishments which can produce an adequate an uninterrupted supply of these substances under adequately competitive conditions for legitimate medical, scientific, research, and industrial purposes.*

21 U.S.C. 823(a)(1) (emphasis added).

As the ALJ observed, DEA has construed paragraph 823(a)(1) in two different ways in prior final orders, both of which were simultaneously upheld in a case that was reviewed by a United States Court of Appeals. ALJ at 82–83. Because of this, I have undertaken an extensive analysis of this provision, which is found in part C of this discussion.[63] For the reasons explained therein, I believe that the most sound reading of the text of paragraph 823(a)(1) requires DEA to consider limiting the number of bulk manufacturers and importers of a given schedule I or II controlled substance to that which can produce an adequate and uninterrupted supply under adequately competitive conditions. The Government so asserted in the Show Cause Order and throughout the proceedings. Although Respondent offered a different interpretation of paragraph 823(a)(1),[64] he asserted that, under any interpretation, this factor weighed in favor of finding the proposed registration consistent with the public interest.[65]

As discussed at length in part C of this discussion, *infra,* to properly construe paragraph 823(a)(1), it must be viewed in comparison with § 823(d)(1). Whereas § 823(d)(1) contains no requirement that DEA consider limiting in any way the total number of registered manufacturers of controlled substances in schedules III, IV, and V, paragraph 823(a)(1) does require DEA to consider limiting the total number of bulk manufacturers of schedule I and II controlled substances. Specifically, paragraph 823(a)(1) calls upon DEA to consider ''limiting'' (i.e., placing an *upper boundary* on) the number of registered bulk manufacturers of a given schedule I or II controlled substance to that ''which can produce an adequate

application to become registered to manufacture marijuana for the purposes of product development. GX 78, at 1–2. In 2005, the University of Mississippi applied for a new registration to manufacture marijuana ''to prepare marihuana extract for further purification into bulk active [THC] for use in launching FDA-approved pharmaceutical products.'' 70 FR 47232; *see also* Tr. 1521. DEA has not yet issued a final order as to this application and the University therefore does not currently have DEA authorization to undertake such activity. As with Respondent's application, DEA may only grant the pending University of Mississippi application if the agency determines that the University has demonstrated that the registration would be consistent with United States treaty obligations and the public interest. *See* GX 79, at 3. In making such determinations, DEA will not simply rely on the prior issuance of registration under the 1999 MOA but will consider the application anew, in view of the current circumstances and consistent with this final order. Among other things that must be considered with respect to the pending University of Mississippi application, I note that the Commentary to the Single Convention states the following with respect to the exemption for ''opium preparations'' under Article 23, paragraph (e): ''Opium-producing countries may thus authorize private manufacture of, and private international and domestic wholesale trade in, medicinal opium and opium preparations. *The opium other than medicinal opium needed for such manufacture must however be procured from the national opium agency.*'' Commentary at 284 (emphasis added). Whether the University of Mississippi's proposed registration would be consistent with this aspect of the treaty has not yet been determined by DEA and is not the subject of this adjudication.

[62] Though the above discussion provides ample basis on which to conclude that Respondent has failed to meet his burden of proving that his proposed registration is consistent with United States obligations under the Single Convention, I also note briefly the following statement in the Commentary regarding the obligation of the United States under article 23, paragraph 2(a) to designate the areas in which cultivation takes place: ''It is also suggested that [such areas] should to the greatest extent possible be located in the same part of the country, and be contiguous, in order to facilitate more effective control.'' Commentary at 280. Thus, in a situation in which a country that is a party to the treaty allows for multiple growers of opium or cannabis with the national agency maintaining control over the distribution of such material in accordance with the Single Convention, the Commentary suggests that proper adherence to the treaty would result in that country keeping the growers located as near as possible to one another.

[63] For ease of exposition, the detailed analysis of the meaning of paragraph 823(a)(1) appears in a separate section of this discussion (part C), due to its length.

[64] *See* note 65, *infra,* regarding Respondent's proposed interpretation of paragraph 823(a)(1).

[65] Because I have concluded, for the reasons set forth in part C of the discussion, that DEA is obligated under the text of paragraph 823(a)(1) to consider limiting the number of bulk manufacturers and importers of a given schedule I or II controlled substance to that which can produce an adequate and uninterrupted supply under adequately competitive conditions, I reject Respondent's alternative reading of paragraph 823(a)(1). Specifically, I reject the interpretation of paragraph 823(a)(1) under which ''the registration should be granted without regard to'' adequacy of competition and supply so long as the ''registration would not interfere with DEA's maintenance of effective diversion controls.'' *See* Respondent's Resp. at 13. Respondent cites *Noramco* v. *DEA,* 375 F.3d 1148 (D.C. Cir. 2004) in support of this interpretation. *Id.*; Resp. Proposed Findings and Conclusion of Law at 36. The *Noramco* decision is examined at length in part C of this discussion. Because I interpret paragraph 823(a)(1) to require consideration of the adequacy of supply and competition, I decline to undertake an analysis of the facts of this case whereby the adequacy of competition and supply is disregarded. However, as indicated above, Respondent has alternatively argued that there is a sufficient basis to grant his application when construing paragraph 823(a)(1) as requiring a showing of inadequate competition or supply, and that argument is addressed at length in this final order.

and uninterrupted supply of these substances under adequately competitive conditions for legitimate medical, scientific, research, and industrial purposes.''

Thus, an applicant seeking to become registered to bulk manufacture a schedule I or II controlled substance bears the burden of demonstrating that the existing registered bulk manufacturers of a given schedule I or II controlled substance are unable to produce an adequate and uninterrupted supply of that substance under adequately competitive conditions. As a threshold matter, Respondent misconstrues this provision as placing the burden on *DEA,* whenever someone applies for registration under 21 U.S.C. 823(a), to demonstrate that competition is already adequate within the meaning of paragraph 823(a)(1). *See* Resp. Proposed Findings and Conclusion of Law at 47 (in which Respondent contends that the ''requirement'' of ''adequately competitive conditions'' ''is not met by the by the current NIDA monopoly''). In fact, the DEA regulations plainly state that every applicant seeking registration under § 823(a) has ''the burden of proving that the requirements for such registration pursuant to [this section] are satisfied.'' 21 CFR 1301.44(a).

Accordingly, the analysis under paragraph 823(a)(1) (and Respondent's burdens thereunder) must be divided into the following parts: (a) an analysis of the adequacy of supply and (b) an analysis of the adequacy of competition. If Respondent can demonstrate by a preponderance of the evidence that either supply or competition is inadequate within the meaning paragraph 823(a)(1), this weighs heavily in favor of granting the registration. If, however, Respondent fails to meet his burden with respect to both supply and competition, this weighs heavily against granting the registration. (See part C of this discussion.)

(a) Adequacy of Supply Within the Meaning of Paragraph 823(a)(1)

The first question under paragraph 823(a)(1) is whether Respondent has demonstrated that the existing supply of marijuana is inadequate to meet the legitimate needs of the United States. As the parties essentially agree, the adequacy of supply of marijuana must be evaluated in two respects: (i) quantity and (ii) quality.

(i) Adequacy of the Quantity of the Existing Supply

With respect to the adequacy of the *quantity* of supply, the record establishes that as of the date of the hearing, there were approximately 1055 kg of marijuana of various potencies in the NIDA vault. RX 53. Moreover, some of this marijuana apparently had been harvested as early as 1997, and it appears that as of the date of the hearing, no marijuana had been grown since 2001. *Id.* For the following reasons, this amount of existing supply far exceeds any present demand for research-grade marijuana as well as any reasonably anticipated demand for such marijuana in the foreseeable future.

Lawful research involving marijuana can be divided into two categories: NIH-funded and privately funded. *See* GX 31, at 3. With respect to NIH-funded research, Respondent does not contend, and there is no basis in the record to conclude, that NIDA has failed to provide, or is incapable of providing, an adequate quantity of marijuana. Rather, to the extent Respondent is claiming that NIDA is unable to provide an adequate quantity of marijuana,[66] this claim relates to privately funded researchers. Yet, even as to this claim, the evidence indicates otherwise.

The record reflects that since HHS changed its policies in 1999 to make marijuana more readily available to researchers (by, among other things, allowing privately funded researchers to obtain marijuana), every one of the 17 CMCR-sponsored pre-clinical or clinical studies that requested marijuana from NIDA was provided with marijuana. GX 31, at 3; Tr. 694–95. Significantly, according to one of the witnesses who testified on behalf of Respondent, CMCR funding of research involving marijuana has currently ended and it appears doubtful that a resumption of such funding is ''on the horizon.'' Tr. at 397–402, 441. Thus, the witness testified, once the research projects sponsored by CMCR that utilize NIDA marijuana reach their conclusion, ''[i]t's likely that the [CMCR] research is done.'' *Id.* at 401–02. Other than the CMCR-sponsored research, the record reveals only one other instance in which a privately funded researcher sought marijuana from NIDA after HHS changed its policies in 1999 to make marijuana more readily available to researchers. That one other instance was the MAPS-sponsored request submitted by Chemic to obtain marijuana to conduct research on the Volcano. *See* RX 52B. According to Mr. Doblin, Chemic ''applied to NIDA to purchase ten grams'' of marijuana. Tr. 531; RX 14. Although, as discussed above, HHS denied that request on scientific grounds (*see* RX 52B), there is no basis to conclude that NIDA was incapable of providing Chemic with the quantity of marijuana it was seeking. Indeed, the ten grams of marijuana that Chemic requested is less then one 100,000th of the amount of marijuana that NIDA has available to supply researchers. *See* RX 53.

Accordingly, the evidence overwhelmingly establishes that NIDA is capable of providing an adequate quantity of marijuana to meet all current and foreseeable research needs of the United States. And while NIDA's existing system for supplying marijuana is quantitatively adequate regardless of how much or how little additional marijuana Respondent seeks to produce, it is notable that the approximately 1055 kg of marijuana currently on hand is more than 90 times the amount of marijuana that Respondent proposes to grow.

Respondent nonetheless contends that the process by which HHS provides marijuana to researchers—which involves a peer review of the scientific merits of the research proposal[67]—results in a barrier to research that effectively renders the supply of marijuana inadequate. Respondent points to three prior incidents to support his contention that the HHS scientific review process impedes research. As discussed above, the first two of these incidents (those involving Dr. Abrams and Dr. Russo) are irrelevant as they occurred before HHS adopted its new procedures in 1999 for making marijuana more widely available to researchers.[68] The third incident involved the application of Chemic to obtain marijuana to conduct research on the Volcano. As discussed above, HHS

[66] Respondent appears to challenge the process by which NIDA supplies marijuana to researchers and the quality of the marijuana, rather than the quantity. *See, e.g.*, Respondent's Resp. at 15–16. The ALJ's recommendation regarding the adequacy of supply also focused on the process by which NIDA supplies marijuana, and she was not of the opinion actual quantity of marijuana supplied by NIDA was inadequate. *See* ALJ at 84. Nonetheless, for the sake of completeness, and in accordance with 21 U.S.C. 823(a)(1), I am addressing the adequacy of supply from a quantitative perspective.

[67] Tr. at 1626–28, 1635. In his testimony, Dr. Gust explained the term ''peer review'' as follows: ''Peer review is a process that has been used, certainly by NIH, and I think in other agencies in the Department of Health and Human Services, and probably the Federal Government, where outside expertise is acquired and outside opinions on the scientific merit of specific research proposals.'' *Id.* at 1627. Dr. Gust added that the NIH peer review committees ''review proposals three times a year for the NIH, and there are—occasionally a Federal employee participates in one of those reviews, but probably 90 percent or more of the participants are researchers who are in the private sector, for the most part in academic institutions.'' *Id.* at 1627–28.

[68] Further, as discussed above, the evidence indicates that the denials involving of Dr. Abrams and Dr. Russo were based on HHS finding their protocols to be lacking in scientific merit.

declined to supply Chemic with marijuana in 2005 based on scientific considerations, finding that Chemic's then-latest proposed study was duplicative of prior and ongoing research and not likely to provide useful data. Thus, the success of Respondent's claim that the HHS scientific review process renders the existing supply of marijuana inadequate depends on whether one accepts Respondent's assumption that anyone in the United States who has a proposed research project involving marijuana should be entitled to obtain marijuana—regardless of whether the competent Government authority finds the research to be lacking in scientific merit.[69]

Respondent's assumption about who is entitled to conduct research with marijuana is directly undercut by the text of the CSA. As set forth in 21 U.S.C. 823(f), persons seeking to conduct research with schedule I controlled substances (such as marijuana) may only obtain a DEA registration ''for the purpose of *bona fide* research'' (emphasis added), with the Secretary of HHS being responsible for determining ''the qualifications and competency'' of the applicant ''as well as the merits of the research protocol.'' The process HHS has established to assess the scientific merit of proposed research studies involving marijuana is that described in the 1999 HHS announcement of its new procedures.[70] GXs 24 & 31; Tr. at 1626–35. That Respondent finds this process to be scientifically rigorous[71]—and thereby not automatically accepting of any proposed study sponsored by MAPS—provides no basis for any valid objection or any contention that the HHS supply of marijuana is inadequate.[72]

(ii) Adequacy of the Quality of the Existing Supply

As for Respondent's contention that the *quality* of marijuana supplied by NIDA is unsatisfactory and that this renders the supply of marijuana inadequate within the meaning of 21 U.S.C. 823(a)(1), the ALJ rejected this contention, finding that a preponderance of the evidence established that ''the quality is generally adequate.'' ALJ at 84. In this regard, Respondent contended that NIDA's marijuana was of inconsistent potency, that it was of too low a potency, that it included stems and seeds, that it was not fresh, and that some of the patients had complained that it ''was the worst marijuana they had ever sampled.'' Resp. Proposed Findings at 16–27 & 49.

As found above, Respondent's contentions rest largely on snippets taken from questionnaires which were completed by a number of researchers. On balance, however, the researchers indicated their overall satisfaction with NIDA's marijuana and noted that the agency had been accommodating and responsive to their concerns. *See, e.g.*, GX 16, at 6 & 19. Moreover, most of the researchers indicated that the potency of NIDA's product was adequate and had not compromised their research. *See, e.g.*, GX 16, at 6 & 15; GX 17, at 9. Furthermore, while Respondent notes that several researchers stated that it would be beneficial to evaluate a higher potency product, he produced no evidence that any researcher had obtained approval from FDA and other reviewing authorities to conduct clinic trials with such a product. *See* GX 21, at 9 (researcher explaining that he ''wanted to use a higher potency product but there were questions from the [scientific review board] and the'' CMCR). In any event, the evidence establishes that NIDA's stock includes substantial quantities of high THC content marijuana and that its contractor is capable of producing marijuana with a THC content of up to twenty percent.[73] Tr. 1203–05.

Related to this argument, Respondent also contends that NIDA's marijuana has stems and seeds and that some patients complained that ''that the marijuana is inferior in sensory qualities (taste, harshness) than the marijuana they smoke outside the laboratory. Some have stated it was the worst marijuana they had ever sampled.'' Resp. Proposed Findings at 20 (other citation omitted); *see also id.* at 49. The evidence establishes, however, that the contractor has rectified the problem with respect to the stems and seeds. Tr. 1301.

As for the complaints regarding the sensory qualities of NIDA's products, only a small percentage of the numerous studies' subjects complained about the harshness of NIDA's marijuana, and as one researcher explained, it is not clear whether it was placebo or actual marijuana that was the cause of the complaints. GX 18, at 7. Relatedly, it seems a strained argument for Respondent to make that experienced

[69] It is not even clear whether Respondent continues to cite the Chemic situation of an example of supposedly ''legitimate research'' for which HHS declined to provide marijuana. While Respondent did so characterize the Chemic situation in his proposed findings of fact and conclusions of law (at 14), in his subsequently filed response to the Government's exceptions to the ALJ recommendation, he listed only Dr. Abrams and Dr. Russo as examples of ''legitimate research'' for which marijuana was not supplied. Respondent's Resp. at 16. As noted, the incidents involving Dr. Abrams and Dr. Russo occurred prior to HHS's promulgation of the 1999 guidelines. As such, these incidents are not probative of the current availability of research-grade marijuana from HHS.

[70] Respondent points out that the Secretary of HHS has delegated to the FDA Commissioner the Secretary's functions under 21 U.S.C. 823(f) relating to research with controlled substances in schedule I. Respondent's Resp. at 4–5 (citing FDA Staff Manual Guides 1410.10). While this is correct as a general matter for schedule I controlled substances, the record plainly indicates that with specific regard to research involving marijuana, HHS has retained its authority to determine the qualifications and competency of the researcher, as well as the merits of the research protocol, for purposes of § 823(f). *See* GX 24. Indeed, the 1999 HHS announcement of its policies for providing marijuana to researchers expressly states: ''To receive such a registration [under § 823(f)], a researcher must first be determined *by HHS* to be qualified and competent, and the proposed research must be determined *by HHS* to have merit.'' *Id.* at 1 (emphasis added). Dr. Gust's testimony confirms that, in fact, HHS—through its peer review process—does make these determinations for persons seeking to conduct research with marijuana. Tr. 1626–35.

Moreover, as discussed above, Respondent produced no evidence showing that HHS has denied marijuana to any clinical researcher with an FDA-approved protocol subsequent to the adoption of the 1999 guidelines. The lone applicant whose post-1999 request for marijuana was denied (Chemic) submitted its request to, and had it reviewed by HHS—not FDA. *See* GXs 49 & 52B. For all these reasons, it is unfounded for Respondent to suggest that the supply of marijuana is somehow inadequate because HHS has not assigned FDA sole responsibility for determining what research proposals involving marijuana are scientifically meritorious.

[71] Any suggestion that the HHS scientific review process is unduly rigorous is belied by the testimony of Dr. Gust that the ''scientific bar has been set very low, [so] that any project that has scientific merit is approved,'' and that ''anything that gets approved gets NIDA marijuana'' (Tr. at 1700–01) as well as the uncontroverted evidence that every one of the 17 CMCR-sponsored research protocols submitted to HHS was deemed scientifically meritorious by HHS and was supplied with marijuana (GX 31, at 3; Tr. 694–95).

[72] For the same reasons, I find wholly unpersuasive the ALJ's recommended finding that the supply of marijuana is inadequate because of the HHS scientific review process.

[73] Despite Respondent's suggestion that human research subjects should be given marijuana of higher potencies than that supplied by NIDA (*see, e.g.*, Tr. 552, 567 (testimony of Mr. Doblin)), there is no basis in the record to conclude that it would be medically or scientifically appropriate to do so. To the contrary, Dr. ElSohly testified that he was told by CMCR researchers that they did *not* want Dr. ElSohly to supply them with marijuana with a THC content as high as eight percent because, based on their prior observations of research subjects being given NIDA marijuana containing eight percent THC, ''the subject couldn't tolerate that, and if we can make a six percent, that would be more appropriate.'' Tr. 1280. Dr. ElSohly also testified that other scientists expressed the same opinion that six percent THC content was preferable because the research subjects ''would not tolerate'' marijuana with eight percent THC. Tr. 1295. Large doses of marijuana (in terms of the amount of THC administered) have been found to cause adverse mood reactions, including anxiety, paranoia, panic, depression, dysphoria, depersonalization, delusions, illusions, and hallucinations. RX 1, at 102. A primary reason that researchers are required to submit an IND to FDA prior to engaging in research with human subjects is ''to assure the safety and rights of subjects.'' 21 CFR 312.22(a).

marijuana smokers reported, after consuming a hallucinogenic substance, that they found NIDA's marijuana to be less pleasing to their senses than the marijuana they had illegally obtained and used. People generally take medicines—which marijuana is not—for their therapeutic benefits and not their taste. And in any event, Respondent has not established that NIDA's products were unsuitable for their intended use.[74]

For these reasons, I accept the ALJ's recommended finding that Respondent did not meet his burden of demonstrating that NIDA is incapable of providing marijuana of sufficient quality to meet the legitimate research needs of the United States.

Thus, I conclude that the evidence does not support Respondent's contention that the supply of marijuana is inadequate—in terms of quantity or quality—within the meaning of paragraph 823(a)(1).

(b) Adequacy of Competition Within the Meaning of Paragraph 823(a)(1)

The second question under paragraph 823(a)(1) is whether Respondent has demonstrated that the existing supply of marijuana is not being produced under adequately competitive conditions to meet the legitimate needs of the United States. Again, as explained below in part C of this discussion, paragraph 823(a)(1) does *not* require DEA simply to register as many bulk manufacturers of a given schedule I or II controlled substance as the market will bear. Nor does paragraph 823(a)(1) require the registration of an additional bulk manufacturer based merely on the assertion the additional registration will result in some vague, theoretical incremental increase in competition. If such a theoretical assertion would suffice, then the language of paragraph 823(a)(1) requiring DEA to consider ''limiting'' the number of registered bulk manufacturers would be rendered meaningless. This is because every person seeking to enter the market as a new bulk manufacturer of a given schedule I or II controlled substance could make the theoretical claim that every new registrant increases the overall amount of competition.

Thus, to avoid reading the limiting language of paragraph 823(a)(1) in a superfluous manner, in final orders where DEA has analyzed competition under paragraph 823(a)(1), DEA has looked to empirical data; specifically, DEA has focused on the historical and present prices charged to those who lawfully acquire the controlled substance from the existing registered bulk manufacturers.[75] This approach is consistent with the following statement made by the Department of Justice stated during Congressional hearings leading up to the enactment of the CSA:

> There is no reason to assume that the Attorney General will prejudice his primary objectives of effective control by excessive licensing. Nor will he undertake direct price control. He will be empowered to take cognizance of evidence showing that prices are clearly and persistently excessive. The criteria for determining whether prices far exceed that which is reasonable relate to reasonable costs and reasonable profits. * * * If evidence indicates that additional licensing will result in more reasonable prices with no significant diminution in the effectiveness of drug control, the Attorney General should be able to license the additional manufacturers.[76]

Here, the evidence demonstrates that NIDA has always provided marijuana to researchers at cost or for free—and at no profit to NIDA. Privately funded researchers receive marijuana at NIDA's cost[77] and HHS-funded researchers (who have historically comprised the bulk of the marijuana recipients) receive the marijuana at no cost. GX 24, at 2; GX 31, at 3; Tr. 1212, 1633, 1670–71. Thus, there is no basis to suggest that the cost to any researcher under the existing supply arrangement is unreasonable. Respondent himself does not so contend; nor does he claim that the cost to any researcher of obtaining marijuana would be lower if Respondent became registered to grow marijuana. Respondent hypothesizes that ''if another manufacturer could produce suitable medical marijuana for a lower cost, competitive conditions would, as they usually do, benefit the researcher-consumer.'' Resp. Prop. Findings at 48. However, Respondent provides no evidentiary basis for the proposition that he (or anyone else) could produce marijuana at a lower cost than NIDA. Moreover, Mr. Doblin acknowledged that MAPS would have a ''profit-making'' motivation as part of its ''operation'' to supply marijuana for the purposes of drug development, and that this would impact ''costs.'' Tr. 605–606. In contrast, there is no evidence that HHS or NIDA is driven in any respect by a profit motive in deciding to whom and at what cost to supply marijuana. Even accepting, *arguendo*, Mr. Doblin's testimony that ''we [MAPS] would either provide [marijuana] free or at cost through donations to MAPS to other researchers who are not doing MAPS funded projects'' (Tr. at 589), this would still not demonstrate a lowering of the cost to researchers. This is because, if MAPS were so willing to fund all researchers, they could do so under the existing system by paying NIDA on a cost-reimbursable basis for the marijuana, allowing the researchers to obtain the marijuana at no cost to the researchers. Thus, Respondent has not demonstrated that competition is inadequate in the way that other applicants for registration under § 823(a) have successfully done in prior final orders; i.e., by focusing on prices charged by the existing registrants that supply the market for the schedule I or II controlled substance in question and showing those prices to be unreasonable.[78]

Respondent also claims that the process by which the NIDA contract is awarded is not adequately competitive because the contract requires not only that the contractor manufacture marijuana, but also that it analyze marijuana samples sent in by law enforcement agencies. *Id.* at 48. Respondent further contends that the NIDA process ''does not ensure that researchers pay a competitive price [because] NIDA sets the price and there is no evidence as to how that price is set.'' *Id.* Finally, Respondent rehashes his argument regarding the quality of NIDA's marijuana contending that granting his application would promote competition and improvement in the quality of research marijuana. *Id.* at 49.

The ALJ agreed with Respondent and rejected the Government's contention that the NIDA process provides for adequate competition because demand for research grade marijuana is limited, the contract is periodically put up for

[74] Moreover, Respondent presented no evidence to show that he is capable of producing marijuana with any degree of quality control—let alone the type of evidence that would allow an inference that he could improve upon the quality of marijuana produced at the University of Mississippi. To the contrary, as explained below in the discussion of public interest factor five, Respondent's lack of experience in growing marijuana is in stark contrast to Dr. ElSohly's decades of experience in manufacturing, analyzing, and publishing scientific articles on the subject.

[75] See *Penick Corporation Inc.*, 68 FR 6947 (2003); *Roxane Laboratories, Inc.*, 63 FR 55891 (1998).

[76] *Hearings Before the Subcomm. to Investigate Juvenile Delinquency of the Comm. on the Judiciary, United States Senate,* 91st Cong. 372 (1969) (discussed more fully in part C of this discussion).

[77] According to Dr. ElSohly, where marijuana is supplied to privately funded researchers, ''the researchers would just pay the production costs.'' RX 5, at 2.

[78] *See Penick Corporation, supra; Roxane Laboratories, supra* (both of which are examined in part C of this discussion). As one DEA scientist testified in this proceeding, based on his experience, when the agency has historically considered the adequacy of competition within the meaning of paragraph 823(a)(1), the analyses ''all seem to be geared around the economics.'' Tr. at 945.

competitive bidding, and the Convention requires that the Government maintain a monopoly on the wholesale distribution of the substance. More specifically, the ALJ reasoned that ''[t]he question is not * * * whether the NIDA process addresses that agency's needs, but whether marijuana is made available to all researchers who have a legitimate need for it in their research.'' ALJ at 85. Based on her finding that NIDA denied marijuana to two researchers, the ALJ ''answer[ed] that question in the negative.'' *Id.*

The ALJ also reasoned that analyzing marijuana samples was ''a separate activity from cultivating marijuana for research purposes and a requirement that a qualified cultivator may not be able to fulfill.'' *Id.* The ALJ thus concluded that ''the NIDA contractual process does not * * * render competition in the manufacture of marijuana adequate.'' *Id.*

I reject both the ALJ's legal conclusions and Respondent's arguments. As for the ALJ's (and Respondent's) reasoning that the NIDA contractual process does not render competition adequate because the contract requires the analyzing of marijuana samples, in executing its authority under § 823(a), DEA does not act as a board of contract appeals. In any event, the contract does not prohibit the contractor from subcontracting this function. *See* GX 15, at 4 (Request for Proposal) (''As this procurement may require expertise in several scientific areas, *offerors are encouraged* to solicit subcontractors or expert consultants as appropriate.'') (emphasis added).[79]

Finally, as for the contention that granting his application would provide for competition and thereby promote improvement in the quality of research-grade marijuana,[80] if Respondent believes that he can produce a higher-quality product than the current contractor, he should bid on the contract.[81] If he prevails, and demonstrates that his project will implement effective controls against diversion, he can establish that his registration would be consistent with the public interest. Respondent, however, has not been awarded a contract to supply NIDA, which, consistent with the Single Convention, is the only lawfully authorized wholesale distributor of plant-form marijuana.

Thus, whether viewing the competition aspect of paragraph 823(a)(1) by considering the reasonableness of prices paid by those who lawfully acquire bulk marijuana for research or by considering the adequacy of the competitiveness of the process by which persons may bid to become the grower of marijuana for NIDA, Respondent has failed to meet his burden. This combined with his failure to meet his burden of demonstrating inadequate supply within the meaning of paragraph 823(a)(1) weighs heavily against granting his application. Nonetheless, Respondent raises a host of arguments under the heading of paragraph 823(a)(1) which—though not actually germane to paragraph 823(a)(1)—are addressed below.

(c) Additional Arguments Raised by Respondent Under the Heading of Paragraph 823(a)(1)

In lieu of presenting evidence to show that competition is inadequate by virtue of unreasonable prices for research-grade marijuana or any other economic data, Respondent argues that competition should be deemed inadequate within the meaning of paragraph 823(a)(1) based on his objection to the to ''government monopoly'' whereby HHS distributes marijuana to researchers. In other words, the very monopoly over the wholesale distribution of marijuana that is mandated by the Single Convention (indeed, the element that is at the heart of the structure of cannabis control under the treaty) is the central basis on which Respondent relies in attempting to meet his burden of demonstrating inadequate competition within the meaning of paragraph 823(a)(1). This argument is flawed in the following respects. As explained above and in part C of this discussion, the competition analysis set forth in paragraph 823(a)(1) must be based on actual economic considerations in the existing market—not policy questions about the wisdom of having the Federal Government control the wholesale distribution of marijuana.

In addition, Respondent's suggestion that paragraph 823(a)(1) can be used to defeat the Single Convention's requirement of a government monopoly over wholesale marijuana distribution mistakenly construes the treaty criterion § 823(a) as being in competition with the public interest criterion. In fact, as explained above, an applicant for registration under § 823(a) must demonstrate that the proposed registration is consistent with *both* the Single Convention and the public interest—and neither criterion is at odds with the other. Both the Single Convention and the United States Code are the ''supreme law of the land,'' U.S. Const. art VI, and in enacting the CSA, Congress made clear that § 823(a) should be interpreted in a manner that is consistent with the United States' obligations under the Convention. The Agency's interpretation of paragraph 823(a)(1) must therefore recognize not only the Convention's specific provisions applicable to marijuana, which expressly prohibit competition in the wholesale distribution of the substance, but also the background principles which underlie both the Convention and the CSA. Accordingly, I reject Respondent's invitation to interpret § 823(a) in a manner that would abrogate the United States' obligation under the Convention to maintain a monopoly in the wholesale trade of marijuana.

While § 823(a) was enacted subsequent to the Convention—indeed it implements the Convention[82]—it is a provision of general applicability and contains no explicit reference to marijuana. Under settled principles of statutory construction, while a later enacted law can sometime repeal an earlier provision, '' '[r]epeals by implication are not favored' and will not be presumed unless the 'intention of the legislature to repeal [is] clear and manifest.' '' *National Ass'n of Home Builders* v. *Defenders of Wildlife,* 127 S.Ct. 2518, 2532 (2007) (quoting *Watt* v. *Alaska*, 451 U.S. 259, 267 (1981)). Accordingly, courts ''will not infer a statutory repeal 'unless the later statute expressly contradict[s] the original act' or unless such a construction is 'absolutely necessary * * * in order that [the] words [of the later statute] shall have any meaning at all.' '' *Id.* (quoting *Traynor* v. *Turnage*, 485 U.S. 535, 548 (1988) (int. quotations and other citations omitted)).

[79] The University of Mississippi subcontracts to another entity, Research Triangle Institute (RTI), the responsibilities under the contract to produce the marijuana cigarettes (using marijuana supplied by the University of Mississippi) and deliver them to authorized recipients. Tr. 1162–65, 1168–69; *see also* 72 FR 73369 (notice of registration for RTI).

[80] As discussed above, Respondent failed to put forth any evidence demonstrating that he is capable of any type of quality control relating the manufacture of marijuana and his lack of experience and expertise in this field compared to that of Dr. ElSohly suggests that he is incapable of improving on the quality of marijuana produced by the University of Mississippi.

[81] I also note Respondent's contention that the NIDA process ''does not ensure that researchers pay a competitive price [because] NIDA sets the price and there is no evidence as to how that price is set.'' Resp. Prop. Findings at 48. Even if marijuana were not subject to the Convention's requirement, I would still reject the argument because Respondent had the burden of proving that the prices are excessive.

[82] *See* H.R. Rep. 1444 (91st. Cong., 2d Sess.), *reprinted at* 1970 U.S.C.C.A.N. 4566, 4572.

Here, this rule applies with added force for two reasons. First, Respondent's construction would derogate the sovereign authority of the United States. See, *e.g., E. I. Du Pont de Nemours & Co.* v. *Davis,* 264 U.S. 456, 462 (1924) (noting that in taking over the railroads, ''the United States did so in its sovereign capacity * * * and it may not be held to have waived any sovereign right or privilege unless plainly so provided''); *cf. Federal Power Comm'n* v. *Tuscarora Indian Nation,* 362 U.S. 99, 120 (1960) (quoting *United States* v. *United Mine Workers of America,* 330 U.S. 258, 272 (1947) (''There is an old and well-known rule that statutes which in general terms divest pre-existing rights or privileges will not be applied to the sovereign without express words to that effect.''); *Sea-Land Service, Inc.,* v. *The Alaska R.R.,* 659 F.2d 243, 245 (D.C. Cir. 1981) (holding that ''[t]he Sherman Act * * * does not expose United States instrumentalities to liability, whether legal or equitable in character, for conduct alleged to violate antitrust constraints'').

Second, Respondent's construction would result in the abrogation of the Convention's provision. While Congress may abrogate a treaty, the ''legislation must be clear to ensure that Congress—and the President—have considered the consequences.'' *Roeder* v. *Islamic Republic of Iran,* 333 F.3d 228, 238 (D.C. Cir. 2003). The D.C. Circuit has further explained that ''[t]he 'requirement of [a] clear statement assures that the legislature has in fact faced, and intended to bring into issue, the critical matters involved in the judicial decision.' '' *Id.* (quoting *Gregory* v. *Ashcroft*, 501 U.S. 452, 461 (1991)). *See also Vimar Seguros y Reaserguros, S.A.* v. *M/V Sky Reefer,* 515 U.S. 528, 539 (1995) (''If the United States is to be able to gain the benefits of international accords and have a role as a trusted partner in multilateral endeavors, its courts should be most cautious before interpreting its domestic legislation in such manner as to violate international agreements.''); *George E. Warren Corp.* v. *U.S. E.P.A.,* 159 F.3d 616, 624 (D.C. Cir. 1998) (upholding agency rule which ''avoid[ed] an interpretation that would put a law of the United States into conflict with a treaty obligation of the United States,'' and observing that that ''[s]ince the days of Chief Justice Marshall, the Supreme Court has consistently held that congressional statutes must be construed wherever possible in a manner that will not require the United States to violate the law of nations'') (internal quotations and other citations omitted).

As explained above, § 823(a) is not limited to applicants who seek a registration to manufacture marijuana, but rather is a provision that applies to every person who seeks a registration to manufacture any one of the hundreds of other controlled substances listed in schedules I and II. Paragraph 823(a)(1)'s direction to the Attorney General to consider the adequacy of competition does not provide a clear statement of congressional intent to abrogate the Convention's requirement that the United States Government maintain a monopoly on the wholesale trade in marijuana. Absent the requisite clear statement, I conclude that to the extent the CSA seeks to promote adequate competition in the supply of marijuana, the NIDA process satisfies Congress' purpose by putting the contract up for competitive bidding at periodic intervals then supplying the marijuana to researchers for free or at NIDA's cost.

Respondent also contends that the current NIDA supply is ''inadequate because a pharmaceutical developer could not reasonably rely on NIDA marijuana to take [plant-form] marijuana through the FDA new drug approval process.'' Respondent's Resp. at 16; *see also* Respondent Proposed Findings at 45 (''no rational drug sponsor seeking to develop botanical marijuana as an FDA-approved product could proceed without seeking a source of supply alternative to NIDA's''). Of note in this regard, Mr. Doblin testified that MAPS could take plant-form marijuana through the FDA-approval process for a cost of $5 to $10 million notwithstanding ample evidence that the actual costs would be considerably more, and that he ''disagree[d]'' with the IOM's conclusion that defined and purified cannabinoid compounds ''are preferable to plant products, which are of variable and uncertain composition.'' Tr. 654; RX 1, at 22. *See also* GX 53 (letter of GW Pharmaceuticals; ''[H]erbal cannabis should comprise only the starting material from which a *bona fide* medical product is ultimately derived.''). Mr. Doblin also testified that the safety of smoked marijuana would be only ''slightly different'' from that of drugs containing cannabinoid extracts, Tr. at 605, notwithstanding the IOM's further conclusion that smoking ''is a crude THC delivery system that also delivers harmful substances'' such as those found in tobacco, and that ''there is little future in smoked marijuana as a medically approved medication.'' RX 1, at 195.

Mr. Doblin's testimony hardly suggests that he is a ''rational drug developer.'' But even ignoring his testimony, Respondent's argument is meritless. Respondent's contention that ''MAPS can have no confidence * * * that NIDA would authorize MAPS to rely on'' NIDA's Drug Master File, Resp. Proposed Findings at 44–45, ignores that under the HHS Guidance, NIDA is required to ''provide the researcher with authorization to reference'' it. GX 24, at 4. Moreover, neither Federal law nor FDA's regulations require that a drug developer submit a Drug Master File. FDA, *Guideline for Drug Master Files,* at 2.

Respondent further contends that NIDA would not be willing to serve as supplier to a drug developer because doing so is not part of its mission. It is, however, HHS, and not NIDA (which is only a subcomponent therein) which sets policy on whether to provide marijuana. As for Respondent's insinuation that HHS is biased against research that seeks to develop plant-form marijuana into a prescription medicine, it is true that Dr. Gust testified that HHS ''strongly endorse[s]'' the IOM's view that if marijuana is to provide the basis for a prescription medicine, it will be in a medicine which uses ''a purified constituent'' and a non-smokable delivery system. Tr. 1722. A view based on science is not bias. Moreover, Dr. Gust's testimony made clear that PHS does not have a bias against research that is directed at developing plant-form marijuana, *id.* at 1719–20, 1722; and that whether plant-form marijuana should be approved as a prescription medicine is a question for the FDA-approval process. *Id.* at 1720. Respondent's contention to this effect is therefore rejected.

In sum, under the text of 21 U.S.C. 823(a)(1), to maintain effective controls against diversion, DEA is obligated to consider limiting the number of registered bulk manufacturers of any given schedule I or II controlled substance to that which can produce an adequate and uninterrupted supply of the substance under adequately competitive conditions. Thus, every applicant for registration under § 823(a) bears the burden of demonstrating that either the existing supply or competition is inadequate within the meaning of paragraph 823(a)(1). For the reasons provided above, Respondent has failed to meet this burden. Accordingly, factor one weighs heavily against granting his application.

2. Public Interest Factor Two

The second public interest factor is ''compliance with applicable State and local law.'' 21 U.S.C. 823(a)(2). The ALJ stated: ''There is neither evidence nor

contention that Respondent has not complied with applicable laws and I therefore find that this factor weighs in favor of granting Respondent's application.'' ALJ at 85. In view of this statement, it must be repeated that at any hearing on an application to manufacture a schedule I or II controlled substance, the applicant has the burden of proving that the requirements for registration under 21 U.S.C. 823(a) are satisfied. 21 CFR 1301.44(a). Moreover, the issue under the second public interest factor is not merely whether an applicant has complied in the past with applicable State and local law, but also whether the applicant will do so if he becomes registered. Thus, it was imprecise for the ALJ to suggest that the absence of evidence regarding past compliance with applicable State and local law constitutes a favorable showing on behalf of the applicant for purposes of the second public interest factor. However, the record is not entirely silent with respect to this factor. As the ALJ noted (ALJ at 57), and as Respondent has emphasized (Resp. Prop. Findings at 57), Respondent did testify that he met with ''state investigators'' who told him that ''a state permit would depend on a federal permit being granted.'' Tr. 45. Given that the Government did not contest this part of Respondent's testimony, I will give Respondent the benefit of the doubt by inferring that what he intended to convey was that Massachusetts state officials indicated to him that he would be able to obtain a ''registration'' under Massachusetts law to manufacture marijuana if and when he were to obtain a DEA registration to do so.[83] I do so despite the fact that Respondent did not indicate in his testimony or through the submission of any documentary exhibits whether he had actually filed an application with the state and submitted the appropriate fee for such state registration. Thus, consistent with the ALJ's recommendation, I find Respondent has put forth some evidence which (being unrefuted) allows for a conclusion that his proposed activities would be in compliance with State and local law.

[83] Analogous to federal law, Massachusetts law provides that ''every person who manufactures * * * any controlled substance within the commonwealth shall upon payment of a fee, * * * register with the commissioner of public health, in accordance with his regulations, said registration to be effective for one year from the date of issuance.'' Mass. Gen. Laws Ann. ch. 94C, § 7(a) (West 2008). Massachusetts has adopted the CSA schedules of controlled substances, making marijuana a schedule I controlled substance under state law. *See* Mass. Gen. Laws Ann. ch. 94C, § 2(a).

The Government took exception, however, to the ALJ's recommendation that this factor (paragraph 823(a)(2)) be weighed in favor of granting Respondent's application. Gov. Exceptions at 12–13. The Government argues that this factor ''is most often relevant'' in cases in which practitioners have lost their state controlled substance authorization. *Id.* at 13. Further, the Government contends, ''[w]hile the failure to have a required state or local license would prove fatal to an application, * * * an expectation by Respondent that the required state license will ineluctably follow the granting of a DEA registration and a promise to comply with state and local law in the future simply renders this factor irrelevant and does not weigh in favor of either party.'' *Id.* In response thereto, Respondent asserts that the lack of evidence of noncompliance with state or local law should indeed support a finding that this factor weighs in favor of registration. Respondent's Resp. at 18–19.

It is certainly true, as both parties agree, that the evidence relating to Respondent's proposed activities cannot be deemed as weighing against the pubic interest for purposes of paragraph 823(a)(2). However, whether one characterizes the evidence relevant to this factor as weighing in favor of granting Respondent's application or simply neutral seems somewhat a matter of semantics. Given the nature of the evidence here (Respondent's mere testimony that he anticipates authorization from the state and that he promises to comply with state law), I accept the characterization that the evidence is favorable as to the second public interest factor, with the caveat that this factor is of limited weight commensurate with the nature of the evidence.

3. Public Interest Factor Three

The third public interest factor is ''promotion of technical advances in the art of manufacturing these substances and the development of new substances.'' 21 U.S.C. 823(a)(3). The ALJ found that Respondent has ''considerable experience in cultivating medicinal plants, which might promote technical advances in the cultivation of marijuana or developing new medications from it.'' ALJ at 85–86. The ALJ nonetheless found that ''there is not sufficient evidence in the record on which to base a finding as to whether granting Respondent's registration would promote technical advances.'' Id. at 86. When asked by his own counsel how his registration would promote technical advances, Respondent answered in a vague manner:

> Well, I think there is two answers to that as far as I'm concerned. One is that, yes, it would make an advance in the understanding any possible clinical use of marijuana if we were able to supply this to investigators to run trials, and, secondly, as I've explained to DEA agents that visited, that we would learn more about how the environment affects the constituents in the plant material which would enable, if this does become at some stage down the road here, becomes a useful drug, and that the manufacturer of it has to be controlled under security conditions, they would know the environment it needs to be grown under to produce a clinical marijuana, medical marijuana.

Tr. at 75–76. In the first part of the above answer, it appears that Respondent is simply accepting the word of his sponsor, Mr. Doblin, that his obtaining a DEA registration would result in marijuana being provided to researchers who would not otherwise obtain it. If so, Respondent is relying on a false premise. As discussed at length above, the evidence demonstrates that not one bona fide researcher within the meaning of the CSA (i.e., one whose protocol has been determined by HHS to be scientifically meritorious) has ever been denied marijuana[84] and that, under the new procedures adopted by HHS in 1999, the ''scientific bar'' has been set relatively low, allowing marijuana to be provided to 17 privately funded researchers. As for the second part of his answer, in which Respondent attempted to explain how his registration would result in learning ''more about how the environment affects the constituents in the plant material,'' this explanation is noticeably lacking in detail and without any discernable scientific basis. By his own admission, Respondent is ''not experienced in growing this plant (marijuana).'' Tr. at 40. In comparison, Dr. ElSohly, who has been the principal investigator under the NIDA contract and has overseen the National Center's work with marijuana since 1980 (employing a wide variety of

[84] Even with respect to Dr. Abrams—who MAPS seems to believe was improperly denied marijuana in the pre-1999 era (before HHS changed its policy for providing marijuana to researchers)—Respondent produced no evidence that HHS's denial was lacking in scientific basis. To the contrary, as indicated above, the evidence indicates that NIDA initially denied Dr. Abrams' request based on valid concerns about the design and scientific merit of his protocol. *See* note 24, *supra,* and accompanying text. The record further reflects that Dr. Abrams corrected these deficiencies to NIDA's satisfaction upon submitting a revised protocol and, as a result, received marijuana from NIDA in 1997; NIDA also supplied Dr. Abrams with marijuana for subsequent studies. *Id.*

manufacturing techniques),[85] has at least seven patents relating to the manufacture and identification of marijuana and its derivatives, and has authored numerous articles on these subjects that have been published in scientific journals. Tr. 1136–38, 1331–36; GXs 65–71, 93. Respondent's lack of experience in growing marijuana does not preclude a finding under paragraph 823(a)(3) that his proposed activities would promote technical advances in the art of manufacturing marijuana and developing new substances. Nor does Respondent's lack of expertise in this area compared to that of Dr. ElSohly preclude such a finding as it is conceivable that a newcomer to a field could make scientific discoveries that others have failed to make. However, Respondent's lack of experience and expertise combined with the vagaries of his testimony as to how he would promote technical advances in the art of manufacturing marijuana and developing new substances do not support a finding that he would do so. Thus, I concur with the ALJ's recommendation as to this factor and conclude that Respondent has failed to meet his burden of demonstrating that his proposed activities would promote technical advances in the art of manufacturing marijuana and developing new substances.

4. Public Interest Factor Four

The fourth public interest factor is ''prior conviction record of applicant under Federal and State laws relating to the manufacture, distribution, or dispensing of such substances.'' 21 U.S.C. 823(a)(4). I adopt the ALJ's recommended finding that it was ''undisputed that Respondent has never been convicted of any violation of any law pertaining to controlled substances'' and therefore this factor weighs in favor of granting the application. I reject the Government's contention that the historical and ongoing activities of Mr. Doblin and MAPS relating to controlled substances (which the Government asserts are improper but for which there is no evidence in the record of any criminal convictions) should be considered under this factor.

5. Public Interest Factor Five

The fifth public interest factor is ''past experience in the manufacture of controlled substances, and the existence in the establishment of effective control against diversion.'' 21 U.S.C. 823(a)(5). Both parties and the ALJ agree that Respondent has no past experience in the manufacture of controlled substances, and I so find.[86] Consideration of such experience serves two purposes. First, the review of an applicant's track record provides substantial information as to prior violations and the likelihood of its future compliance with the Act and regulations. *See ALRA Laboratories, Inc.* v. *DEA*, 54 F.3d 450, 452 (7th Cir. 1995) (''An agency rationally may conclude that past performance is the best predictor of future performance.''). Second, the experience factor recognizes that the regulatory scheme is complex and that having effective controls against diversion requires more than simply having a secure building and a policy and procedures manual.[87] Rather, having effective controls requires that those controls be properly performed. Thus, Respondent's lack of experience in the manufacture of controlled substances cannot be dismissed as inconsequential.[88] Indeed, there is agency precedent for concluding, in appropriate circumstances, that lack of such experience can be an independent basis for denial of registration.[89] However, I find in this case that Respondent's lack of experience in handling controlled substances—while a factor weighing against granting his application—should not disqualify him from obtaining a registration to bulk manufacture marijuana.

As to whether there would be, within Respondent's establishment, effective control against diversion,[90] Respondent testified that, although he ''did not have a full-blown plan when [he] applied for the [DEA registration],'' when DEA personnel conducted an on-site inspection of his premises, he assured them that he ''understood the need for security'' and that they thought that his proposed room for growing marijuana ''could be made secure with no problems.'' Tr. 44–45, 355–56. Respondent further testified that he

[85] The National Center grows marijuana both indoors and outdoors and has done so using conventional soil planting from seeds and seedlings, as well as using hydroponics (without soil), vegetative propagation (using cuttings to retain the genetic identity of the ''mother plant''), and micropropagation (vegetative propagation using a very small part of plant material rather than a cutting). Tr. 1187–1263, 1328–30. It has also utilized a variety of harvesting, drying, fertilization, and storage methods to affect the THC content of the marijuana, to promote more effective rolling of cigarettes, and to isolate certain cannabinoids. *Id.* It also has in its inventory seeds from different parts of the world, which can produce marijuana of various potencies. *Id.* Respondent did not identify any cultivation, harvesting, or other manufacturing techniques relating to marijuana in which the National Center lacks expertise.

[86] While the ALJ correctly observed that Respondent has no experience in the in the manufacture of controlled substances, she stated that Respondent ''does have experience in growing medicinal plants.'' ALJ at 86. It is unclear whether the ALJ was taking this into account for purposes of factor 5, or simply noting it in passing, because she ultimately recommended that I conclude ''there is not sufficient evidence in the record on which to base a finding as to whether granting Respondent's registration would promote technical advances.'' *Id.* In any event, under the text of paragraph 823(a)(5), experience in the manufacture of anything other than ''controlled substances'' is immaterial for purposes of factor 5.

[87] The CSA and DEA regulations impose a complex and comprehensive scheme to protect against diversion. These include not only requirements pertaining to the physical security of manufacturing facilities, *see* 21 CFR 1301.73, and employee screening procedures, *id.* 1301.90, but also extensive inventory, record keeping, and reporting requirements. *See* 21 CFR 1304.04 (maintenance of records and inventories); id. 1304.11 (inventory requirements); 1304.22(a) (records for manufacturers); 1304.33 (ARCOS reports); 1301.74(c) (reporting of theft).

[88] Respondent notes the Government's argument that '' '[i]n no case involving applications to handle controlled substances, has 'prior experience' with non-controlled substances ever been considered as support for granting an application.' '' Respondent's Resp. at 24. Respondent maintains that ''this argument is simply wrong,'' and that ''[i]n *Chattem Chemicals, Inc.*, 71 FR 9834, 9838 (2006) * * * the applicant had no prior experience in processing opium alkaloids, the controlled substance for which it sought a manufacturer's registration.'' Respondent's Resp. at 24–25. That much is true. Respondent ignores, however, that Chattem already held registrations to manufacture schedule II controlled substances including morphine, codeine and oxycodone, and to import other controlled substances. *See* 71 FR at 9836. In contrast to Respondent, who has no relevant experience, Chattem had extensive experience in the regulatory scheme and the effective implementation of controls against diversion.

Respondent also notes Dr. ElSohly's testimony to the effect that when the University of Mississippi first applied in 1968 for the contract to grow marijuana for NIDA's predecessor, ''he lacked experience and expertise in security measures relating to controlled substances.'' Respondent Resp. at 27. Respondent ignores, however, that the registration belongs to the University of Mississippi and was issued to it 12 years before Dr. ElSohly took over the project and under a different statutory scheme and further that Dr. ElSohly had been working on the marijuana project for four years at the time he succeeded his predecessor. *See* Tr. at 1131–32, 1152.

[89] *Cf. Stephen J. Heldman*, 72 FR 4032, 4034 (2007) (noting that even ''[w]ere there no evidence of Respondent having engaged in illicit activity * * * his lack of experience bars his registration'').

[90] As explained in part C of the discussion section, this aspect of paragraph 823(a)(5) requires DEA to consider, among other things, whether Respondent has demonstrated that he will have in place appropriate physical security and employee screening as required by the DEA regulations and as confirmed through a DEA on-site inspection of the premises. Also as explained in part C, this aspect of paragraph 823(a)(5)—which involves an evaluation of the applicant's particular facility, proposed security measures, and other controls against diversion to be implemented by the applicant—is best viewed as being distinguished from the requirement under paragraph 823(a)(1) that *DEA* maintain effective controls against diversion ''by limiting the importation and bulk manufacture of such controlled substances to a number of establishments which can produce an adequate and uninterrupted supply of these substances under adequately competitive conditions.''

agreed to meet all DEA security requirements. Tr. 79. The Government did not dispute these assertions. I therefore find that Respondent has met his burden of demonstrating that, if the registration were granted, he would have in place effective controls against diversion.[91] In sum, the evidence bearing on factor five weighs both in favor of and against Respondent's application: it indicates that he has no past experience in the manufacture of controlled substances but that he will have in the establishment effective controls against diversion.

6. Public Interest Factor Six

The sixth and final public interest factor is ''such other factors as may be relevant to and consistent with the public health and safety.'' 21 U.S.C. 823(a)(6). At the outset, it should be noted that, because the text of this provision calls on me to consider ''such *other* factors,'' I will *not* restate in the discussion of factor six the evidence that I have already taken into account for purposes of the first five public interest factors—even though such evidence might be relevant to the determination of whether Respondent's proposed registration would be consistent with the public health and safety.

The most notable evidence relevant to factor six is that relating to Mr. Doblin.[92] Before addressing this evidence, it needs to be made clear that I consider irrelevant for purposes of this application whether Mr. Doblin, in the expression of his political viewpoints, supports the legalization of marijuana and other controlled substances. I also consider irrelevant the political activities of the organization he heads, MAPS. The expression of political viewpoints enjoys the protection of the first amendment. However, it is certainly relevant for purposes of factor six whether a person who might be in a position to directly influence the activities of a registrant has engaged in actual conduct involving controlled substances that fails to comply with the federal or state law.

The evidence indicates that Mr. Doblin has been significantly involved in Respondent's application process and plans to retain a key role in Respondent's activities if the registration is granted. Mr. Doblin came up with the idea of sponsoring an applicant for a DEA registration who would be a supplier of marijuana other than NIDA, and he selected Respondent to be that applicant. Tr. 210–12, 219. Mr. Doblin assisted Respondent in filling out the application, supplied answers to DEA's supplemental written questions, and agreed, on behalf of MAPS, to ''cover all the costs'' associated with the registered activities, including the costs of equipment, manufacturing, and security installations. Tr. 221–22, 351–52; 383, 583; GX 3, at 1. Respondent has agreed that Mr. Doblin, in his role as head of MAPS, will take an active role in deciding to whom Respondent will supply the marijuana. Tr. 224–26, 358–360. Respondent described the process of applying for the DEA registration and the ''project of developing marijuana'' as a ''joint effort'' by Mr. Doblin and himself. Tr. 390–91. Indeed, Respondent testified that his ''understanding'' of his ''role,'' as well as that of Mr. Doblin, was that dictated to him by Mr. Doblin.[93] *Id.* at 358. Another part of Mr. Doblin's role would be to ''route'' the ''investigators'' (those seeking marijuana for research) to Respondent. *Id.* Mr. Doblin would also decide for Respondent the ''strains'' of marijuana to produce and ''allocate'' the marijuana produced in accordance with MAPS's priorities. Tr. 589.

In short, Mr. Doblin has mapped out and assisted in most acts, if not every act, that Respondent has taken toward applying for a registration to manufacture marijuana and, if the registration were granted, Mr. Doblin would continue to maintain responsibility for managing and monitoring the activities of the registrant. Given this level of involvement by Mr. Doblin—and the passive, if not subservient, nature of Respondent's involvement—it is appropriate under factor six to consider the following conduct by Mr. Doblin relating to controlled substances. First, Mr. Doblin admits that he smokes marijuana for ''recreational use'' on a weekly basis. Tr. 716, 718–19. Thus, Mr. Doblin violates federal and state laws relating to controlled substances on a weekly basis.[94] This demonstrates that Mr. Doblin has disregard for the controlled substances laws. It is simply inconceivable that DEA would—consistent with its obligations under the CSA—grant a registration to engage in certain activities involving controlled substances where it is clear that a person who will have *any* role in the oversight and management of such activities routinely engages in the illegal use of controlled substances. It is still more untenable where that person has the level of oversight and management that Mr. Doblin would have—and where the controlled substance he illegally uses is the very controlled substance the applicant seeks to produce. Indeed, it is remarkable that Mr. Doblin would—given his admitted illegal involvement in controlled substances—ask DEA to effectively grant him permission to take on such a prominent role in the manufacture of the most widely abused illegal controlled substance in the United States.

Respondent points to Mr. Doblin's testimony that MAPS has previously sponsored research by DEA registrants involving schedule I controlled substances other than marijuana. Respondent's Resp. at 23 (citing Tr. 482–491). Respondent characterizes such research as having taken place ''all without a hint of * * * diversion.'' *Id.* at 23–24. However, there is nothing in the record that confirms or refutes this

[91] Because the DEA regulations require all registered manufacturers of controlled substances to have certain control measures in place at all times (21 CFR 1301.71–.74, .76), DEA may not issue a certificate of registration to a new applicant until the required security measures are actually in place.

Moreover, while I acknowledge that Respondent testified that he would secure the growing area and meet ''appropriate security conditions'' (Tr. 79), and I find it is highly unlikely that Respondent would personally divert, this does not establish that the risk of diversion is minimal. Respondent testified that he usually does not go down to the greenhouse to water the plants but leaves this task to a technician. Tr. at 254. Moreover, the graduate students and technicians ''would probably do the transplanting'' and the ''daily check on any environmental controls.'' *Id.* at 254–55. Respondent's testimony begs the question of who would be supervising these workers. Furthermore, while Respondent has promised to meet appropriate security conditions, it is undisputed that he has no experience in the manufacture of controlled substances and the regulatory scheme. As he testified: ''I have no experience in the control against diversion.'' Tr. 79.

Thus, my finding under factor five that Respondent would have in place effective controls against diversion might be viewed as being generous toward Respondent.

[92] By its terms, paragraph 823(a)(6) is not limited to conduct on the part of the applicant. Rather, its broad wording indicates that it is a catchall provision that calls on the agency to consider ''such other factors [not covered by factors (a)(1) through (a)(5)] as may be relevant to and consistent with the public health and safety.''

[93] Further indication that MAPS is the driving force behind this application is that, when asked to explain the meaning of one of his written answers to the questions submitted by DEA as a follow up to the application, Respondent admitted that he had ''no idea'' whether he was referring to Chemic when he answered that one of the proposed recipients of the marijuana that he seeks to produce would be an entity that would use ''marijuana delivered through a vaporizer device.'' Tr. at 225–26. Nor did Respondent know if this entity was authorized under the law to conduct such research or the amount of marijuana that would be needed for this research. *Id.* at 229. Respondent said that such questions would have to be referred to Mr. Doblin. *Id.* at 226. Respondent acknowledged that the only entity he had in mind as a recipient of the marijuana he seeks to grow was the researcher that would test the vaporizer. Tr. at 235.

[94] 21 U.S.C. 844; Mass. Gen. Laws Ann. ch. 94C, § 34 (West 2008). Mr. Doblin lives in Massachusetts. Tr. 472.

characterization; nor does the record indicate exactly what role Mr. Doblin played in the prior MAPS-sponsored research.[95] In any event, even assuming that MAPS has previously sponsored DEA-registered researchers without incident, this does not undo the legitimate concerns that came to light in this proceeding about Mr. Doblin's fitness for directing, at least in part, the activities of a DEA-registered bulk manufacturer of marijuana, given Mr. Doblin's routine illegal use of marijuana.

Thus, Mr. Doblin's ongoing illegal marijuana use, by itself (i.e., even putting aside the treaty considerations and Respondent's failure to demonstrate inadequate supply or competition within the meaning of paragraph 823(a)(1)), provides a sufficient independent basis upon which DEA may deny the application.

Accordingly, based on a consideration of all six pubic interest factors set forth in 21 U.S.C. 823(a), I conclude the Respondent has failed to meet his burden of demonstrating that his proposed registration is consistent with the public interest. To the contrary, the evidence is compelling that the registration is inconsistent with the public interest.

C. The Meaning of 21 U.S.C. 823(a)(1)

This section of the discussion contains a far more extensive analysis of 21 U.S.C. 823(a)(1) (hereafter, ''paragraph 823(a)(1)'') than DEA has previously published. As indicated above, for ease of exposition, due to the length of this analysis, it is being presented here as a separate section of the discussion rather than inserting it directly into the above discussion of the public interest factors.

1. The Text of the Statute

The appropriate starting point for the analysis of any statute is the text of the statute itself. The text of § 823(a) remains the same today as it was when the CSA was enacted by Congress in 1970. It states:

> (a) Manufacturers of controlled substances in schedule I or II
>
> The Attorney General shall register an applicant to manufacture controlled substances in schedule I or II if he determines that such registration is consistent with the public interest and with United States obligations under international treaties, conventions, or protocols in effect on May 1, 1971. In determining the public interest, the following factors shall be considered:
>
> (1) Maintenance of effective controls against diversion of particular controlled substances and any controlled substance in schedule I or II compounded therefrom into other than legitimate medical, scientific, research, or industrial channels, by limiting the importation and bulk manufacture of such controlled substances to a number of establishments which can produce an adequate and uninterrupted supply of these substances under adequately competitive conditions for legitimate medical, scientific, research, and industrial purposes;
>
> (2) Compliance with applicable State and local law;
>
> (3) Promotion of technical advances in the art of manufacturing these substances and the development of new substances;
>
> (4) Prior conviction record of applicant under Federal and State laws relating to the manufacture, distribution, or dispensing of such substances;
>
> (5) Past experience in the manufacture of controlled substances, and the existence in the establishment of effective control against diversion; and
>
> (6) Such other factors as may be relevant to and consistent with the public health and safety.

Thus, the statute allows DEA to register an applicant to bulk manufacture a schedule I or II controlled substance only if the Deputy Administrator[96] determines that the proposed registration would be consistent with both (i) the Single Convention and (ii) the public interest. In determining whether the proposed registration is consistent with the public interest, the statute requires DEA to evaluate the above six factors. The first factor, set forth in 21 U.S.C. 823(a)(1) (referred to in this discussion as ''paragraph 823(a)(1)''), requires the Deputy Administrator to consider ''maintenance of effective controls against diversion * * * *by limiting the * * * bulk manufacture of such controlled substances to a number of establishments which can produce an adequate and uninterrupted supply of these substances under adequately competitive conditions* for legitimate medical, scientific, research, and industrial purposes.'' (Emphasis added.) Thus, Congress stated in paragraph 823(a)(1) that—in order to maintain effective controls against diversion of a given schedule I or II controlled substance—DEA must consider limiting the number of registered bulk manufactures of the substance to that ''which can produce an adequate and uninterrupted supply of these substances under adequately competitive conditions.''

While the above-quoted text of paragraph 823(a)(1) is relatively straightforward, consulting the dictionary helps to confirm the meaning. The word ''limiting'' (or ''limit''), when used as a verb, is defined as ''to assign certain limits to; prescribe,'' ''to restrict the bounds or limits of,'' or ''to curtail or reduce in quantity or extent.'' [97] The word ''limit,'' when used as a noun, is defined as ''something that bounds, restrains or confines'' or ''the utmost extent.'' [98] Thus, the command under paragraph 823(a)(1) that DEA consider ''limiting'' the number of registered bulk manufacturers of a given schedule I or II controlled substance can be construed to mean that the *upper boundary* on the number of such manufacturers is that ''which can produce an adequate and uninterrupted supply of these substances under adequately competitive conditions for legitimate medical, scientific, research, and industrial purposes.''

It is notable that, by requiring DEA to consider *limiting* the number of bulk manufactures of a given schedule I controlled substance to that ''which can produce an adequate and uninterrupted supply * * * under adequately competitive conditions,'' paragraph 823(a)(1) does *not* allow DEA simply to register as many bulk manufacturers of a given schedule I or II controlled substance as the market will bear. Rather, DEA is obligated under paragraph 823(a)(1) to consider disallowing additional entrants into the schedule I and II bulk manufacturing market *unless* DEA concludes that addition of a particular applicant is necessary to produce ''an adequate and uninterrupted supply of [a given substance] under adequately competitive conditions.''

This reading of paragraph 823(a)(1) is also consistent with the overall structure of the CSA. The Act places each controlled substance into one of five schedules based on: whether the substance has a currently accepted medical use in the United States; the substance's relative potential for abuse; and the extent to which abuse of the substance may lead to psychological or physical dependence.[99] As the United States Supreme Court has stated, ''[t]he Act then imposes restrictions on the

[95] Respondent does not appear to contend that DEA granted the prior registrations to MAPS-sponsored researchers knowing that MAPS was the sponsor with Mr. Doblin having the same level of involvement that he seeks here, and he cites no part of the record for such a proposition.

[96] Pursuant to 21 U.S.C. 871(a), functions vested in the Attorney General by the CSA have been delegated to the Administrator of DEA. 28 CFR 0.100(b). The function of issuing final orders regarding applications for registration has been further delegated to the Deputy Administrator. 28 CFR 0.104, appendix to subpart R, sec. 7(a).

[97] Merriam-Webster OnLine, *http://www.merriam-webster.com/dictionary* (2008).

[98] *Id.*

[99] 21 U.S.C. 812(b).

manufacturing and distribution of the substance according to the schedule in which it has been placed.'' [100] ''Schedule I,'' as the Court observed, ''is the most restrictive schedule.'' This is commensurate with the fact that schedule I controlled substances are the only controlled substances with no currently accepted medical use in treatment in the United States. Schedule II restrictions are the next most restrictive (less restrictive than those for schedule I controls but more restrictive than those for schedules III, IV, and V)—commensurate with schedule II substances having the highest potential for abuse of those controlled substances that have a currently accepted medical use (those in schedules II through V).

Consistent with this basic CSA principle of applying greater controls to the substances that are most subject to abuse and most harmful when abused, the CSA is structured to apply certain critical control provisions to schedule I and II substances but not to those in schedules III, IV, and V. For example, the CSA imposes quota restrictions and order form requirements for schedule I and II controlled substances but not for those in schedules III, IV, and V.[101] Paragraph 823(a)(1) is another example of this principle. The required consideration in paragraph 823(a)(1) of limiting the number of bulk manufacturers of schedule I and II controlled substances (to that which can produce an adequate and uninterrupted supply of a given substance under adequately competitive conditions) is noticeably absent from paragraph 823(d)(1), which governs the registration of manufacturers of schedule III, IV, and V controlled substances. This contrast between the presence of the ''limiting'' language in paragraph 823(a)(1) and its absence from paragraph 823(d)(1) underscores the importance of this requirement—particularly in view of Congress's overall scheme of placing the greatest restrictions on substances in schedules I and II.

Another consideration when interpreting the language of paragraph 823(a)(1) is a comparison of its terms with those of paragraph 823(a)(5). As indicated above, paragraph 823(a)(5) is one of the six factors DEA must consider when evaluating an application for registration to bulk manufacture a schedule I or II controlled substance. Paragraph 823(a)(5) requires consideration of, among other things, ''the existence *in the establishment* of effective control against diversion.'' (Emphasis added.) The plain meaning of this language is that the Deputy Administrator must evaluate whether the particular facility in which the applicant proposes to manufacture the schedule I or II controlled substance will have in place effective safeguards to prevent diversion. This would include, among other considerations, appropriate physical security and employee screening as required by the DEA regulations [102] as confirmed through a DEA on-site inspection of the premises. That paragraph 823(a)(5) expressly requires the Deputy Administrator to consider ''the existence *in the establishment* of effective control against diversion'' is a further indication that paragraph 823(a)(1) is not intended to cover precisely the same consideration. To restate this interpretation somewhat, whereas paragraph 823(a)(1) can be viewed as preventing diversion on a registrant-wide scale (by directing the agency to consider limiting the total number of registered bulk manufacturers and importers of schedule I and II controlled based on the principle—discussed below—that fewer registrants decreases the likelihood of diversion), paragraph 823(a)(5) can be viewed as preventing diversion on an individual-registrant basis (by directing the agency to consider whether the applicant will have in place, in its particular establishment, effective controls against diversion).[103]

In sum, for the preceding reasons, examining the text of paragraph 823(a)(1) can lead squarely to the conclusion that it requires DEA to maintain effective controls against diversion by considering ''limiting the * * * bulk manufacture of [schedule I and II] controlled substances to a number of establishments which can produce an adequate and uninterrupted supply of these substances under adequately competitive conditions.''

2. Legislative History of the Statute

Congress derived paragraph 823(a)(1) from the Narcotics Manufacturing Act of 1960 [104] (which was superseded by the CSA in 1970). Under the 1960 Act, a person seeking to manufacture a basic class of narcotic drugs was required to obtain a license from the Secretary of the Treasury Department. Within the Treasury Department, this function was delegated to the Commissioner of the Bureau of Narcotics (a predecessor of DEA). Section 8 of the 1960 Act set forth the criteria that the Commissioner was required to consider in determining whether to issue a narcotics manufacturing license. Paragraph (a)(1) of section 8 of the 1960 Act was the analog to paragraph 823(a)(1) of the CSA. Paragraph (a)(1) provided that, in determining whether to issue a license to an applicant seeking to manufacture a basic class of narcotic drug, the Commissioner was required to consider:

> Maintenance of effective controls against the diversion of the particular basic class of narcotic drug and of narcotic drugs compounded therefrom into other than legitimate medical and scientific channels *through limitation of manufacture of the particular basic class of narcotic drug to the smallest number of establishments which will produce an adequate and uninterrupted supply* of narcotic drugs of or derived from such basis class of narcotic drugs for medical and scientific purposes, consistent with the public interest.

(Emphasis added.)

As the italicized language above indicates, the 1960 Act reflected the then-policy of the United States to limit the number of licensed manufacturers ''to the smallest number of establishments which will produce an adequate and uninterrupted supply''—without regard to whether there was adequate competition. Plainly, there are both similarities to and distinctions between this provision of the 1960 Act and its counterpart in the CSA. The CSA carried forward the concept of ''limiting'' the number of registered manufacturers (with respect to schedule I and II controlled substances). However, the CSA modified this requirement by providing that this limitation on the number of manufacturers be based not only on that which can produce ''an adequate and uninterrupted supply,'' but also on that which provides for ''adequately competitive conditions.'' Put slightly differently, when Congress enacted the CSA, it raised the ceiling on the number of manufacturers from that which can produce ''an adequate and uninterrupted supply'' to a consideration of that which can produce ''an adequate and uninterrupted supply * * * under adequately competitive conditions.'' [105] The policies underlying

[100] OCBC, 532 U.S. at 492 (2001).

[101] 21 U.S.C. 826 & 828.

[102] *See* 21 CFR 1301.71–1301.93.

[103] As discussed below, some prior DEA final orders have construed paragraph 823(a)(1) to require consideration of the existence in the establishment of effective control against diversion. While this factor must be considered in evaluating any application for registration under § 823(a), it is best considered only for purposes of paragraph 823(a)(5) and not mingled with the analysis under paragraph 823(a)(1).

[104] 74 Stat. 55 (1960).

[105] To be precise, the text of the CSA (in contrast to that of the 1960 Act) does not unambiguously impose an absolute ceiling on the number of registered manufacturers (that which can produce an adequate and uninterrupted supply under adequately competitive conditions). Rather, as indicated above, the text of the CSA requires DEA

this change in the law are summarized in the following exchange during the Congressional hearings on the enactment of the CSA. The exchange was between Senator Hruska (one of the co-sponsors of the various bills that led up to the CSA) and then-Attorney General Mitchell:

Senator Hruska: We have two national policies involved here. One is the anticompetitive situation policy. The antitrust law is a very well-established concept * * *. We also have another national policy have we not, Mr. Attorney General? We have entered into a global series of agreements in which we undertake in joint action with other nations the business of controlling the manufacture and distribution of the opiates and final derivatives of opium. Among those agreements is this principle: That we urge upon nations to keep the number of producers down to as low a point as possible to facilitate and to make more certain their ability to control and supervise the output and to keep it in normal and proper legal channels. We have these two national policies involved here, have we not?

Mr. Mitchell: Yes sir, you have both of them, and there is no intention on the part of the Justice Department nor the Bureau of Narcotics and Dangerous Drugs by this provision to expand beyond necessity, and of course those are the key words, any manufacturers in this particular area. We felt it was necessary to maintain the protection of the consumer from the price structure point of view and that is why the additional provisions have been added.[106]

During that same hearing, the Department of Justice submitted in writing its position regarding a proposed version of what would become paragraph 823(a)(1). In that document, the Department of Justice stated the following with respect to the then-pending proposal to deviate in the CSA from the 1960 Act by adding the consideration of adequacy of competition, and how the Department would carry out such proposal, if enacted:

There is no reason to assume that the Attorney General will prejudice his primary objectives of effective control by excessive licensing. Nor will he undertake direct price control. He will be empowered to take cognizance of evidence showing that prices are clearly and persistently excessive. The criteria for determining whether prices far exceed that which is reasonable relate to reasonable costs and reasonable profits. No explicit statement of criteria is needed. If evidence indicates that additional licensing will result in more reasonable prices with no significant diminution in the effectiveness of drug control, the Attorney General should be able to license the additional manufacturers.[107]

Consistent with the foregoing statements made during the Senate hearings, a subsequent Senate report contained the following statement, which echoes the language of what is now in paragraph 823(a)(1): ''[T]he Attorney General must limit the importation and manufacture of schedules I and II substances to a number of establishments which can produce an adequate and uninterrupted supply under adequately competitive conditions for legitimate purposes.'' [108]

Thus, the legislative history reaffirms several principles already evident from the text of paragraph 823(a)(1) and expands upon those principles. The legislative history confirms that paragraph 823(a)(1) indeed was designed to require the Attorney General to take into account limiting the number of bulk manufacturers (and importers) of schedule I and II controlled substances. However, this limit was not as restrictive as under the law that preceded the CSA. Whereas under the 1960 Act, additional manufacturers could only be added if supply was inadequate, the CSA added the consideration of adequacy of competition. Nonetheless, as the legislative history reflects, Congress under the CSA placed the burden on the applicant seeking to become registered to bulk manufacture a schedule I or II controlled substance to put forth evidence demonstrating either inadequate supply or inadequate competition.

The legislative history also reflects the recognition by Congress of a crucial principle underlying paragraph 823(a)(1): That the risk of diversion tends to increase with each new registered bulk manufacturer of a schedule I or II controlled substance. At the same time, the language of paragraph 823(a)(1) reflects the determination by Congress that—despite the increased risk of diversion resulting from the addition of each new registered manufacturer—it is beneficial to the public interest to allow the registration of additional manufacturers where the Attorney General finds that doing so is necessary to produce an adequate and uninterrupted supply of a given substance under adequately competitive conditions.[109]

3. Treaty Considerations

The principle that limiting the number of producers of narcotics and other schedule I and II controlled substances tends to promote more effective control has long been a part of United States policy and incorporated into the international drug control treaties to which the United States has been a party and which predate the CSA. Under the Single Convention, article 29 addresses the manufacture of narcotic drugs. Paragraph 2(b) of article 29 requires parties to the treaty to ''[c]ontrol under license the establishment and premises in which such manufacture may take place.'' With respect to this provision, the Commentary to the Single Convention states: ''It is suggested that, in order to facilitate control, the licensing system under subparagraph (b) should be employed to ensure that the manufacture of drugs, their salts and preparations is restricted to as small a number of establishments and premises as is practicable.'' Commentary at 322 (emphasis added); *see also id.* at 319 (discussing how the concept of limiting the number of manufacturers of narcotic drugs was inherent in the international drug control treaties that preceded the Single Convention).[110] This is the same

to ''consider * * * limiting'' the number of manufacturers to such a number (along with considering the other public interest factors). It should also be noted that, whereas the 1960 Act referred to allowing only ''the *smallest* number of establishments which will produce an adequate and uninterrupted supply'' (emphasis added), the CSA does not contain the term ''smallest'' in paragraph 823(a)(1). Nonetheless, as explained above, the use of the term ''limiting'' in paragraph 823(a)(1) can be construed to mean that DEA, when evaluating an application under § 823(a), must consider keeping as the upper boundary on the number of manufacturers that which can produce an adequate and uninterrupted supply under adequately competitive conditions. In other words, even though Congress when it enacted the CSA did not carry forward from the 1960 Act the term ''smallest,'' because it did carry forward the term ''limiting,'' it retained the concept of an upper limit on the number of manufacturers as a factor to be considered when evaluating an application for registration under § 823(a).

[106] *Hearings Before the Subcomm. to Investigate Juvenile Delinquency of the Comm. on the Judiciary, United States Senate*, 91st Cong. 261–262 (1969).

[107] *Id.* at 372. Although this statement by the Department of Justice was commenting on an earlier version of the bill, the modified version of the bill that ultimately was enacted retained the same principles as the earlier version under which the adequacy of competition would become a consideration in determining whether to grant applications to become registered to manufacture schedule I or II controlled substances.

[108] *Controlled Dangerous Substances Act of 1969: Report of the Comm. on the Judiciary, United States Senate*, 91st Cong. 7 (1969).

[109] As the statute states, an application for registration under § 823(a) may only be granted if DEA determines that such registration is consistent with *both* the public interest and United States obligations under the Single Convention. Thus, even if a proposed registration were found by DEA to be consistent with the public interest based on a consideration of the six public interest factors of § 823(a), the registration must be denied if DEA finds it would be inconsistent with United States obligations under the Single Convention.

[110] Also illustrative of this point are the following statements contained in a 1979 resolution issued by the United Nations Commission on Narcotic Drugs, which DEA has cited in a prior **Federal Register** publication: ''Recalling the relevant provisions of

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principle as that referred to in the legislative history of the CSA (in the above-quoted exchange between Senator Hruska and the then-Attorney General).

4. Pertinent Provision of the DEA Regulations

The only applications for registration for which the DEA regulations require the agency to publish notice in the **Federal Register** are those by persons seeking to bulk manufacture and import schedule I and II controlled substances. 21 CFR 1301.33(a) & 1301.34(a). These are the applications governed by 21 U.S.C. 823(a). In the cases of such applications, the regulations further require DEA to mail (simultaneously with the publication in the **Federal Register**) a copy of the **Federal Register** notice to each person registered as a bulk manufacturer of the particular schedule I or II controlled substance and to each person who has submitted a pending application therefor. *Id.* Any such person may also file written comments or objections to the proposed registration. *Id.*

That the regulations provide the foregoing procedures in the case of applications filed pursuant to 21 U.S.C. 823(a)—and for no other categories of applications—is indicative of the distinction between the statutory factors for registration contained in subsection 823(a) and those contained in all other subsections of § 823. As explained above in the discussion of the text of the statute, whereas paragraph 823(a)(1) requires DEA to consider limiting the number of registered bulk manufacturers and importers of a given schedule I or II controlled substance to that which can produce an adequate and uninterrupted supply under adequately competitive conditions, this consideration appears nowhere else in § 823 (i.e., it is inapplicable to all other applications for registration). Moreover, the consideration of adequacy of supply and competition is the *only* factor that is unique to subsection 823(a). It is therefore implicit that the notice-and-comment provisions of the regulations listed above (those contained in 21 CFR 1301.33(a) and 1301.34(a)) are designed to effectuate the consideration by DEA of adequacy of supply and competition. This implication is also consistent with the view that, in addition to DEA and the applicant itself, those registrants that constitute the existing suppliers (bulk manufacturers) of a given schedule I or II controlled substance have the requisite knowledge to comment on whether the existing market is capable of producing an adequate and interrupted supply under adequately competitive conditions.

Thus, the notice-and-comment provisions of 21 CFR 1301.33(a) and 1301.34(a) provide further support for interpreting paragraph 823(a)(1) as requiring DEA to consider, for purposes of determining the public interest, limiting the number of registered bulk manufacturers and importers of schedule I and II controlled substances to that which can produce an adequate and uninterrupted supply under adequately competitive conditions.

Another provision of the regulations that warrants discussion is 21 CFR 1301.33(b), which states:

> In order to provide adequate competition, the Administrator shall not be required to limit the number of manufacturers in any basic class to a number less than that consistent with maintenance of effective controls against diversion solely because a smaller number is capable of producing an adequate and uninterrupted supply.

Although this provision is somewhat awkwardly phrased, a careful examination reveals that it is merely a corollary to paragraph 823(a)(1). In construing subsection 1301.33(b), it is important to bear in mind that an agency regulation cannot deviate from any mandate imposed by Congress under the statute that the regulation implements. Thus, any reading of subsection 1301.33(b) must be consistent with Congress's direction in paragraph 823(a)(1) that DEA consider limiting the number of bulk manufacturers of schedule I and II controlled substances to that which can produce an adequate and uninterrupted supply under adequately competitive conditions.

With the foregoing principles in mind, subsection 1301.33(b) can be broken down into its constituent elements for purposes of analysis as follows:

■ ''In order to provide adequate competition''; i.e., if it has been determined under paragraph 823(a)(1) that granting a particular applicant a registration to bulk manufacture a given schedule I or II controlled substance is necessary to provide an adequate and uninterrupted supply of that substance under adequately competitive conditions,

■ ''The Administrator shall not be required to limit the number of manufacturers in any basic class to a number less than that consistent with maintenance of effective controls against diversion''; i.e., if granting the applicant's registration (based on a finding of inadequate competition) will bring the total number of registered bulk manufacturers of a given schedule I or II controlled substance to a number which remains consistent with maintenance of effective controls against diversion, DEA is not obligated to keep the total *less than* that number,

■ ''Solely because a smaller number is capable of producing an adequate and uninterrupted supply''; i.e., based solely on the fact that the existing number of manufacturers already produces an adequate and uninterrupted supply (but under *in*adequately competitive conditions).

Viewing these elements together, it is apparent that subsection 1301.33(b) merely states what are direct outgrowths of 21 U.S.C. 823(a)(1):

(1) That the existence of an adequate and uninterrupted supply of a given schedule I or II controlled substance is *not* a sufficient basis to deny an application by a person seeking to become an additional manufacturer of that substance (since inadequate competition may provide an independent basis for registration under paragraph 823(a)(1)) and

(2) That DEA need not keep the number of registered bulk manufacturers to a number *below* that which is consistent with maintenance of effective controls against diversion where adding an additional manufacturer is necessary to provide for adequate competition.

Thus, 21 CFR 1301.33(b) can be reconciled with the statutory text (paragraph 823(a)(1))—as must be the case for the regulation to be valid.[111]

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the Single Convention * * * to limit cultivation, production, manufacture and use of narcotic drugs to an amount required for medical and scientific purposes * * *'' and ''Bearing in mind that the treaties which establish this system are based on the concept that the number of producers of narcotic materials for export should be limited in order to facilitate effective control. * * *'' Cited in 44 FR 33695 (1979) and available at *http://daccessdds.un.org/doc/RESOLUTION/GEN/NR0/638/29/IMG/NR063829.pdf?OpenElement.*

[111] It is unclear why subsection 1301.33(b) was written in the manner that it was. Given that the regulation was promulgated shortly after the enactment of the CSA in 1970, it is possible that it was written to emphasize how paragraph 823(a)(1) represented a departure from the provision it superseded in the 1960 Narcotic Manufacturing Act. As explained above, the 1960 Act limited the number of licensed manufacturers ''to the smallest number of establishments which will produce an adequate and uninterrupted supply''—without regard to whether there was adequate competition. In contrast, when Congress enacted the CSA, it raised the ceiling on the number manufacturers to that which can produce an adequate and uninterrupted supply *under adequately competitive conditions.* Subsection 1301.33(b) seems to emphasize this distinction between the 1960 Act and the CSA by pointing out that, under the latter, DEA may not deny an application based solely on the existence of an adequate and uninterrupted supply.

In 2004, the Department of Justice provided Congress with an explanation of subsection 1301.33(b) that is consistent with the explanation

5. Prior DEA Statements Regarding the Meaning of Paragraph 823(a)(1)

As discussed above, I now conclude that the text of paragraph 823(a)(1) indicates a directive, which is confirmed by the legislative history, that the agency consider limiting the number of registered bulk manufacturers and importers of controlled substances in schedules I and II to that which can produce an adequate and uninterrupted supply under adequately competitive conditions. Yet, in various final orders and other statements issued by DEA over the years, the agency has at times followed this approach and at other times failed to do so.

For example, in *Roxane Laboratories, Inc.,* 63 FR 55891 (1998), the agency applied paragraph 823(a)(1) consistent with the interpretation that requires the applicant to demonstrate that the existing manufacturer of the controlled substance in question is unable to provide an adequate and uninterrupted supply of the substance under adequately competitive conditions. Roxane Laboratories, Inc. (Roxane) was a company that applied to become registered to import cocaine hydrochloride, a schedule II controlled substance, for use in pharmaceutical products. As § 823(a) states, both an application to import a schedule I or II controlled substance and an application to bulk manufacture such a substance must be evaluated under the same criteria set forth in § 823(a).[112] Thus, in *Roxane,* the Acting Deputy Administrator had to evaluate whether the proposed registration was consistent with the public interest in view of the six public interest factors of § 823(a), including paragraph 823(a)(1).

Consistent with the interpretation of paragraph 823(a)(1) under which the adequacy of supply and competition must be considered, the parties in *Roxane* presented extensive evidence as to whether there was adequate competition within the meaning of the statute.[113] Toward that end, much of the testimony and other evidence introduced in the proceedings focused on the historical and prevailing prices for bulk cocaine hydrochloride charged by what was then the only registered importer of that substance. In addition to presenting factual evidence regarding such prices, each side presented its own economic expert to testify whether, in view of the prices, competition in the market was adequate within the meaning of paragraph 823(a)(1).[114] Ultimately, the Acting Deputy Administrator found that the applicant had met its burden under paragraph 823(a)(1) of demonstrating that competition was inadequate and, in view of all the applicable statutory factors, granted Roxane's application to become registered as an importer of cocaine hydrochloride.

Four years later, in *Johnson Matthey, Inc.*, 67 FR 39041 (2002), DEA again addressed the paragraph 823(a)(1) issue. As in *Roxane,* Johnson Matthey had applied to become registered as, among other things, an importer of schedule II controlled substances. Thus, as in *Roxane,* one of the central issues in *Johnson Matthey* was whether granting the application was necessary to provide adequate competition within the meaning of paragraph 823(a)(1).[115] The application was opposed by two firms that were already registered as importers of the same substances that Johnson Matthey sought to import. These competing firms contended at the administrative hearing that they maintained an adequate and uninterrupted supply of the substances under adequately competitive conditions. The two firms therefore objected to the proposed registration under paragraph 823(a)(1), among other grounds.

The final order in *Johnson Matthey* contains no description of the evidence presented by the parties during the administrative hearing on the competition issue as the final order expressly declared such evidence to be irrelevant. Nor does the *Johnson Matthey* final order contain a recitation of the text of paragraph 823(a)(1) or an independent analysis of the statutory text. Instead, the *Johnson Matthey* final order simply adopted a proposed rule that was published 18 years earlier by DEA and subsequently withdrawn by the agency. In that subsequently withdrawn 1974 proposed rule (39 FR 12138 (1974)), DEA proposed to revise its regulations to state that, during an administrative hearing on an application to manufacture a controlled substance in schedule I or II, if the ALJ determines that the registration would be consistent with maintenance of effective controls against diversion, he shall exclude as irrelevant evidence bearing on whether existing manufacturers are capable of producing an adequate and uninterrupted supply under adequately competitive conditions.

The *Johnson Matthey* final order failed to state that, two months after DEA published the aforementioned proposed rule in 1974, the agency published a notice in the **Federal Register** that three firms (which were then registered bulk manufacturers under § 823(a)) filed objections to, and requested a hearing on, the proposed rule, asserting that ''the Controlled Substances Act requires a finding respecting the adequacy of competition prior to registering any person to engage in the bulk manufacture of a schedule I or II substance.'' 39 FR 20382 (1974). These objections that were submitted in response to the 1974 proposed rule reflect precisely the same conclusion regarding the meaning of paragraph 823(a)(1) that I find—for the reasons discussed above—to be most

provided in the text above. *See Marijuana and Medicine: The Need for a Science-Based Approach: Hearing Before the Subcomm. on Criminal Justice, Drug Policy and Human Resources*, 108th Cong. 208 (2004) (letter from Assistant Attorney General William Moschella to Subcomm. Chairman Rep. Souder) (''The meaning of [21 CFR 1301.33(b)] can be restated as follows: *If DEA determines there is inadequate economic competition among the existing manufacturers of the particular controlled substance that the applicant seeks to produce* (e.g., substantial overcharging by the existing manufacturers due to an insufficient number of competing manufacturers of that controlled substance), and provided further that granting the applicant's registration (and thereby increasing the total number of manufacturers) is consistent with maintenance of effective controls against diversion, DEA is not required to deny the application solely because the number of manufacturers currently registered can adequately supply the market for that controlled substance in terms of quantity and quality of product.'') (emphasis in original).

[112] *See also* 21 U.S.C. 958(a) (a registration to import a schedule I or II controlled substance must be consistent with the public interest, based on consideration of the six criteria of § 823(a)). Further, 21 U.S.C. 952(a)(2)(B) requires a person seeking to become registered to import a schedule I or II controlled substance to demonstrate not only that competition among domestic manufacturers of the particular substance is inadequate but also that competition ''will not be rendered adequate by the registration of additional [domestic] manufacturers under section 823.'' Thus, an applicant to import a schedule I or II substance must make an additional showing beyond that required for an applicant to bulk manufacture such a substance. However, as § 823(a) indicates, both the applicant seeking to import and the applicant seeking to bulk manufacture are subject to the same 823(a) criteria, including the same determination under paragraph 823(a)(1) regarding the adequacy of competition.

[113] That the existing supply of cocaine hydrochloride was adequate within the meaning of paragraph 823(a)(1) was not in dispute in *Roxane*.

[114] As indicated above, because *Roxane* involved an application to import a schedule II controlled substance, the applicant was required demonstrate that competition was inadequate not only within the meaning of paragraph 823(a)(1), but also within the meaning of 21 U.S.C. 952(a)(2)(B). As to the latter, the DEA regulations require consideration of the factors set forth in 21 CFR 1301.34(d). These factors are specifically designed to assess competition in the context of an import application. However, as § 823(a) indicates, an application to import a schedule I or II controlled substance must also be evaluated under paragraph 823(a)(1) regarding the adequacy of competition.

[115] As Johnson Matthey had applied to import narcotic raw materials, the application also had to be evaluated under 21 U.S.C. 952(a)(1).

reconcilable with the text of the statute. That DEA withdrew the 1974 proposed rule a month after publishing these objections (39 FR 26031 (1974)) is consistent with the conclusion that the proposed rule could not be firmly reconciled with the statute.[116]

Thus, the *Johnson Matthey* final order appears to have been flawed both procedurally (by relying entirely upon a proposed rule that was withdrawn) and substantively (by relying on an interpretation of paragraph 823(a)(1) that is, in my view, difficult to reconcile with the statutory text). Nonetheless, it must be recognized that the *Johnson Matthey* final order was upheld on appeal in *Noramco* v. *DEA*, 375 F.3d 1148 (D.C. Cir. 2004). Examining the *Noramco* decision is therefore warranted. Before doing so, however, it is necessary to review another DEA final order that was issued shortly after *Johnson Matthey*.

In *Penick Corporation Inc.*, 68 FR 6947 (2003), DEA evaluated the paragraph 823(a)(1) issue in a different manner than it had done eight months earlier in the *Johnson Matthey* final order. As in *Roxane* and *Johnson Matthey*, Penick had applied with DEA to become registered as, among other things, an importer of schedule II controlled substances. Also as in *Roxane* and *Johnson Matthey*, the applicant's competitors (who were already in the market as registered importers of the same substances) objected to the proposed registration contending, among other things, that the applicant had failed to demonstrate the existence of inadequate competition within the meaning of paragraph 823(a)(1). However, in contrast to the *Johnson Matthey* final order, the *Penick* final order did not disregard the competition issue as irrelevant. Nor did the *Penick* final order mention the 1974 proposed rule (that was subsequently withdrawn), which was relied upon in *Johnson Matthey*. Rather, the *Penick* final order did examine the evidence presented on the competition issue and ultimately concluded: ''Having found that the market is not adequately competitive, the Deputy Administrator concludes that this factor weighs in favor of granting Penick's application, even though *Noramco* and Mallinckrodt are capable of maintaining an adequate and uninterrupted supply.'' [117] The *Penick* final order did not address the *Johnson Matthey* final order or why the two final orders took a differing approach as to the competition issue.

Both the *Johnson Matthey* final order and the *Penick* final order were challenged by a competitor (Noramco) in *Noramco* v. *DEA*. The United States Court of Appeals for the D.C. Circuit consolidated Noramco's two petitions for review into one appellate proceeding. With respect to the *Johnson Matthey* final order, Noramco contended that DEA erred by failing to consider the adequacy of competition and limit the number of importers to that which can produce an adequate and uninterrupted supply under adequately competitive conditions as paragraph 823(a)(1) requires. The D.C. Circuit panel reviewed DEA's decision ''under the familiar two-step *Chevron* framework.'' [118] Under this framework, if the reviewing court finds that the statute does not directly address ''the precise question at issue'' (step one), the court must sustain the agency's interpretation if it is ''based on a permissible construction of the statute'' (step two).[119] The court of appeals in *Noramco* upheld the *Johnson Matthey* final order, under *Chevron* step two, finding that DEA's decision to disregard competition to be a ''permissible interpretation'' of paragraph 823(a)(1).[120] Simultaneously, the court of appeals in *Noramco* upheld the *Penick* final order after reciting how DEA did consider the competition issue as paragraph 823(a)(1) directs. That the final orders in *Johnson Matthey* and *Penick* were inconsistent with one another as to the interpretation of paragraph 823(a)(1) was rejected by the court of appeals as a basis for reversal.[121]

It is especially important to note here that, under *Chevron* step two, ''[t]he court need not conclude that the agency construction was the only one it permissibly could have adopted to uphold the construction, or even the reading the court would have reached if the question initially had arisen in a judicial proceeding.'' [122] Accordingly, when the court in *Noramco* upheld the final order in *Johnson Matthey,* it was not offering an opinion whether that final order had interpreted paragraph 823(a)(1) in the best manner; rather, the court was merely stating that DEA (being owed the measure of *Chevron* deference accorded to an agency that administers a statute) had put forth a ''permissible interpretation'' of the statute. This point is underscored by the fact that the court in *Noramco* also upheld the *Penick* final order, which interpreted paragraph 823(a)(1) in a notably different manner than did the *Johnson Matthey* final order.

Thus, nothing in the *Noramco* decision constrains DEA from concluding, as I now do, that the most sound reading of the text of paragraph 823(a)(1) is that which requires the agency to consider limiting the number of bulk manufacturers and importers of schedule I and II controlled substances to that which can produce an adequate and uninterrupted supply of a given substance under adequately competitive conditions.

In 2006, another final order was issued involving the competition issue. In *Chattem Chemicals, Inc.*, 71 FR 9834 (2006), *petition for review denied, Penick Corp., Inc.* v. *DEA*, 491 F3d 483 (D.C. Cir. 2007), the applicant sought to become registered to import a schedule II controlled substance, just as Roxane, Johnson Matthey, and Penick had previously done. In the final order, which I issued, I followed the *Johnson Matthey* approach of declining to consider the adequacy of competition or supply. In doing so, I expressly noted that this approach had been ''approved by the appellate court in *Noramco*.'' [123] Upon review of the *Chattem* final order, the court of appeals likewise reaffirmed that, under *Noramco*, this approach of not considering adequacy of competition was a permissible reading of the statute. *Penick*, 491 F.3d at 491 n.11. However, for the reasons discussed at length above, I now believe that this approach—though deemed permissible upon *Chevron* review—must be rejected in favor of that which more accurately follows the text of the statute; i.e., the approach that was taken in *Roxane* and *Penick* of considering limiting the number of bulk manufacturers and importers of a given schedule I or II controlled substance to that which can produce an adequate and uninterrupted supply under adequately competitive conditions.[124] In addition

[116] The notice of withdrawal of the proposed rule stated that DEA was in the midst of reviewing and revising all the agency regulations in their entirety and that the proposed amendments regarding the competition issue ''are withdrawn so that all proposed changes to the regulations may be published together.'' However, DEA never again proposed to amend its regulations to eliminate the consideration—that paragraph 823(a)(1) mandates—of adequacy of supply and competition.

[117] 68 FR at 6950.

[118] 375 F.3d at 1152 (citing *Chevron U.S.A, Inc.* v. *Natural Res. Def. Council*, 467 U.S. 837, 842–43 (1983)).

[119] *Id.*

[120] 375 F.3d at 1153.

[121] 375 F.3d at 1157 n.8.

[122] 467 U.S. at 843 n.11.

[123] 71 FR at 9838.

[124] While it is certainly preferable that an agency interpret a statutory provision that it administers in a consistent manner throughout the agency's existence, the head of an agency ''is not estopped from changing a view she believes to have been grounded upon a mistaken legal interpretation.'' *See Thomas Jefferson University* v. *Shalala*, 512 U.S. 504, 517 (1994); *cf. Chevron*, 467 U.S. at 863 (''The fact that the agency has from time to time

to finding this interpretation to be that which most closely mirrors the text of the statute, I believe that, upon consideration of the legislative history and treaty considerations discussed above, this interpretation most effectively achieves the principles underlying the statutory text: Balancing the overarching goal of preventing the United States from being a source of domestic and international diversion by limiting the number of bulk manufacturers of schedule I and II controlled substances with the desire to ensure a level of competition adequate to prevent legitimate purchasers of these substances from being charged unreasonable prices.[125] The alternative interpretation, though found to be permissible, does not give full effect to these principles and provides no mechanism to prevent the proliferation of bulk suppliers of schedule I and II controlled substances beyond that necessary to adequately supply the legitimate United States demand for these materials under adequately competitive conditions. It is axiomatic that the proliferation of suppliers of bulk schedule I and II controlled substances heightens the risk of oversupply, which in turn increases the risk of diversion. The alternative interpretation, therefore, does not effectuate the statute and its underlying purposes as well as the interpretation followed in this final order.

D. Summary of the Discussion

For the reasons indicated above, I have determined that Respondent's proposed registration is inconsistent with United States obligations under the Single Convention and with the public interest based on a consideration of the factors set forth in 21 U.S.C. 823(a). With respect to the Single Convention, Respondent's desire to become registered in order to achieve MAPS's goal of ending the Federal Government's monopoly on the wholesale distribution of marijuana cannot be squared with the requirement under the Convention that there be precisely such a monopoly. With respect to the public interest, Respondent's failure to demonstrate that the longstanding existing system in the United States of producing and distributing research-grade marijuana under the oversight of HHS and NIDA is inadequate within the meaning of 21 U.S.C. 823(a)(1) weighs heavily against granting his application. Also with respect to the public interest, the admitted conduct relating to controlled substances of Respondent's sponsor, Mr. Doblin (in particular, Mr. Doblin's past and ongoing conduct relating to marijuana) is unacceptable for anyone seeking to have a prominent role in overseeing the controlled substance activities of a DEA registrant—especially where the registrant's proposed activities are the manufacture and distribution of the very drug marijuana. In sum, there are three independent grounds, any of which, standing alone, provide a sufficient (indeed, compelling) legal basis for denying Respondent's application.

Order

Pursuant to the authority vested in me by 21 U.S.C. 823(a), as well as 28 CFR 0.100(b) & 0.104, appendix to subpart R, sec. 7(a), I order that the application of Lyle E. Craker, Ph.D., for a DEA certificate of registration as a manufacturer of marijuana be, and hereby is, denied. This order is effective February 13, 2009.

Dated: January 7, 2009.

Michele M. Leonhart,

Deputy Administrator.

[FR Doc. E9–521 Filed 1–13–09; 8:45 am]

BILLING CODE 4410–09–P

changed its interpretation of [a statutory provision] does not * * * lead us to conclude that no deference should be accorded the agency's interpretation of the statute.'').

[125] DEA has never invoked the ''limiting'' language of paragraph 823(a)(1) as a basis to revoke the registration of an existing bulk manufacturer that is currently utilizing its registration to supply the market for a given schedule I or II controlled substance, and this final order should not be construed as suggesting a departure from such practice.

DEPARTMENT OF JUSTICE

Foreign Claims Settlement Commission of the United States

Privacy Act of 1974; System of Records

AGENCY: Foreign Claims Settlement Commission of the United States.

ACTION: Notice of a New System of Records.

SUMMARY: Pursuant to the Privacy Act of 1974 (5 U.S.C. 552a), the Foreign Claims Settlement Commission (Commission), Department of Justice, proposes to establish a new system of records to enable the Commission to carry out its statutory responsibility to determine the validity and amount of the claims submitted to the Commission against Libya. The Claims Against Libya System will include documentation provided by the claimant as well as background material that will assist the Commission in the processing of their claims. The system will also include the final decision of the Commission regarding the claim.

DATES: In accordance with 5 U.S.C. 552a(e)(4) and (11), the public is given a 30-day period in which to comment; and the Office of Management and Budget (OMB), which has oversight responsibility under the Act, requires a 40-day period in which to conclude its review of the system. Accordingly, please submit any comments by February 17, 2009.

ADDRESSES: The public, OMB, and Congress are invited to submit any comments to the Foreign Claims Settlement Commission of the United States, 600 E Street, NW., Suite 6002, Washington, DC 20579.

FOR FURTHER INFORMATION CONTACT: The Administrative Office, Foreign Claims Settlement Commission, U.S. Department of Justice, 600 E Street, NW., Suite 6002, Washington, DC 20579, or by telephone at 202–616–6975. In accordance with 5 U.S.C. 552a(r), the Department has provided a report to OMB and the Congress on the new system of records.

Dated: January 9, 2009.

Mauricio Tamargo,

Chairman.

JUSTICE/FCSC–29

SYSTEM NAME:

Libya, Claims Against.

SYSTEM LOCATION:

Offices of the Foreign Claims Settlement Commission, 600 E Street, NW., Suite 6002, Washington, DC 20579.

CATEGORIES OF INDIVIDUALS COVERED BY THE SYSTEM:

Persons with claims against Libya covered by the August 14, 2008 Claims Settlement Agreement Between the United States of America and the Great Socialist People's Libyan Arab Jamahiriya and referred by the Department of State to the Foreign Claims Settlement Commission.

CATEGORIES OF RECORDS IN THE SYSTEM:

Claim information, including name and address of claimant and representative, if any; date and place of birth or naturalization; nature of claim; description of loss or injury including medical records; and other evidence establishing entitlement to compensation.

AUTHORITY FOR MAINTENANCE OF THE SYSTEM:

Authority to establish and maintain this system is contained in 5 U.S.C. 301 and 44 U.S.C. 3101, which authorize the Chairman of the Commission to create

FEDERAL REGISTER

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Part IV

Department of Justice

Drug Enforcement Administration

21 CFR Chapter II

Denial of Petition To Initiate Proceedings To Reschedule Marijuana; Proposed Rule

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Chapter II

[Docket No. DEA–352N]

Denial of Petition To Initiate Proceedings To Reschedule Marijuana

AGENCY: Drug Enforcement Administration (DEA), Department of Justice.

ACTION: Denial of petition to initiate proceedings to reschedule marijuana.

SUMMARY: By letter dated June 21, 2011, the Drug Enforcement Administration (DEA) denied a petition to initiate rulemaking proceedings to reschedule marijuana.[1] Because DEA believes that this matter is of particular interest to members of the public, the agency is publishing below the letter sent to the petitioner (denying the petition), along with the supporting documentation that was attached to the letter.

FOR FURTHER INFORMATION CONTACT: Imelda L. Paredes, Office of Diversion Control, Drug Enforcement Administration, 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone (202) 307–7165.

SUPPLEMENTARY INFORMATION:

June 21, 2011.

Dear Mr. Kennedy:

On October 9, 2002, you petitioned the Drug Enforcement Administration (DEA) to initiate rulemaking proceedings under the rescheduling provisions of the Controlled Substances Act (CSA). Specifically, you petitioned DEA to have marijuana removed from schedule I of the CSA and rescheduled as cannabis in schedule III, IV or V.

You requested that DEA remove marijuana from schedule I based on your assertion that:

(1) Cannabis has an accepted medical use in the United States;

(2) Cannabis is safe for use under medical supervision;

(3) Cannabis has an abuse potential lower than schedule I or II drugs; and

(4) Cannabis has a dependence liability that is lower than schedule I or II drugs.

In accordance with the CSA rescheduling provisions, after gathering the necessary data, DEA requested a scientific and medical evaluation and scheduling recommendation from the Department of Health and Human Services (DHHS). DHHS concluded that marijuana has a high potential for abuse, has no accepted medical use in the United States, and lacks an acceptable level of safety for use even under medical supervision. Therefore, DHHS recommended that marijuana remain in schedule I. The scientific and medical evaluation and scheduling recommendation that DHHS submitted to DEA is attached hereto.

Based on the DHHS evaluation and all other relevant data, DEA has concluded that there is no substantial evidence that marijuana should be removed from schedule I. A document prepared by DEA addressing these materials in detail also is attached hereto. In short, marijuana continues to meet the criteria for schedule I control under the CSA because:

(1) *Marijuana has a high potential for abuse.* The DHHS evaluation and the additional data gathered by DEA show that marijuana has a high potential for abuse.

(2) *Marijuana has no currently accepted medical use in treatment in the United States.* According to established case law, marijuana has no ''currently accepted medical use'' because: The drug's chemistry is not known and reproducible; there are no adequate safety studies; there are no adequate and well-controlled studies proving efficacy; the drug is not accepted by qualified experts; and the scientific evidence is not widely available.

(3) *Marijuana lacks accepted safety for use under medical supervision.* At present, there are no U.S. Food and Drug Administration (FDA)-approved marijuana products, nor is marijuana under a New Drug Application (NDA) evaluation at the FDA for any indication. Marijuana does not have a currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions. At this time, the known risks of marijuana use have not been shown to be outweighed by specific benefits in well-controlled clinical trials that scientifically evaluate safety and efficacy.

You also argued that cannabis has a dependence liability that is lower than schedule I or II drugs. Findings as to the physical or psychological dependence of a drug are only one of eight factors to be considered. As discussed further in the attached documents, DHHS states that long-term, regular use of marijuana can lead to physical dependence and withdrawal following discontinuation as well as psychic addiction or dependence.

The statutory mandate of 21 U.S.C. 812(b) is dispositive. Congress established only one schedule, schedule I, for drugs of abuse with ''no currently accepted medical use in treatment in the United States'' and ''lack of accepted safety for use under medical supervision.'' 21 U.S.C. 812(b).

Accordingly, and as set forth in detail in the accompanying DHHS and DEA documents, there is no statutory basis under the CSA for DEA to grant your petition to initiate rulemaking proceedings to reschedule marijuana. Your petition is, therefore, hereby denied.

Sincerely,

Michele M. Leonhart,

Administrator.

Attachments:

Marijuana. Scheduling Review Document: Eight Factor Analysis

Basis for the recommendation for maintaining marijuana in schedule I of the Controlled Substances Act

Date: June 30, 2011

Michele M. Leonhart

Administrator

Department of Health and Human Services,

Office of the Secretary Assistant Secretary for Health, Office of Public Health and Science Washington, D.C. 20201.

December 6, 2006.

The Honorable Karen P. Tandy

Administrator, Drug Enforcement Administration, U.S. Department of Justice, Washington, D.C. 20537

Dear Ms. Tandy:

This is in response to your request of July 2004, and pursuant to the Controlled Substances Act (CSA), 21 U.S.C. 811(b), (c), and (f), the Department of Health and Human Services (DHHS) recommends that marijuana continue to be subject to control under Schedule I of the CSA.

Marijuana is currently controlled under Schedule I of the CSA. Marijuana continues to meet the three criteria for placing a substance in Schedule I of the CSA under 21 U.S.C. 812(b)(l). As discussed in the attached analysis, marijuana has a high potential for abuse, has no currently accepted medical use in treatment in the United States, and has a lack of an accepted level of safety for use under medical supervision. Accordingly, HHS recommends that marijuana continue to be subject to control under Schedule I of the CSA. Enclosed is a document prepared by FDA's Controlled Substance Staff that is the basis for this recommendation.

Should you have any questions regarding this recommendation, please contact Corinne P. Moody, of the Controlled Substance Staff, Center for Drug Evaluation and Research. Ms. Moody can be reached at 301–827–1999.

Sincerely yours,

John O. Agwunobi,

Assistant Secretary for Health.

Enclosure:

[1] Note that ''marihuana'' is the spelling originally used in the Controlled Substances Act (CSA). This document uses the spelling that is more common in current usage, ''marijuana.''

Basis for the Recommendation for Maintaining Marijuana in Schedule I of the Controlled Substances Act

BASIS FOR THE RECOMMENDATION FOR MAINTAINING MARIJUANA IN SCHEDULE I OF THE CONTROLLED SUBSTANCES ACT

On October 9, 2002, the Coalition for Rescheduling Cannabis (hereafter known as the Coalition) submitted a petition to the Drug Enforcement Administration (DEA) requesting that proceedings be initiated to repeal the rules and regulations that place marijuana in Schedule I of the Controlled Substances Act (CSA). The petition contends that cannabis has an accepted medical use in the United States, is safe for use under medical supervision, and has an abuse potential and a dependency liability that is lower than Schedule I or II drugs. The petition requests that marijuana be rescheduled as ''cannabis'' in either Schedule III, IV, or V of the CSA. In July 2004, the DEA Administrator requested that the Department of Health and Human Services (HHS) provide a scientific and medical evaluation of the available information and a scheduling recommendation for marijuana, in accordance with the provisions of 21 U.S.C. 811(b).

In accordance with 21 U.S.C. 811(b), DEA has gathered information related to the control of marijuana (*Cannabis sativa*) [2] under the CSA. Pursuant to 21 U.S.C. 811(b), the Secretary is required to consider in a scientific and medical evaluation eight factors determinative of control under the CSA. Following consideration of the eight factors, if it is appropriate, the Secretary must make three findings to recommend scheduling a substance in the CSA. The findings relate to a substance's abuse potential, legitimate medical use, and safety or dependence liability.

Administrative responsibilities for evaluating a substance for control under the CSA are performed by the Food and Drug Administration (FDA), with the concurrence of the National Institute on Drug Abuse (NIDA), as described in the Memorandum of Understanding (MOU) of March 8, 1985 (50 FR 9518–20).

In this document, FDA recommends the continued control of marijuana in Schedule I of the CSA. Pursuant to 21 U.S.C. 811(c), the eight factors pertaining to the scheduling of marijuana are considered below.

1. ITS ACTUAL OR RELATIVE POTENTIAL FOR ABUSE

The first factor the Secretary must consider is marijuana's actual or relative potential for abuse. The term ''abuse'' is not defined in the CSA. However, the legislative history of the CSA suggests the following in determining whether a particular drug or substance has a potential for abuse:

a. Individuals are taking the substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community.

b. There is a significant diversion of the drug or substance from legitimate drug channels.

c. Individuals are taking the substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such substances.

d. The substance is so related in its action to a substance already listed as having a potential for abuse to make it likely that it will have the same potential for abuse as such substance, 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.

Comprehensive Drug Abuse Prevention and Control Act of 1970, H.R. Rep. No. 91–1444, 91st Cong., Sess. 1 (1970) reprinted in U.S.C.C.A.N. 4566, 4603.

In considering these concepts in a variety of scheduling analyses over the last three decades, the Secretary has analyzed a range of factors when assessing the abuse liability of a substance. These factors have included the prevalence and frequency of use in the general public and in specific sub-populations, the amount of the material that is available for illicit use, the ease with which the substance may be obtained or manufactured, the reputation or status of the substance ''on the street,'' as well as evidence relevant to population groups that may be at particular risk.

Abuse liability is a complex determination with many dimensions. There is no single test or assessment procedure that, by itself, provides a full and complete characterization. Thus, no single measure of abuse liability is ideal. Scientifically, a comprehensive evaluation of the relative abuse potential of a drug substance can include consideration of the drug's receptor binding affinity, preclinical pharmacology, reinforcing effects, discriminative stimulus effects, dependence producing potential, pharmacokinetics and route of administration, toxicity, assessment of the clinical efficacy-safety database relative to actual abuse, clinical abuse liability studies, and the public health risks following introduction of the substance to the general population. It is important to note that abuse may exist independent of a state of tolerance or physical dependence, because drugs may be abused in doses or in patterns that do not induce these phenomena. Animal data, human data, and epidemiological data are all used in determining a substance's abuse liability. Epidemiological data can also be an important indicator of actual abuse. Finally, evidence of clandestine production and illicit trafficking of a substance are also important factors.

a. There is evidence that individuals are taking the substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community.

Marijuana is a widely abused substance. The pharmacology of the psychoactive constituents of marijuana, including delta^{9}-tetrahydrocannabinol (delta^{9}-THC), the primary psychoactive ingredient in marijuana, has been studied extensively in animals and humans and is discussed in more detail below in Factor 2, ''Scientific Evidence of its Pharmacological Effects, if Known.'' Data on the extent of marijuana abuse are available from HHS through NIDA and the Substance Abuse and Mental Health Services Administration (SAMHSA). These data are discussed in detail under Factor 4, ''Its History and Current Pattern of Abuse;'' Factor 5, ''The Scope, Duration, and Significance of Abuse;'' and Factor 6, ''What, if any, Risk There is to the Public Health?''

According to SAMHSA's 2004 National Survey on Drug Use and Health (NSDUH; the database formerly known as the National Household Survey on Drug Abuse (NHSDA)), the latest year for which complete data are available, 14.6 million Americans have used marijuana in the past month. This is an increase of 3.4 million individuals since 1999, when 11.2 million individuals reported using marijuana monthly. (See the discussion of NSDUH data under Factor 4).

The Drug Abuse Warning Network (DAWN), sponsored by SAMHSA, is a national probability survey of U.S. hospitals with emergency departments (EDs) designed to obtain information on ED visits in which recent drug use is implicated; 2003 is the latest year for which complete data are available. Marijuana was involved in 79,663 ED visits (13 percent of drug-related visits). There are a number of risks resulting from both acute and chronic use of marijuana which are discussed in full below under Factors 2 and 6.

b. There is significant diversion of the substance from legitimate drug channels.

At present, cannabis is legally available through legitimate channels for research purposes only and thus has a limited potential for diversion. In addition, the lack of significant diversion of investigational supplies may result from the ready availability of illicit cannabis of equal or greater quality. The magnitude of the demand for illicit marijuana is evidenced by DEA/Office of National Drug Control Policy (ONDCP) seizure statistics. Data on marijuana seizures can often highlight trends in the overall trafficking patterns. DEA's Federal-Wide Drug Seizure System (FDSS) provides information on total federal drug seizures. FDSS reports total federal seizures of 2,700,282 pounds of marijuana in 2003, the latest year for which complete data are available (DEA, 2003). This represents nearly a doubling of marijuana seizures since 1995, when 1,381,107 pounds of marijuana were seized by federal agents.

c. Individuals are taking the substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such substances.

[2] The CSA defines marijuana as the following: all parts of the plant Cannabis Sativa L., whether growing or not; the seeds thereof; the resin extracted from any part of such plant; and every compound, manufacture, salt, derivative, mixture, or preparation of such plant, its seeds or resin. Such term does not include the mature stalks of such plant, fiber produced from such stalks, oil or cake made from the seeds of such plant, any other compound, manufacture, salt, derivative, mixture, or preparation of such mature stalks (except the resin extracted there from), fiber, oil, or cake, or the sterilized seed of such plant which is incapable of germination (21 U.S.C. 802(16)).

The 2004 NSDUH data show that 14.6 million American adults use marijuana on a monthly basis (SAMHSA, 2004), confirming that marijuana has reinforcing properties for many individuals. The FDA has not evaluated or approved a new drug application (NDA) for marijuana for any therapeutic indication, although several investigational new drug (IND) applications are currently active. Based on the large number of individuals who use marijuana, it can be concluded that the majority of individuals using cannabis do so on their own initiative, not on the basis of medical advice from a practitioner licensed to administer the drug in the course of professional practice.

d. The substance is so related in its action to a substance already listed as having a potential for abuse to make it likely that it will have the same potential for abuse as such substance, 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.

The primary psychoactive compound in botanical marijuana is delta^9-THC. Other cannabinoids also present in the marijuana plant likely contribute to the psychoactive effects.

There are two drug products containing cannabinoid compounds that are structurally related to the active components in marijuana. Both are controlled under the CSA. Marinol is a Schedule III drug product containing synthetic delta^9-THC, known generically as dronabinol, formulated in sesame oil in soft gelatin capsules. Dronabinol is listed in Schedule I. Marinol was approved by the FDA in 1985 for the treatment of two medical conditions: nausea and vomiting associated with cancer chemotherapy in patients that had failed to respond adequately to conventional anti-emetic treatments, and for the treatment of anorexia associated with weight loss in patients with acquired immunodeficiency syndrome or AIDS. Cesamet is a drug product containing the Schedule II substance, nabilone, that was approved for marketing by the FDA in 1985 for the treatment of nausea and vomiting associated with cancer chemotherapy. All other structurally related cannabinoids in marijuana are already listed as Schedule I drugs under the CSA.

2. SCIENTIFIC EVIDENCE OF ITS PHARMACOLOGICAL EFFECTS, IF KNOWN

The second factor the Secretary must consider is scientific evidence of marijuana's pharmacological effects. There are abundant scientific data available on the neurochemistry, toxicology, and pharmacology of marijuana. This section includes a scientific evaluation of marijuana's neurochemistry, pharmacology, and human and animal behavioral, central nervous system, cognitive, cardiovascular, autonomic, endocrinological, and immunological system effects. The overview presented below relies upon the most current research literature on cannabinoids.

Neurochemistry and Pharmacology of Marijuana

Some 483 natural constituents have been identified in marijuana, including approximately 66 compounds that are classified as cannabinoids (Ross and El Sohly, 1995). Cannabinoids are not known to exist in plants other than marijuana, and most of the cannabinoid compounds that occur naturally have been identified chemically. Delta^9-THC is considered the major psychoactive cannabinoid constituent of marijuana (Wachtel et al., 2002). The structure and function of delta^9-THC was first described in 1964 by Gaoni and Mechoulam.

The site of action of delta^9-THC and other cannabinoids was verified with the cloning of cannabinoid receptors, first from rat brain tissue (Matsuda et al., 1990) and then from human brain tissue (Gerard et al., 1991). Two cannabinoid receptors, CB_1 and CB_2, have subsequently been characterized (Piomelli, 2005).

Autoradiographic studies have provided information on the distribution of cannabinoid receptors. CB_1 receptors are found in the basal ganglia, hippocampus, and cerebellum of the brain (Howlett et al., 2004) as well as in the immune system. It is believed that the localization of these receptors may explain cannabinoid interference with movement coordination and effects on memory and cognition. The concentration of CB_1 receptors is considerably lower in peripheral tissues than in the central nervous system (Henkerham et al., 1990 and 1992).

CB_2 receptors are found primarily in the immune system, predominantly in B lymphocytes and natural killer cells (Bouaboula et al., 1993). It is believed that the CB_2-type receptor is responsible for mediating the immunological effects of cannabinoids (Galiegue et al., 1995).

However, CB_2 receptors also have recently been localized in the brain, primarily in the cerebellum and hippocampus (Gong et al., 2006).

The cannabinoid receptors belong to the family of G-protein-coupled receptors and present a typical seven transmembrane-spanning domain structure. Many G-protein-coupled receptors are linked to adenylate cyclase either positively or negatively, depending on the receptor system. Cannabinoid receptors are linked to an inhibitory G-protein (Gi), so that when the receptor is activated, adenylate cyclase activity is inhibited, which prevents the conversion of adenosine triphosphate (ATP)to the second messenger cyclic adenosine monophosphate (cAMP). Examples of inhibitory-coupled receptors include: opioid, muscarinic cholinergic, alpha $_2$-adrenoreceptors, dopamine (D_2), and serotonin ($5\text{–}HT_1$).

It has been shown that CB_1, but not CB_2 receptors, inhibit N- and P/Q type calcium channels and activate inwardly rectifying potassium channels (Mackie et al., 1995; Twitchell et al., 1997). Inhibition of the N-type calcium channels decreases neurotransmitter release from several tissues and this may be the mechanism by which cannabinoids inhibit acetylcholine, norepinephrine, and glutamate release from specific areas of the brain. These effects might represent a potential cellular mechanism underlying the antinociceptive and psychoactive effects of cannabinoids (Ameri, 1999). When cannabinoids are given subacutely to rats, there is a down-regulation of CB_1 receptors, as well as a decrease in GTPgammaS binding, the second messenger system coupled to CB_1 receptors (Breivogel et al., 2001).

Delta^9-THC displays similar affinity for CB_1 and CB_2 receptors but behaves as a weak agonist for CB_2 receptors, based on inhibition of adenylate cyclase. The identification of synthetic cannabinoid ligands that selectively bind to CB_2 receptors but do not have the typical delta^9-THC-like psychoactive properties suggests that the psychotropic effects of cannabinoids are mediated through the activation of CB_1-receptors (Hanus et al., 1999). Naturally-occurring cannabinoid agonists, such as delta^9-THC, and the synthetic cannabinoid agonists such as WIN–55,212–2 and CP–55,940 produce hypothermia, analgesia, hypoactivity, and cataplexy in addition to their psychoactive effects.

In 2000, two endogenous cannabinoid receptor agonists, anandamide and arachidonyl glycerol (2–AG), were discovered. Anandamide is a low efficacy agonist (Breivogel and Childers, 2000), 2–AG is a highly efficacious agonist (Gonsiorek et al., 2000). Cannabinoid endogenous ligands are present in central as well as peripheral tissues. The action of the endogenous ligands is terminated by a combination of uptake and hydrolysis. The physiological role of endogenous cannabinoids is an active area of research (Martin et al., 1999).

Progress in cannabinoid pharmacology, including further characterization of the cannabinoid receptors, isolation of endogenous cannabinoid ligands, synthesis of agonists and antagonists with variable affinity, and selectivity for cannabinoid receptors, provide the foundation for the potential elucidation of cannabinoid-mediated effects and their relationship to psychomotor disorders, memory, cognitive functions, analgesia, anti-emesis, intraocular and systemic blood pressure modulation, bronchodilation, and inflammation.

Central Nervous System Effects

Human Physiological and Psychological Effects

Subjective Effects

The physiological, psychological, and behavioral effects of marijuana vary among individuals. Common responses to cannabinoids, as described by Adams and Martin (1996) and others (Hollister, 1986 and 1988; Institute of Medicine, 1982) are listed below:

1) Dizziness, nausea, tachycardia, facial flushing, dry mouth, and tremor initially

2) Merriment, happiness, and even exhilaration at high doses

3) Disinhibition, relaxation, increased sociability, and talkativeness

4) Enhanced sensory perception, giving rise to increased appreciation of music, art, and touch

5) Heightened imagination leading to a subjective sense of increased creativity
6) Time distortions
7) Illusions, delusions, and hallucinations, especially at high doses
8) Impaired judgment, reduced co-ordination and ataxia, which can impede driving ability or lead to an increase in risk-taking behavior
9) Emotional lability, incongruity of affect, dysphoria, disorganized thinking, inability to converse logically, agitation, paranoia, confusion, restlessness, anxiety, drowsiness, and panic attacks, especially in inexperienced users or in those who have taken a large dose
10) Increased appetite and short-term memory impairment

These subjective responses to marijuana are pleasurable to many humans and are associated with drug-seeking and drug-taking (Maldonado, 2002).

The short-term perceptual distortions and psychological alterations produced by marijuana have been characterized by some researchers as acute or transient psychosis (Favrat et al., 2005). However, the full response to cannabinoids is dissimilar to the DSM–IV–TR criteria for a diagnosis of one of the psychotic disorders (DSM–IV–TR, 2000).

As with many psychoactive drugs, an individual's response to marijuana can be influenced by that person's medical/psychiatric history and history with drugs. Frequent marijuana users (greater than 100 times) were better able to identify a drug effect from low dose delta^{9}-THC than infrequent users (less than 10 times) and were less likely to experience sedative effects from the drug (Kirk and deWit, 1999). Dose preferences have been demonstrated for marijuana in which higher doses (1.95 percent delta^{9}-THC) are preferred over lower doses (0.63 percent delta^{9}-THC) (Chait and Burke, 1994).

Behavioral Impairment

Acute administration of smoked marijuana impairs performance on tests of learning, associative processes, and psychomotor behavior (Block et al., 1992). These data demonstrate that the short-term effects of marijuana can interfere significantly with an individual's ability to learn in the classroom or to operate motor vehicles. Administration to human volunteers of 290 micrograms per kilogram (μg/kg) delta^{9}-THC in a smoked marijuana cigarette resulted in impaired perceptual motor speed and accuracy, two skills that are critical to driving ability (Kurzthaler et al., 1999). Similarly, administration of 3.95 percent delta^{9}-THC in a smoked marijuana cigarette increased disequilibrium measures, as well as the latency in a task of simulated vehicle braking, at a rate comparable to an increase in stopping distance of 5 feet at 60 mph (Liguori et al., 1998).

The effects of marijuana may not fully resolve until at least 1 day after the acute psychoactive effects have subsided, following repeated administration. Heishman et al. (1990) showed that impairment on memory tasks persists for 24 hours after smoking marijuana cigarettes containing 2.57 percent delta^{9}-THC. However, Fant et al. (1998) showed minimal residual alterations in subjective or performance measures the day after subjects were exposed to 1.8 percent or 3.6 percent smoked delta^{9}-THC.

The effects of chronic marijuana use have also been investigated. Marijuana did not appear to have residual effects on performance of a comprehensive neuropsychological battery when 54 monozygotic male twins (one of whom used marijuana, one of whom did not) were compared 1–20 years after cessation of marijuana use (Lyons et al., 2004). This conclusion is similar to the results from an earlier study of marijuana's effects on cognition in 1,318 participants over a 15-year period, where there was no evidence of long-term residual effects (Lyketsos et al., 1999). In contrast, Solowij et al. (2002) demonstrated that 51 long-term cannabis users did less well than 33 non-using controls or 51 short-term users on certain tasks of memory and attention, but users in this study were abstinent for only 17 hours at time of testing. A recent study noted that heavy, frequent cannabis users, abstinent for at least 24 hours, performed significantly worse than controls on verbal memory and psychomotor speed tests (Messinis et al, 2006).

Pope et al. (2003) reported that no differences were seen in neuropsychological performance in early- or late-onset users compared to non-using controls, after adjustment for intelligence quotient (IQ). In another cohort of chronic, heavy marijuana users, some deficits were observed on memory tests up to a week following supervised abstinence, but these effects disappeared by day 28 of abstinence (Harrison et al., 2002). The authors concluded that, ''cannabis-associated cognitive deficits are reversible and related to recent cannabis exposure, rather than irreversible and related to cumulative lifetime use.'' Other investigators have reported neuropsychological deficits in memory, executive functioning, psychomotor speed, and manual dexterity in heavy marijuana smokers who had been abstinent for 28 days (Bolla et al., 2002). A follow up study of heavy marijuana users noted decision-making deficits after 25 days of abstinence (Bolla et al., 2005). Finally, when IQ was contrasted in adolescents at 9–12 years and at 17–20 years, current heavy marijuana users showed a 4-point reduction in IQ in later adolescence compared to those who did not use marijuana (Fried et al., 2002).

Age of first use may be a critical factor in persistent impairment resulting from chronic marijuana use. Individuals with a history of marijuana-only use that began before the age of 16 were found to perform more poorly on a visual scanning task measuring attention than individuals who started using marijuana after age 16 (Ehrenreich et al., 1999). Kandel and Chen (2000) assert that the majority of early-onset marijuana users do not go on to become heavy users of marijuana, and those that do tend to associate with delinquent social groups.

Heavy marijuana users were contrasted with an age matched control group in a case-control design. The heavy users reported lower educational achievement and lower income than controls, a difference that persisted after confounding variables were taken into account. Additionally, the users also reported negative effects of marijuana use on cognition, memory, career, social life, and physical and mental health (Gruber et al., 2003).

Association with Psychosis

Extensive research has been conducted recently to investigate whether exposure to marijuana is associated with schizophrenia or other psychoses. While many studies are small and inferential, other studies in the literature utilize hundreds to thousands of subjects.

At present, the data do not suggest a causative link between marijuana use and the development of psychosis. Although some individuals who use marijuana have received a diagnosis of psychosis, most reports conclude that prodromal symptoms of schizophrenia appear prior to marijuana use (Schiffman et al., 2005). When psychiatric symptoms are assessed in individuals with chronic psychosis, the ''schizophrenic cluster'' of symptoms is significantly observed among individuals who do not have a history of marijuana use, while ''mood cluster'' symptoms are significantly observed in individuals who do have a history of marijuana use (Maremmani et al., 2004).

In the largest study evaluating the link between psychosis and drug use, 3 percent of 50,000 Swedish conscripts who used marijuana more than 50 times went on to develop schizophrenia (Andreasson et al., 1987). This was interpreted by the authors to suggest that marijuana use increased the risk for the disorder only among those individuals who were predisposed to develop psychosis. A similar conclusion was drawn when the prevalence of schizophrenia was modeled against marijuana use across birth cohorts in Australia between the years 1940 to 1979 (Degenhardt et al., 2003). Although marijuana use increased over time in adults born during the 4-decade period, there was not a corresponding increase in diagnoses for psychosis in these individuals. The authors conclude that marijuana may precipitate schizophrenic disorders only in those individuals who are vulnerable to developing psychosis. Thus, marijuana per se does not appear to induce schizophrenia in the majority of individuals who try or continue to use the drug.

However, as might be expected, the acute intoxication produced by marijuana does exacerbate the perceptual and cognitive deficits of psychosis in individuals who have been previously diagnosed with the condition (Schiffman et al., 2005; Hall et al., 2004; Mathers and Ghodse, 1992; Thornicroft, 1990). This is consistent with a 25-year longitudinal study of over 1,000 individuals who had a higher rate of experiencing some symptoms of psychosis (but who did not receive a diagnosis of psychosis) if they were daily marijuana users than if they were not (Fergusson et al., 2005). A shorter, 3-year longitudinal study with over 4,000 subjects similarly showed that psychotic symptoms, but not diagnoses, were more prevalent in subjects who used marijuana (van Os et al., 2002).

Additionally, schizophrenic individuals stabilized with antipsychotics do not respond differently to marijuana than healthy controls (D'Souza et al., 2005), suggesting that psychosis and/or antipsychotics do not biochemically alter cannabinoid systems in the brain.

Interestingly, cannabis use prior to a first psychotic episode appeared to spare neurocognitive deficits compared to patients who had not used marijuana (Stirling et al., 2005). Although adolescents diagnosed with a first psychotic episode used more marijuana than adults who had their first psychotic break, adolescents and adults had similar clinical outcomes 2 years later (Pencer et al., 2005).

Heavy marijuana users, though, do not perform differently than non-users on the Stroop task, a classic psychometric instrument that measures executive cognitive functioning. Since psychotic individuals do not perform the Stroop task well, alterations in executive functioning consistent with a psychotic profile were not apparent following chronic exposure to marijuana (Gruber and Yurgelun-Todd, 2005; Eldreth et al., 2004).

Alteration in Brain Structure

Although evidence suggests that some drugs of abuse can lead to changes in the density or structure of the brain in humans, there are currently no data showing that exposure to marijuana can induce such alterations. A recent comparison of long-term marijuana smokers to non-smoking control subjects using magnetic resonance imaging (MRI) did not reveal any differences in the volume of grey or white matter, in the hippocampus, or in cerebrospinal fluid volume, between the two groups (Tzilos et al., 2005).

Behavioral Effects of Prenatal Exposure

The impact of in utero marijuana exposure on performance in a series of cognitive tasks has been studied in children at different stages of development. However, since many marijuana users have abused other drugs, it is difficult to determine the specific impact of marijuana on prenatal exposure.

Differences in several cognitive domains distinguished the 4-year-old children of heavy marijuana users. In particular, memory and verbal measures are negatively associated with maternal marijuana use (Fried and Watkinson, 1987). Maternal marijuana use is predictive of poorer performance on abstract/visual reasoning tasks, although it is not associated with an overall lowered IQ in 3-year old children (Griffith et al., 1994). At 6 years of age, prenatal marijuana history is associated with an increase in omission errors on a vigilance task, possibly reflecting a deficit in sustained attention (Fried et al., 1992). When the effect of prenatal exposure in 9–12 year old children is analyzed, in utero marijuana exposure is negatively associated with executive function tasks that require impulse control, visual analysis, and hypothesis testing, and it is not associated with global intelligence (Fried et al., 1998).

Marijuana as a ''Gateway Drug''

The Institute of Medicine (IOM) reported that the widely held belief that marijuana is a ''gateway drug,'' leading to subsequent abuse of other illicit drugs, lacks conclusive evidence (Institute of Medicine, 1999). Recently, Fergusson et al. (2005) in a 25-year study of 1,256 New Zealand children concluded that use of marijuana correlates to an increased risk of abuse of other drugs, including cocaine and heroin. Other sources, however, do not support a direct causal relationship between regular marijuana and other illicit drug use. In general, such studies are selective in recruiting individuals who, in addition to having extensive histories of marijuana use, are influenced by myriad social, biological, and economic factors that contribute to extensive drug abuse (Hall and Lynskey, 2005). For most studies that test the hypothesis that marijuana causes abuse of harder drugs, the determinative measure of choice is any drug use, rather than DSM–IV–TR criteria for drug abuse or dependence (DSM–IV–TR, 2000).

According to Golub & Johnson (2001), the rate of progression to hard drug use by youth born in the 1970's, as opposed to youth born between World War II and the 1960's, is significantly decreased, although overall marijuana use among youth appears to be increasing. Nace et al. (1975) reported that even in the Vietnam-era soldiers who extensively abused marijuana and heroin, there was a lack of correlation of a causal relationship demonstrating marijuana use leading to heroin addiction. A recent longitudinal study of 708 adolescents demonstrated that early onset marijuana use did not lead to problematic drug use (Kandel and Chen, 2000). Similarly, among 2,446 adolescents followed longitudinally, cannabis dependence was uncommon but when it did occur, it was predicted primarily by parental death, deprived socio-economic status, and baseline use of illicit drugs other than marijuana (von Sydow et al., 2002).

Animal behavioral effects

Self-Administration

Self-administration is a method that assesses whether a drug produces rewarding effects that increase the likelihood of behavioral responses in order to obtain additional drug. Drugs that are self-administered by animals are likely to produce rewarding effects in humans, which is indicative of abuse liability. Generally, a good correlation exists between those drugs that are self-administered by rhesus monkeys and those that are abused by humans (Balster and Bigelow, 2003).

Interestingly, self-administration of hallucinogenic-like drugs, such as cannabinoids, lysergic acid diethylamide (LSD), and mescaline, has been difficult to demonstrate in animals (Yanagita, 1980). However, when it is known that humans voluntarily consume a particular drug (such as cannabis) for its pleasurable effects, the inability to establish self-administration with that drug in animals has no practical importance in the assessment of abuse potential. This is because the animal test is a predictor of human behavioral response in the absence of naturalistic data.

The experimental literature generally reports that naïve animals will not self-administer cannabinoids unless they have had previous experience with other drugs of abuse. However, when squirrel monkeys are first trained to self-administer intravenous cocaine, they will continue to bar-press at the same rate as when delta^9-THC is substituted for cocaine, at doses that are comparable to those used by humans who smoke marijuana (Tanda et al., 2000). This effect is blocked by the cannabinoid receptor antagonist, SR 141716. New studies show that monkeys without a history of any drug exposure can be successfully trained to self-administer delta^9-THC intravenously (Justinova et al., 2003). The maximal rate of responding is 4 µg/kg/injection, which is 2–3 times greater than that observed in previous studies using cocaine-experienced monkeys.

These data demonstrate that under specific pretreatment conditions, an animal model of reinforcement by cannabinoids now exists for future investigations. Rats will self-administer delta^9-THC when it is applied intracerebroventricularly (i.c.v.), but only at the lowest doses tested (0.01–0.02 µg/infusion) (Braida et al., 2004). This effect is antagonized by the cannabinoid antagonist SR141716 and by the opioid antagonist naloxone (Braida et al., 2004). Additionally, mice will self-administer WIN 55212, a CB_1 receptor agonist with a non-cannabinoid structure (Martellotta et al., 1998).

There may be a critical dose-dependent effect, though, since aversive effects, rather than reinforcing effects, have been described in rats that received high doses of WIN 55212 (Chaperon et al., 1998) or delta^9-THC (Sanudo-Pena et al., 1997). SR 141716 reversed these aversive effects in both studies.

Conditioned Place Preference

Conditioned place preference (CPP) is a less rigorous method than self-administration of determining whether drugs have rewarding properties. In this behavioral test, animals are given the opportunity to spend time in two distinct environments: one where they previously received a drug and one where they received a placebo. If the drug is reinforcing, animals will choose to spend more time in the environment paired with the drug than the one paired with the placebo, when both options are presented simultaneously.

Animals show CPP to delta^9-THC, but only at the lowest doses tested (0.075–0.75 mg/kg, i.p.) (Braida et al., 2004). This effect is antagonized by the cannabinoid antagonist, SR141716, as well as by the opioid antagonist, naloxone (Braida et al., 2004). However, SR141716 may be a partial agonist, rather than a full antagonist, since it is also able to induce CPP (Cheer et al., 2000). Interestingly, in knockout mice, animals without µ-opioid receptors do not develop CPP to delta^9-THC (Ghozland et al., 2002).

Drug Discrimination Studies

Drug discrimination is a method in which animals indicate whether a test drug produces physical or psychic perceptions similar to those produced by a known drug of abuse. In this test, an animal learns to press one bar when it receives the known drug of abuse and another bar when it receives placebo. A challenge session with the test drug determines which of the two

bars the animal presses more often, as an indicator of whether the test drug is like the known drug of abuse.

Animals, including monkeys and rats (Gold et al., 1992), as well as humans (Chait, 1988), can discriminate cannabinoids from other drugs or placebo. Discriminative stimulus effects of delta9-THC are pharmacologically specific for marijuana-containing cannabinoids (Balster and Prescott, 1992; Barnett et al., 1985; Browne and Weissman, 1981; Wiley et al., 1993; Wiley et al., 1995). Additionally, the major active metabolite of delta9-THC, 11-hydroxy-delta9-THC, also generalizes to the stimulus cue elicited by delta9-THC (Browne and Weissman, 1981). Twenty-two other cannabinoids found in marijuana also fully substitute for delta9-THC.

The discriminative stimulus effects of the cannabinoid group appear to provide unique effects because stimulants, hallucinogens, opioids, benzodiazepines, barbiturates, NMDA antagonists, and antipsychotics do not fully substitute for delta9-THC.

Tolerance and Physical Dependence

Tolerance is a state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time (American Academy of Pain Medicine, American Pain Society and American Society of Addiction Medicine consensus document, 2001). Physical dependence is a state of adaptation manifested by a drug class-specific withdrawal syndrome produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist (*ibid*).

The presence of tolerance or physical dependence does not determine whether a drug has abuse potential, in the absence of other abuse indicators such as rewarding properties. Many medications that are not associated with abuse or addiction, such as antidepressants, beta-blockers, and centrally acting antihypertensive drugs, can produce physical dependence and withdrawal symptoms after chronic use.

Tolerance to the subjective and performance effects of marijuana has not been demonstrated in studies with humans. For example, reaction times are not altered by acute administration of marijuana in long term marijuana users (Block and Wittenborn, 1985). This may be related to recent electrophysiological data showing that the ability of delta9-THC to increase neuronal firing in the ventral tegmental area (a region known to play a critical role in drug reinforcement and reward) is not reduced following chronic administration of the drug (Wu and French, 2000). On the other hand, tolerance can develop in humans to marijuana-induced cardiovascular and autonomic changes, decreased intraocular pressure, and sleep alterations (Jones et al., 1981). Down-regulation of cannabinoid receptors has been suggested as the mechanism underlying tolerance to the effects of marijuana (Rodriguez de Fonseca et al., 1994; Oviedo et al., 1993).

Acute administration of marijuana containing 2.1 percent delta9-THC does not produce ''hangover effects'' (Chait et al., 1985). In chronic marijuana users, though, a marijuana withdrawal syndrome has been described that consists of restlessness, irritability, mild agitation, insomnia, sleep EEG disturbances, nausea, and cramping that resolves within a few days (Haney et al., 1999). However, the American Psychiatric Association's Diagnostic and Statistical Manual (DSM–IV–TR, 2000) does not include a listing for cannabis withdrawal syndrome because, ''symptoms of cannabis withdrawal . . . have been described . . . but their clinical significance is uncertain.'' A review of all current clinical studies on cannabis withdrawal led to the recommendation by Budney et al. (2004) that the DSM introduce a listing for cannabis withdrawal that includes such symptoms as sleep difficulties, strange dreams, decreased appetite, decreased weight, anger, irritability, and anxiety. Based on clinical descriptions, this syndrome appears to be mild compared to classical alcohol and barbiturate withdrawal syndromes, which can include more serious symptoms such as agitation, paranoia, and seizures. A recent study comparing marijuana and tobacco withdrawal symptoms in humans demonstrated that the magnitude and timecourse of the two withdrawal syndromes are similar (Vandrey et al., 2005).

The production of an overt withdrawal syndrome in animals following chronic delta9-THC administration has been variably demonstrated under conditions of natural discontinuation. This may be the result of the slow release of cannabinoids from adipose storage, as well as the presence of the major psychoactive metabolite, 11-hydroxy-delta9-THC. When investigators have shown such a withdrawal syndrome in monkeys following the termination of cannabinoid administration, the behaviors included transient aggression, anorexia, biting, irritability, scratching, and yawning (Budney et al., 2004). However, in rodents treated with a cannabinoid antagonist following subacute administration of delta9-THC, pronounced withdrawal symptoms, including wet dog shakes, can be provoked (Breivogel et al., 2003).

Behavioral Sensitization

Sensitization to the effects of drugs is the opposite of tolerance: instead of a reduction in behavioral response upon repeated drug administration, animals that are sensitized demonstrate an increase in behavioral response. Cadoni et al. (2001) demonstrated that repeated exposure to delta9-THC can induce sensitization to a variety of cannabinoids. These same animals also have a sensitized response to administration of opioids, an effect known as cross-sensitization. Conversely, when animals were sensitized to the effects of morphine, there was cross-sensitization to cannabinoids. Thus, the cannabinoid and opioids systems appear to operate symmetrically in terms of cross-sensitization.

Cardiovascular and Autonomic Effects

Single smoked or oral doses of delta9-THC produce tachycardia and may increase blood pressure (Capriotti et al., 1988; Benowitz and Jones, 1975). However, prolonged delta9-THC ingestion produces significant heart rate slowing and blood pressure lowering (Benowitz and Jones, 1975). Both plant-derived cannabinoids and endocannabinoids have been shown to elicit hypotension and bradycardia via activation of peripherally-located CB_1 receptors (Wagner et al., 1998). This study suggests that the mechanism of this effect is through presynaptic CB_1 receptor-mediated inhibition of norepinephrine release from peripheral sympathetic nerve terminals, with possible additional direct vasodilation via activation of vascular cannabinoid receptors.

The impaired circulatory responses following delta9-THC administration to standing, exercise, Valsalva maneuver, and cold pressor testing suggest that cannabinoids induce a state of sympathetic insufficiency. In humans, tolerance can develop to the orthostatic hypotension (Jones, 2002; Sidney, 2002), possibly related to plasma volume expansion, but does not develop to the supine hypotensive effects (Benowitz and Jones, 1975). During chronic marijuana ingestion, nearly complete tolerance develops to tachycardia and psychological effects when subjects are challenged with smoked marijuana. Electrocardiographic changes are minimal even after large cumulative doses of delta9-THC. (Benowitz and Jones, 1975).

It is notable that marijuana smoking by older patients, particularly those with some degree of coronary artery or cerebrovascular disease, poses risks related to increased cardiac work, increased catecholamines, carboxyhemoglobin, and postural hypotension (Benowitz and Jones, 1981; Hollister, 1988).

Respiratory Effects

Transient bronchodilation is the most typical effect following acute exposure to marijuana (Gong et al., 1984). Long-term use of marijuana can lead to an increased frequency of chronic bronchitis and pharyngitis, as well as chronic cough and increased sputum. Pulmonary function tests reveal that large-airway obstruction can occur with chronic marijuana smoking, as can cellular inflammatory histopathological abnormalities in bronchial epithelium (Adams and Martin, 1996; Hollister, 1986).

The evidence that marijuana may lead to cancer associated with respiratory effects is inconsistent, with some studies suggesting a positive correlation while others do not (Tashkin, 2005). Several cases of lung cancer have been reported in young marijuana users with no history of tobacco smoking or other significant risk factors (Fung et al., 1999). Marijuana use may dose-dependently interact with mutagenic sensitivity, cigarette smoking and alcohol use to increase the risk of head and neck cancer (Zhang et al., 1999). However, in the largest study to date with 1,650 subjects, no positive association was found between marijuana use and lung cancer (Tashkin et al., 2006). This finding held true regardless of extent of marijuana use, when tobacco use and other potential confounding factors were controlled.

The lack of evidence for carcinogenicity related to cannabis may be related to the fact that intoxication from marijuana does not require large amounts of smoked material.

This may be especially pertinent since marijuana is reportedly more potent today than a generation ago. Thus, individuals may consume much less marijuana than in previous decades to reach the desired subjective effects, exposing them to less potential carcinogens.

Endocrine System

The presence of in vitro delta^{9}-THC reduces binding of the corticosteroid, dexamethasone, in hippocampal tissue from adrenalectomized rats, suggesting an interaction with the glucocorticoid receptor (Eldridge et al., 1991). Acute delta^{9}-THC releases corticosterone, but tolerance develops to this effect with chronic administration (Eldridge et al., 1991).

Experimental administration of marijuana to humans does not consistently alter endocrine parameters. In an early study, male subjects who experimentally received smoked marijuana showed a significant depression in luteinizing hormone and a significant increase in cortisol were observed (Cone et al., 1986). However, two later studies showed no changes in hormones. Male subjects who were experimentally exposed to smoked delta^{9}-THC (18 mg/marijuana cigarette) or oral delta^{9}-THC (10 mg t.i.d. for 3 days and on the morning of the fourth day) showed no changes in plasma prolactin, ACTH, cortisol, luteinizing hormone, or testosterone levels (Dax et al., 1989). Similarly, a study with 93 men and 56 women showed that chronic marijuana use did not significantly alter concentrations of testosterone, luteinizing hormone, follicle stimulating hormone, prolactin, or cortisol (Block et al., 1991).

Relatively little research has been performed on the effects of experimentally administered marijuana on female reproductive system functioning. In monkeys, delta^{9}-THC administration suppressed ovulation (Asch et al., 1981) and reduced progesterone levels (Almirez et al., 1983). However, when women were studied following experimental exposure to smoked marijuana, no hormonal or menstrual cycle changes were observed (Mendelson and Mello, 1984). Brown and Dobs (2002) suggest that the discrepancy between animal and human hormonal response to cannabinoids may be attributed to the development of tolerance in humans.

Recent data suggest that cannabinoid agonists may have therapeutic value in the treatment of prostate cancer, a type of carcinoma in which growth is stimulated by androgens. Research with prostate cancer cells shows that the mixed CB_1/CB_2 agonist, WIN–55212–2, induces apoptosis in prostate cancer cell growth, as well as decreases in expression of androgen receptors and prostate-specific antigens (Sarfaraz et al., 2005).

Immune System

Immune functions are altered by cannabinoids, but there can be differences between the effects of synthetic, natural, and endogenous cannabinoids, often in an apparently biphasic manner depending on dose (Croxford and Yamamura, 2005).

Abrams et al. (2003) investigated the effect of marijuana on immunological functioning in 62 AIDS patients who were taking protease inhibitors. Subjects received one of the following three times a day: smoked marijuana cigarette containing 3.95 percent delta^{9}-THC; oral tablet containing delta^{9}-THC (2.5 mg oral dronabinol); or oral placebo. There were no changes in CD4+ and CD8+ cell counts or HIV RNA levels or protease inhibitor levels between groups, demonstrating no short-term adverse virologic effects from using cannabinoids in individuals with compromised immune systems.

These human data contrast with data generated in immunodeficient mice showing that exposure to delta^{9}-THC in vivo suppresses immune function, increases HIV co-receptor expression, and acts as a cofactor to enhance HIV replication (Roth et al., 2005).

3. THE STATE OF CURRENT SCIENTIFIC KNOWLEDGE REGARDING THE DRUG OR OTHER SUBSTANCE

The third factor the Secretary must consider is the state of current scientific knowledge regarding marijuana. Thus, this section discusses the chemistry, human pharmacokinetics, and medical uses of marijuana.

Chemistry

According to the DEA, Cannabis sativa is the primary species of cannabis currently marketed illegally in the United States of America. From this plant, three derivatives are sold as separate illicit drug products: marijuana, hashish, and hashish oil.

Each of these derivatives contains a complex mixture of chemicals. Among the components are the 21 carbon terpenes found in the plant as well as their carboxylic acids, analogues, and transformation products known as cannabinoids (Agurell et al., 1984 and 1986; Mechoulam, 1973). The cannabinoids appear to naturally occur only in the marijuana plant and most of the botanically-derived cannabinoids have been identified. Among the cannabinoids, delta^{9}-THC (alternate name delta^{1}-THC) and delta-8-tetrahydrocannabinol (delta^{8}-THC, alternate name delta^{6}-THC) are both found in marijuana and are able to produce the characteristic psychoactive effects of marijuana. Because delta^{9}-THC is more abundant than delta^{8}-THC, the activity of marijuana is largely attributed to the former. Delta^{8}-THC is found only in few varieties of the plant (Hively et al., 1966).

Delta^{9}-THC is an optically active resinous substance, insoluble in water, and extremely lipid soluble. Chemically delta^{9}-THC is (6aR-trans)-6a,7,8,10a-tetrahydro-6,6,9-trimethyl-3-pentyl-6H-dibenzo-[b,d]pyran-1-ol or (-)-delta^{9}-(trans)-tetrahydrocannabinol. The (-)-trans isomer of delta^{9}-THC is pharmacologically 6 to 100 times more potent than the (+)-trans isomer (Dewey et al., 1984).

Other cannabinoids, such as cannabidiol (CBD) and cannabinol (CBN), have been characterized. CBD is not considered to have cannabinol-like psychoactivity, but is thought to have significant anticonvulsant, sedative, and anxiolytic activity (Adams and Martin, 1996; Agurell et al., 1984 and 1986; Hollister, 1986).

Marijuana is a mixture of the dried flowering tops and leaves from the plant and is variable in content and potency (Agurell et al., 1984 and 1986; Graham, 1976; Mechoulam, 1973). Marijuana is usually smoked in the form of rolled cigarettes while hashish and hash oil are smoked in pipes. Potency of marijuana, as indicated by cannabinoid content, has been reported to average from as low as 1 to 2 percent to as high as 17 percent.

The concentration of delta^{9}-THC and other cannabinoids in marijuana varies with growing conditions and processing after harvest. Other variables that can influence the strength, quality, and purity of marijuana are genetic differences among the cannabis plant species and which parts of the plant are collected (flowers, leaves, stems, etc.) (Adams and Martin, 1996; Agurell et al., 1984; Mechoulam, 1973). In the usual mixture of leaves and stems distributed as marijuana, the concentration of delta^{9}-THC ranges widely from 0.3 to 4.0 percent by weight. However, specially grown and selected marijuana can contain even 15 percent or greater delta^{9}-THC. Thus, a 1 gm marijuana cigarette might contain as little as 3 mg or as much as 150 mg or more of delta^{9}-THC.

Hashish consists of the cannabinoid-rich resinous material of the cannabis plant, which is dried and compressed into a variety of forms (balls, cakes, etc.). Pieces are then broken off, placed into a pipe and smoked. DEA reports that cannabinoid content in hashish averages 6 percent.

Hash oil is produced by solvent extraction of the cannabinoids from plant material. Color and odor of the extract vary, depending on the type of solvent used. Hash oil is a viscous brown or amber-colored liquid that contains approximately 15 percent cannabinoids. One or two drops of the liquid placed on a cigarette purportedly produce the equivalent of a single marijuana cigarette (DEA, 2005).

The lack of a consistent concentration of delta^{9}-THC in botanical marijuana from diverse sources complicates the interpretation of clinical data using marijuana. If marijuana is to be investigated more widely for medical use, information and data regarding the chemistry, manufacturing, and specifications of marijuana must be developed.

Human Pharmacokinetics

Marijuana is generally smoked as a cigarette (weighing between 0.5 and 1.0 gm), or in a pipe. It can also be taken orally in foods or as extracts of plant material in ethanol or other solvents.

The absorption, metabolism, and pharmacokinetic profile of delta^{9}-THC (and other cannabinoids) in marijuana or other drug products containing delta^{9}-THC vary with route of administration and formulation (Adams and Martin, 1996; Agurell et al., 1984 and 1986). When marijuana is administered by smoking, delta^{9}-THC in the form of an aerosol is absorbed within seconds. The psychoactive effects of marijuana occur immediately following absorption, with mental and behavioral effects measurable up to 6 hours (Grotenhermen, 2003; Hollister,

1986 and 1988). Delta9-THC is delivered to the brain rapidly and efficiently as would be expected of a very lipid-soluble drug.

The bioavailability of the delta9-THC from marijuana in a cigarette or pipe can range from 1 to 24 percent with the fraction absorbed rarely exceeding 10 to 20 percent (Agurell et al., 1986; Hollister, 1988). The relatively low and variable bioavailability results from the following: significant loss of delta9-THC in side-stream smoke, variation in individual smoking behaviors, cannabinoid pyrolysis, incomplete absorption of inhaled smoke, and metabolism in the lungs. A individual's experience and technique with smoking marijuana is an important determinant of the dose that is absorbed (Herning et al., 1986; Johansson et al., 1989).

After smoking, venous levels of delta9-THC decline precipitously within minutes, and within an hour are about 5 to 10 percent of the peak level (Agurell et al., 1986; Huestis et al., 1992a and 1992b). Plasma clearance of delta9-THC is approximately 950 ml/min or greater, thus approximating hepatic blood flow. The rapid disappearance of delta9-THC from blood is largely due to redistribution to other tissues in the body, rather than to metabolism (Agurell et al., 1984 and 1986). Metabolism in most tissues is relatively slow or absent. Slow release of delta9-THC and other cannabinoids from tissues and subsequent metabolism results in a long elimination half-life. The terminal half-life of delta9-THC is estimated to range from approximately 20 hours to as long as 10 to 13 days (Hunt and Jones, 1980), though reported estimates vary as expected with any slowly cleared substance and the use of assays of variable sensitivities. Lemberger et al. (1970) determined the half-life of delta9-THC to range from 23 to 28 hours in heavy marijuana users to 60 to 70 hours in naïve users.

Characterization of the pharmacokinetics of delta9-THC and other cannabinoids from smoked marijuana is difficult (Agurell et al., 1986; Herning et al., 1986; Huestis et al., 1992a), in part because a subject's smoking behavior during an experiment is variable. Each puff delivers a discrete dose of delta9-THC. An experienced marijuana smoker can titrate and regulate the dose to obtain the desired acute psychological effects and to avoid overdose and/or minimize undesired effects. For example, under naturalistic conditions, users will hold marijuana smoke in the lungs for an extended period of time, in order to prolong absorption and increase psychoactive effects. The effect of experience in the psychological response may explain why venous blood levels of delta9-THC correlate poorly with intensity of effects and level of intoxication (Agurell et al., 1986; Barnett et al., 1985; Huestis et al., 1992a).

Additionally, puff and inhalation volume changes with phase of smoking, tending to be highest at the beginning and lowest at the end of smoking a cigarette. Some studies found frequent users to have higher puff volumes than less frequent marijuana users. During smoking, as the cigarette length shortens, the concentration of delta9-THC in the remaining marijuana increases; thus, each successive puff contains an increasing concentration of delta9-THC.

In contrast to smoking, the onset of effects after oral administration of delta9-THC or marijuana is 30 to 90 min, which peaks after 2 to 3 hours and continues for 4 to 12 hours (Grotenhermen, 2003; Adams and Martin, 1996; Agurell et al., 1984 and 1986). Oral bioavailability of delta9-THC, whether pure or in marijuana, is low and extremely variable, ranging between 5 and 20 percent (Agurell et al., 1984 and 1986). Following oral administration of radioactive-labeled delta9-THC, delta9-THC plasma levels are low relative to those levels after smoking or intravenous administration. There is inter- and intra-subject variability, even when repeated dosing occurs under controlled conditions. The low and variable oral bioavailability of delta9-THC is a consequence of its first-pass hepatic elimination from blood and erratic absorption from stomach and bowel. It is more difficult for a user to titrate the oral delta9-THC dose than marijuana smoking because of the delay in onset of effects after an oral dose (typically 1 to 2 hours).

Cannabinoid metabolism is extensive. Delta9-THC is metabolized via microsomal hydroxylation to both active and inactive metabolites (Lemberger et al., 1970, 1972a, and 1972b; Agurell et al., 1986; Hollister, 1988) of which the primary active metabolite was 11-hydroxy-delta9-THC. This metabolite is approximately equipotent to delta9-THC in producing marijuana-like subjective effects (Agurell et al., 1986; Lemberger and Rubin, 1975). After oral administration, metabolite levels may exceed that of delta9-THC and thus contribute greatly to the pharmacological effects of oral delta9-THC or marijuana. In addition to 11-hydroxy-delta9-THC, some inactive carboxy metabolites have terminal half-lives of 50 hours to 6 days or more. The latter substances serve as long-term markers of earlier marijuana use in urine tests. The majority of the absorbed delta9-THC dose is eliminated in feces, and about 33 percent in urine. Delta9-THC enters enterohepatic circulation and undergoes hydroxylation and oxidation to 11-nor-9-carboxy-delta9-THC. The glucuronide is excreted as the major urine metabolite along with about 18 nonconjugated metabolites. Frequent and infrequent marijuana users are similar in the way they metabolize delta9-THC (Agurell et al., 1986).

Medical Uses for Marijuana

A NDA for marijuana/cannabis has not been submitted to the FDA for any indication and thus no medicinal product containing botanical cannabis has been approved for marketing. However, small clinical studies published in the current medical literature demonstrate that research with marijuana is being conducted in humans in the United States under FDA-authorized investigational new drug (IND) applications.

HHS states in a published guidance that it is committed to providing ''research-grade marijuana for studies that are the most likely to yield usable, essential data'' (HHS, 1999). The opportunity for scientists to conduct clinical research with botanical marijuana has increased due to changes in the process for obtaining botanical marijuana from NIDA, the only legitimate source of the drug for research in the United States. In May 1999, HHS provided guidance on the procedures for providing research-grade marijuana to scientists who intend to study marijuana in scientifically valid investigations and well-controlled clinical trials (DHHS, 1999). This action was prompted by the increasing interest in determining whether cannabinoids have medical use through scientifically valid investigations.

In February 1997, a National Institutes of Health (NIH)-sponsored workshop analyzed available scientific information and concluded that ''in order to evaluate various hypotheses concerning the potential utility of marijuana in various therapeutic areas, more and better studies would be needed'' (NIH, 1997). In addition, in March 1999, the Institute of Medicine (IOM) issued a detailed report that supported the need for evidence-based research into the effects of marijuana and cannabinoid components of marijuana, for patients with specific disease conditions. The IOM report also emphasized that smoked marijuana is a crude drug delivery system that exposes individuals to a significant number of harmful substances and that ''if there is any future for marijuana as a medicine, it lies in its isolated components, the cannabinoids and their synthetic derivatives.'' As such, the IOM recommended that clinical trials should be conducted with the goal of developing safe delivery systems (Institute of Medicine, 1999). Additionally, state-level public initiatives, including referenda in support of the medical use of marijuana, have generated interest in the medical community for high quality clinical investigation and comprehensive safety and effectiveness data.

For example, in 2000, the state of California established the Center for Medicinal Cannabis Research (CMCR) (*www.cmcr.ucsd.edu*) ''in response to scientific evidence for therapeutic possibilities of cannabis and local legislative initiatives in favor of compassionate use'' (Grant, 2005). State legislation establishing the CMCR called for high quality medical research that will ''enhance understanding of the efficacy and adverse effects of marijuana as a pharmacological agent,'' but stressed that the project ''should not be construed as encouraging or sanctioning the social or recreational use of marijuana.'' CMCR has thus far funded studies on the potential use of cannabinoids for the treatment of multiple sclerosis, neuropathic pain, appetite suppression and cachexia, and severe pain and nausea related to cancer or its treatment by chemotherapy. To date, though, no NDAs utilizing marijuana for these indications have been submitted to the FDA.

However, FDA approval of an NDA is not the sole means through which a drug can be determined to have a ''currently accepted medical use'' under the CSA. According to established case law, a drug has a ''currently accepted medical use'' if all of the following five elements have been satisfied:

a. the drug's chemistry is known and reproducible;

b. there are adequate safety studies;

c. there are adequate and well-controlled studies proving efficacy;

d. the drug is accepted by qualified experts; and

e. the scientific evidence is widely available.

[*Alliance for Cannabis Therapeutics* v. *DEA*, 15 F.3d 1131, 1135 (D.C. Cir. 1994)]

Although the structures of many cannabinoids found in marijuana have been characterized, a complete scientific analysis of all the chemical components found in marijuana has not been conducted. Safety studies for acute or subchronic administration of marijuana have been carried out through a limited number of Phase 1 clinical investigations approved by the FDA, but there have been no NDA-quality studies that have scientifically assessed the efficacy and full safety profile of marijuana for any medical condition. A material conflict of opinion among experts precludes a finding that marijuana has been accepted by qualified experts. At this time, it is clear that there is not a consensus of medical opinion concerning medical applications of marijuana. Finally, the scientific evidence regarding the safety or efficacy of marijuana is typically available only in summarized form, such as in a paper published in the medical literature, rather than in a raw data format. As such, there is no opportunity for adequate scientific scrutiny of whether the data demonstrate safety or efficacy.

Alternately, a drug can be considered to have ''a currently accepted medical use with severe restrictions'' (21 U.S.C. 812(b)(2)(B)), as allowed under the stipulations for a Schedule II drug. However, as stated above, a material conflict of opinion among experts precludes a finding that marijuana has been accepted by qualified experts, even under conditions where its use is severely restricted. Thus, to date, research on the medical use of marijuana has not progressed to the point that marijuana can be considered to have a ''currently accepted medical use'' or a ''currently accepted medical use with severe restrictions.''

4. ITS HISTORY AND CURRENT PATTERN OF ABUSE

The fourth factor the Secretary must consider is the history and current pattern of abuse of marijuana. A variety of sources provide data necessary to assess abuse patterns and trends of marijuana. The data indicators of marijuana use include NSDUH, Monitoring the Future (MTF), DAWN, and Treatment Episode Data Set (TEDS), which are described below:

National Survey on Drug Use and Health

The National Survey on Drug Use and Health (NSDUH, 2004; *http://oas.samhsa.gov/nsduh.htm*) is conducted annually by SAMHSA, an agency of HHS. NSDUH provides estimates of the prevalence and incidence of illicit drug, alcohol, and tobacco use in the United States. This database was known until 2001 as the National Household Survey on Drug Abuse. The survey is based on a nationally representative sample of the civilian, non-institutionalized population 12 years of age and older. The survey identifies whether an individual used a drug during a certain period, but not the amount of the drug used on each occasion. Excluded groups include homeless people, active military personnel, and residents of institutions, such as jails.

According to the 2004 NSDUH, 19.1 million individuals (7.9 percent of the U.S. population) illicitly used drugs other than alcohol and nicotine on a monthly basis, compared to 14.8 million (6.7 percent of the U.S. population) users in 1999. This is an increase from 1999 of 4.3 million (2.0 percent of the U.S. population). The most frequently used illicit drug was marijuana, with 14.6 million individuals (6.1 percent of the U.S. population) using it monthly. Thus, regular illicit drug use, and more specifically marijuana use, for rewarding responses is increasing. The 2004 NSDUH estimated that 96.8 million individuals (40.2 percent of the U.S. population) have tried marijuana at least once during their lifetime. Thus, 15 percent of those who have tried marijuana on one occasion go on to use it monthly, but 85 percent of them do not.

Monitoring the Future

MTF (2005, *http://www.monitoringthefuture.org*) is a NIDA-sponsored annual national survey that tracks drug use trends among adolescents in the United States. The MTF surveys 8th, 10th, and 12th graders every spring in randomly selected U.S. schools. The MTF survey has been conducted since 1975 for 12th graders and since 1991 for 8th and 10th graders by the Institute for Social Research at the University of Michigan under a grant from NIDA. The 2005 sample sizes were 17,300—8th graders; 16,700—10th graders; and 15,400—12th graders. In all, a total of 49,300 students in 402 schools participated.

Since 1999, illicit drug use among teens decreased and held steady through 2005 in all three grades (Table 1). Marijuana remained the most widely used illicit drug, though its use has steadily decreased since 1999. For 2005, the annual prevalence rates for marijuana use in grades 8, 10, and 12 were, respectively, 12.2 percent, 26.6 percent, and 33.6 percent. Current monthly prevalence rates for marijuana use were 6.6 percent, 15.2 percent, and 19.8 percent. (See Table 1). According to Gruber and Pope (2002), when adolescents who used marijuana reach their late 20's, the vast majority of these individuals will have stopped using marijuana.

TABLE 1—TRENDS IN ANNUAL AND MONTHLY PREVALENCE OF USE OF VARIOUS DRUGS FOR EIGHTH, TENTH, AND TWELFTH GRADERS, FROM MONITORING THE FUTURE. PERCENTAGES REPRESENT STUDENTS IN SURVEY RESPONDING THAT THEY HAD USED A DRUG EITHER IN THE PAST YEAR OR IN THE PAST 30 DAYS

	Annual			30-Day		
	2003	2004	2005	2003	2004	2005
Any illicit drug (a):						
8th Grade	16.1	15.2	15.5	9.7	8.4	8.5
10th Grade	32.0	31.1	29.8	19.5	18.3	17.3
12th Grade	39.3	38.8	38.4	24.1	23.4	23.1
Any illicit drug other than cannabis (a):						
8th Grade	8.8	7.9	8.1	4.7	4.1	4.1
10th Grade	13.8	13.5	12.9	6.9	6.9	6.4
12th Grade	19.8	20.5	19.7	10.4	10.8	10.3
Marijuana/hashish:						
8th Grade	12.8	11.8	12.2	7.5	6.4	6.6
10th Grade	28.2	27.5	26.6	17.0	15.9	15.2
12th Grade	34.9	34.3	33.6	21.2	19.9	19.8

SOURCE: The Monitoring the Future Study, the University of Michigan.

a. For 12th graders only, ''any illicit drug'' includes any use of marijuana, LSD, other hallucinogens, crack, other cocaine, or heroin, or any use of other opiates, stimulants, barbiturates, or tranquilizers not under a doctor's orders. For 8th and 10th graders, the use of other opiates and barbiturates was excluded.

Drug Abuse Warning Network

DAWN (2006, *http://dawninfo.samhsa.gov/*) is a national probability survey of U.S. hospitals with EDs designed to obtain information on ED visits in which recent drug use is implicated. The ED data from a representative sample of hospital emergency departments are weighted to produce national estimates. It is critical to note that DAWN data and estimates for 2004 are not comparable to those for any prior years because of vast

changes in the methodology used to collect the data. Further, estimates for 2004 are the first to be based on a new, redesigned sample of hospitals. Thus, the most recent estimates available are for 2004.

Many factors can influence the estimates of ED visits, including trends in the ED usage in general. Some drug users may have visited EDs for a variety of reasons, some of which may have been life-threatening, whereas others may have sought care at the ED for detoxification because they needed certification before entering treatment. DAWN data do not distinguish the drug responsible for the ED visit from others used concomitantly. As stated in a recent DAWN report, ''Since marijuana/hashish is frequently present in combination with other drugs, the reason for the ED contact may be more relevant to the other drug(s) involved in the episode.''

For 2004, DAWN estimates a total of 1,997,993 (95 percent confidence interval [CI]: 1,708,205 to 2,287,781) drug-related ED visits for the entire United States. During this period, DAWN estimates 940,953 (CI: 773,124 to 1,108,782) drug-related ED visits involved a major drug of abuse. Thus, nearly half of all drug-related visits involved alcohol or an illicit drug. Overall, drug-related ED visits averaged 1.6 drugs per visit, including illicit drugs, alcohol, prescription and over-the-counter (OTC) pharmaceuticals, dietary supplements, and non-pharmaceutical inhalants.

Marijuana was involved in 215,665 (CI: 175,930 to 255,400) ED visits, while cocaine was involved in 383,350 (CI: 284,170 to 482,530) ED visits, heroin was involved in 162,137 (CI: 122,414 to 201,860) ED visits, and stimulants, including amphetamine and methamphetamine, were involved in 102,843 (CI: 61,520 to 144,166) ED visits. Other illicit drugs, such as PCP, MDMA, and GHB, were much less frequently associated with ED visits.

Approximately 18 percent of ED visits involving marijuana were for patients under the age of 18, whereas this age group accounts for less than 1 percent of the ED visits involving heroin/morphine and approximately 3 percent of the visits involving cocaine. Since the size of the population differs across age groups, a measure standardized for population size is useful to make comparisons. For marijuana, the rates of ED visits per 100,000 population were highest for patients aged 18 to 20 (225 ED visits per 100,000) and for patients aged 21 to 24 (190 ED visits per 100,000).

Treatment Episode Data Set

TEDS (TEDS, 2003; *http://oas.samhsa.gov/dasis.htm#teds2*) system is part of SAMHSA's Drug and Alcohol Services Information System (Office of Applied Science, SAMHSA). TEDS comprises data on treatment admissions that are routinely collected by States in monitoring their substance abuse treatment systems. The TEDS report provides information on the demographic and substance use characteristics of the 1.8 million annual admissions to treatment for abuse of alcohol and drugs in facilities that report to individual State administrative data systems.

TEDS is an admission-based system, and TEDS admissions do not represent individuals. Thus, a given individual admitted to treatment twice within a given year would be counted as two admissions. Additionally, TEDS does not include all admissions to substance abuse treatment. TEDS includes facilities that are licensed or certified by the States to provide substance abuse treatment and that are required by the States to provide TEDS client-level data. Facilities that report TEDS data are those that receive State alcohol and/or drug agency funds for the provision of alcohol and/or drug treatment services. The primary goal for TEDS is to monitor the characteristics of treatment episodes for substance abusers.

Primary marijuana abuse accounted for 15.5 percent of TEDS admissions in 2003, the latest year for which data are available. Three-quarters of the individuals admitted for marijuana were male and 55 percent of the admitted individuals were white. The average age at admission was 23 years. The largest proportion (84 percent) of admissions to ambulatory treatment was for primary marijuana abuse. More than half (57 percent) of marijuana treatment admissions were referred through the criminal justice system.

Between 1993 and 2003, the percentage of admissions for primary marijuana use increased from 6.9 percent to 15.5 percent, comparable to the increase for primary opioid use from 13 percent in 1993 to 17.6 percent in 2003. In contrast, the percentage of admissions for primary cocaine use declined from 12.6 percent in 1993 to 9.8 percent in 2003, and for primary alcohol use from 56.9 percent in 1993 to 41.7 percent in 2003.

Twenty-six percent of those individuals who were admitted for primary use of marijuana reported its daily use, although 34.6 percent did not use marijuana in the past month. Nearly all (96.2 percent) of primary marijuana users utilized the drug by smoking it. Over 90 percent of primary marijuana admissions used marijuana for the first time before the age of 18.

5. THE SCOPE, DURATION, AND SIGNIFICANCE OF ABUSE

The fifth factor the Secretary must consider is the scope, duration, and significance of marijuana abuse. According to 2004 data from NSDUH and MTF, marijuana remains the most extensively used illegal drug in the United States, with 40.6 percent of U.S. individuals over age 12 (96.6 million) and 44.8 percent of 12th graders having used marijuana at least once in their lifetime. While the majority of individuals over age 12 (85 percent) who have used marijuana do not use the drug monthly, 14.6 million individuals (6.1 percent of the U.S. population) report that they used marijuana within the past 30 days. An examination of use among various age cohorts in NSDUH demonstrates that monthly use occurs primarily among college age individuals, with use dropping off sharply after age 25.

DAWN data show that marijuana was involved in 79,663 ED visits, which amounts to 13 percent of all drug-related ED visits. Minors accounted for 15 percent of these marijuana-related visits, making marijuana the drug most frequently associated with ED visits for individuals under the age of 18 years.

Data from TEDS show that 15.5 percent of all admissions were for primary marijuana abuse. Approximately 90 percent of these primary marijuana admissions were for individuals under the age of 18 years.

6. WHAT, IF ANY, RISK THERE IS TO THE PUBLIC

The sixth factor the Secretary must consider is the risk marijuana poses to the public health. The risk to the public health as measured by emergency room episodes, marijuana-related deaths, and drug treatment admissions is discussed in full under Factors 1, 4, and 5, above. Accordingly, Factor 6 focuses on the health risks to the individual user.

All drugs, both medicinal and illicit, have a broad range of effects on the individual user that are dependent on dose and duration of use among others. FDA-approved drug products can produce adverse events (or ''side effects'') in some individuals even at doses in the therapeutic range. When determining whether a drug product is safe and effective for any indication, FDA performs an extensive risk-benefit analysis to determine whether the risks posed by the drug product's potential or actual side effects are outweighed by the drug product's potential benefits. As marijuana is not FDA-approved for any medicinal use, any potential benefits attributed to marijuana use have not been found to be outweighed by the risks. However, cannabinoids are generally potent psychoactive substances and are pharmacologically active on multiple organ systems.

The discussion of marijuana's central nervous system, cognitive, cardiovascular, autonomic, respiratory, and immune system effects are fully discussed under Factor 2. Consequences of marijuana use and abuse are discussed below in terms of the risk from acute and chronic use of the drug to the individual user (Institute of Medicine, 1999).

Risks from acute use of marijuana

Acute use of marijuana impairs psychomotor performance, including performance of complex tasks, which makes it inadvisable to operate motor vehicles or heavy equipment after using marijuana (Ramaekers et al., 2004). Dysphoria and psychological distress, including prolonged anxiety reactions, are potential responses in a minority of individuals who use marijuana (Haney et al., 1999).

Risks from chronic use of marijuana

Chronic exposure to marijuana smoke is considered to be comparable to tobacco smoke with respect to increased risk of cancer, lung damage, and poor pregnancy outcome. Although a distinctive marijuana withdrawal syndrome has been identified, indicating that marijuana produces physical dependence, this phenomenon is mild and short-lived (Budney et al., 2004), as described above under Factor 2.

The Diagnostic and Statistical Manual (DSM–IV–TR, 2000) of the American Psychiatric Association states that the

consequences of cannabis abuse are as follows:

[P]eriodic cannabis use and intoxication can interfere with performance at work or school and may be physically hazardous in situations such as driving a car. Legal problems may occur as a consequence of arrests for cannabis possession. There may be arguments with spouses or parents over the possession of cannabis in the home or its use in the presence of children. When psychological or physical problems are associated with cannabis in the context of compulsive use, a diagnosis of Cannabis Dependence, rather than Cannabis Abuse, should be considered.

Individuals with Cannabis Dependence have compulsive use and associated problems. Tolerance to most of the effects of cannabis has been reported in individuals who use cannabis chronically. There have also been some reports of withdrawal symptoms, but their clinical significance is uncertain. There is some evidence that a majority of chronic users of cannabinoids report histories of tolerance or withdrawal and that these individuals evidence more severe drug-related problems overall. Individuals with Cannabis Dependence may use very potent cannabis throughout the day over a period of months or years, and they may spend several hours a day acquiring and using the substance. This often interferes with family, school, work, or recreational activities. Individuals with Cannabis Dependence may also persist in their use despite knowledge of physical problems (e.g., chronic cough related to smoking) or psychological problems (e.g., excessive sedation and a decrease in goal-oriented activities resulting from repeated use of high doses).

7. ITS PSYCHIC OR PHYSIOLOGIC DEPENDENCE LIABILITY

The seventh factor the Secretary must consider is marijuana's psychic or physiologic dependence liability. Physical dependence is a state of adaptation manifested by a drug class-specific withdrawal syndrome produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist (American Academy of Pain Medicine, American Pain Society and American Society of Addiction Medicine consensus document, 2001). Long-term, regular use of marijuana can lead to physical dependence and withdrawal following discontinuation as well as psychic addiction or dependence. The marijuana withdrawal syndrome consists of symptoms such as restlessness, mild agitation, insomnia, nausea, and cramping that may resolve after 4 days, and may require in-hospital treatment. It is distinct from the withdrawal syndromes associated with alcohol and heroin use (Budney et al., 1999; Haney et al., 1999). Lane and Phillips-Bute (1998) describes milder cases of dependence including symptoms that are comparable to those from caffeine withdrawal, including decreased vigor, increased fatigue, sleepiness, headache, and reduced ability to work. The marijuana withdrawal syndrome has been reported in adolescents who were admitted for substance abuse treatment or in individuals who had been given marijuana on a daily basis during research conditions. Withdrawal symptoms can also be induced in animals following administration of a cannabinoid antagonist after chronic delta^{9}-THC administration (Breivogel et al., 2003).

Tolerance is a state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time (American Academy of Pain Medicine, American Pain Society and American Society of Addiction Medicine consensus document, 2001). Tolerance can develop to marijuana-induced cardiovascular and autonomic changes, decreased intraocular pressure, sleep and sleep EEG, and mood and behavioral changes (Jones et al., 1981). Down-regulation of cannabinoid receptors has been suggested as the mechanism underlying tolerance to the effects of marijuana (Rodriguez de Fonseca et al., 1994). Pharmacological tolerance does not indicate the physical dependence liability of a drug.

8. WHETHER THE SUBSTANCE IS AN IMMEDIATE PRECURSOR OF A SUBSTANCE ALREADY CONTROLLED UNDER THIS ARTICLE

The eighth factor the Secretary must consider is whether marijuana is an immediate precursor of a controlled substance. Marijuana is not an immediate precursor of another controlled substance.

RECOMMENDATION

After consideration of the eight factors discussed above, HHS recommends that marijuana remain in Schedule I of the CSA. Marijuana meets the three criteria for placing a substance in Schedule I of the CSA under 21 U.S.C. 812(b)(1):

1) Marijuana has a high potential for abuse:

The large number of individuals using marijuana on a regular basis, its widespread use, and the vast amount of marijuana that is available for illicit use are indicative of the high abuse potential for marijuana. Approximately 14.6 million individuals in the United States (6.1 percent of the U.S. population) used marijuana monthly in 2003. A 2003 survey indicates that by 12th grade, 33.6 percent of students report having used marijuana in the past year, and 19.8 percent report using it monthly. In Q3 to Q4 2003, 79,663 ED visits were marijuana-related, representing 13 percent of all drug-related episodes. Primary marijuana use accounted for 15.5 percent of admissions to drug treatment programs in 2003. Marijuana has dose-dependent reinforcing effects, as demonstrated by data that humans prefer higher doses of marijuana to lower doses. In addition, there is evidence that marijuana use can result in psychological dependence in at risk individuals.

2) Marijuana has no currently accepted medical use in treatment in the United States:

The FDA has not yet approved an NDA for marijuana. The opportunity for scientists to conduct clinical research with marijuana exists under the HHS policy supporting clinical research with botanical marijuana. While there are INDs for marijuana active at the FDA, marijuana does not have a currently accepted medical use for treatment in the United States, nor does it have an accepted medical use with severe restrictions.

A drug has a ''currently accepted medical use'' if all of the following five elements have been satisfied:

a. The drug's chemistry is known and reproducible;

b. There are adequate safety studies;

c. There are adequate and well-controlled studies proving efficacy;

d. The drug is accepted by qualified experts; and

e. The scientific evidence is widely available.

[*Alliance for Cannabis Therapeutics* v. *DEA,* 15 F.3d 1131, 1135 (D.C. Cir. 1994)]

Although the structures of many cannabinoids found in marijuana have been characterized, a complete scientific analysis of all the chemical components found in marijuana has not been conducted. Safety studies for acute or subchronic administration of marijuana have been carried out through a limited number of Phase 1 clinical investigations approved by the FDA, but there have been no NDA-quality studies that have scientifically assessed the efficacy of marijuana for any medical condition. A material conflict of opinion among experts precludes a finding that marijuana has been accepted by qualified experts. At this time, it is clear that there is not a consensus of medical opinion concerning medical applications of marijuana. Finally, the scientific evidence regarding the safety or efficacy of marijuana is typically available only in summarized form, such as in a paper published in the medical literature, rather than in a raw data format. As such, there is no opportunity for adequate scientific scrutiny of whether the data demonstrate safety or efficacy.

Alternately, a drug can be considered to have ''a currently accepted medical use with severe restrictions'' (21 U.S.C. 812(b)(2)(B)), as allowed under the stipulations for a Schedule II drug. However, as stated above, a material conflict of opinion among experts precludes a finding that marijuana has been accepted by qualified experts, even under conditions where its use is severely restricted. To date, research on the medical use of marijuana has not progressed to the point that marijuana can be considered to have a ''currently accepted medical use'' or a ''currently accepted medical use with severe restrictions.''

3) There is a lack of accepted safety for use of marijuana under medical supervision.

At present, there are no FDA-approved marijuana products, nor is marijuana under NDA evaluation at the FDA for any indication. Marijuana does not have a currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions. The Center for Medicinal Cannabis Research in California, among others, is conducting research with marijuana at the IND level, but these studies have not yet progressed to the stage of submitting an NDA. Thus, at this time, the known risks of marijuana use have

not been shown to be outweighed by specific benefits in well-controlled clinical trials that scientifically evaluate safety and efficacy.

In addition, the agency cannot conclude that marijuana has an acceptable level of safety without assurance of a consistent and predictable potency and without proof that the substance is free of contamination. If marijuana is to be investigated more widely for medical use, information and data regarding the chemistry, manufacturing, and specifications of marijuana must be developed. Therefore, HHS concludes that, even under medical supervision, marijuana has not been shown at present to have an acceptable level of safety.

REFERENCES

Abrams, D.I., Hilton, J.F., Leiser, R.J., Shade, S.B., Elbeik, T.A., Aweeka, F.T., Benowitz, N.L., Bredt, B.M., Kosel, B., Aberg, J.A., Deeks, S.G., Mitchell, T.F., Mulligan, K., Bacchetti, P., McCune, J.M., and Schambelan, M. Short-term effects of cannabinoids in patients with HIV–1 infection: a randomized, placebo-controlled clinical trial. *Ann Intern Med.* 2003 Aug 19: 139(4): 258–66.

Adams, I.B. and Martin, B.R. Cannabis: Pharmacology and toxicology in animals and humans. *Addiction.* 1996: 91(11): 1585–1614.

Agurell, S., Dewey, W.L., and Willett, R.E., eds. The Cannabinoids: Chemical, Pharmacologic, and Therapeutic Aspects. *New York: Academic Press.* 1984.

Agurell, S., Halldin, M., Lindgren, J.E., Ohlsson, A., Widman, M., Gillespie, H., and Hollister, L. Pharmacokinetics and metabolism of delta 1-tetrahydrocannabinol and other cannabinoids with emphasis on man. *Pharmacol Rev.* 1986: 38(1): 21–43.

Almirez, R.G., Smith, C.G., and Asch, R.H. The effects of marijuana extract and delta 9-tetrahydrocannabinol on luteal function in the rhesus monkey. *Fertil Steril.* 1983 Feb: 39(2): 212–7.

Ameri, A. The effects of cannabinoids on the brain. *Progress in Neurobiology.* 1999: 58 (4): 315–348.

American Academy of Pain Medicine, American Pain Society and American Society of Addiction Medicine Consensus Document. Definitions related to the use of opioids for the treatment of pain. 2001.

Andreasson, S., Allebeck, .P, Engstrom, A., and Rydberg, U. Cannabis and schizophrenia. A longitudinal study of Swedish conscripts. *Lancet.* 1987 Dec 26: 2(8574): 1483–6.

Asch, R.H., Smith, C.G., Siler-Khodr, T.M., and Pauerstein, C.J. Effects of delta 9-tetrahydrocannabinol during the follicular phase of the rhesus monkey (Macaca mulatta). *J Clin Endocrinol Metab.* 1981 Jan: 52(1): 50–5.

Balster, R.L. and Prescott, W.R., delta^{9}-Tetrahydrocannabinol discrimination in rats as a model for cannabis intoxication. *Neurosci. & Biobehav. Rev.* 1992: 16(1): 55–62.

Balster, R.L. and Bigelow, G.E. Guidelines and methodological reviews concerning drug abuse liability assessment. *Drug and Alcohol Dependence.* 2003: 70: S13–S40.

Barnett, G., Licko, V., and Thompson, T. Behavioral pharmacokinetics of marijuana. *Psychopharmacology.* 1985: 85(1): 51–56.

Benowitz, N.L. and Jones, R.T. Cardiovascular effects of prolonged delta-9-tetrahydrocannabinol ingestion. *Clin Pharmacol Ther.* 1975 Sep: 18(3): 287–97.

Benowitz, N.L. and Jones, R.T. Cardiovascular and metabolic considerations in prolonged cannabinoid administration in man. *J Clin Pharmacol.* 1981 Aug–Sep: 21(8–9 Suppl): 214S–223S.

Block, R.I. and Wittenborn, J.R. Marijuana effects on associative processes. *Psychopharmacology (Berl).* 1985: 85(4): 426–30.

Block, R.I., Farinpour, R., and Schlechte, J.A. Effects of chronic marijuana use on testosterone, luteinizing hormone, follicle stimulating hormone, prolactin and cortisol in men and women. *Drug Alcohol Depend.* 1991 Aug: 28(2): 121–8.

Block, R.I., Farinpour, R., and Braverman, K. Acute effects of marijuana on cognition: relationships to chronic effects and smoking techniques. *Pharmacol Biochem Behav.* 1992 Nov: 43(3): 907–17.

Bolla, K.I., Brown, K., Eldreth, D., Tate, K., and Cadet, J.L. Dose-related neurocognitive effects of marijuana use. *Neurology.* 2002: 59: 1337–1343.

Bolla, K.I., Eldreth, D.A., Matochik, J.A., and Cadet, J.L. Neural substrates of faulty decision-making in abstinent marijuana users. *NeuroImage.* 2005: 26: 480–492.

Bouaboula, M., Rinaldi, M., Carayon, P., Carillon, C., Delpech, B., Shire, D., Le Fur, G., and Casellas, P. Cannabinoid-receptor expression in human leukocytes. *Eur J Biochem.* 1993 May 15: 214(1): 173–80.

Braida, D., Iosue, S., Pegorini, S., and Sala, M. Delta9-tetrahydrocannabinol-induced conditioned place preference and intracerebroventricular self-administration in rats. *Eur J Pharmacol.* 2004 Dec 3: 506(1): 63–9.

Breivogel, C.S. and Childers, S.R. Cannabinoid agonist signal transduction in rat brain: comparison of cannabinoid agonists in receptor binding, G-protein activation, and adenylyl cyclase inhibition. *J Pharmacol Exp Ther.* 2000 Oct: 295(1): 328–36.

Breivogel, C.S., Griffin, G., Di Marzo, V., and Martin, B.R. Evidence for a new G protein-coupled cannabinoid receptor in mouse brain. *Mol Pharmacol.* 2001 Jul: 60(1): 155–63.

Breivogel, C.S., Scates, S.M., Beletskaya, I.O., Lowery, O.B., Aceto, M.D., and Martin, B.R. The effects of delta9-tetrahydrocannabinol physical dependence on brain cannabinoid receptors. *Eur J Pharmacol.* 2003 Jan 17: 459(2–3): 139–50.

Brown, T.T. and Dobs, A.S. Endocrine effects of marijuana. *J Clin Pharmacol.* 2002 Nov: 42(11 Suppl): 90S–96S.

Browne, R.G. and Weissman, A. Discriminative stimulus properties of delta 9-tetrahydrocannabinol: mechanistic studies. *J Clin Pharmacol.* 1981 Aug–Sep: 21(8–9 Suppl): 227S–234S.

Budney, A.J., Novy, P.L., and Hughes, J.R. Marijuana withdrawal among adults seeking treatment for marijuana dependence. *Addiction.* 1999: 94(9): 1311–22

Budney, A.J., Hughes, J.R., Moore, B.A., and Vandrey, R. Review of the validity and significance of cannabis withdrawal syndrome. *Am J Psychiatry.* 2004 Nov: 161(11): 1967–77.

Cadoni, C., Pisanu, A., Solinas, M., Acquas, E., and Di Chiara, G. Behavioural sensitization after repeated exposure to Delta 9-tetrahydrocannabinol and cross-sensitization with morphine. *Psychopharmacology (Berl).* 2001 Nov: 158(3): 259–66.

Capriotti, R.M., Foltin, R.W., Brady, J.V., and Fischman, M.W. Effects of marijuana on the task-elicited physiological response. *Drug Alcohol Depend.* 1988 Jul: 21(3): 183–7.

Chait, L.D., Fischman, M.W., and Schuster, C.R. '"Hangover' effects the morning after marijuana smoking. *Drug Alcohol Depend.* 1985 Jun:15(3): 229–38.

Chait, L.D., Evans, S.M., Grant, K.A., Kamien, J.B., Johanson, C.E., and Schuster, C.R. Discriminative stimulus and subjective effects of smoked marijuana in humans. *Psychopharmacology (Berl).* 1988: 94(2): 206–12.

Chait, L.D. and Burke, K.A. Preference for high- versus low-potency marijuana. *Pharmacol Biochem Behav.* 1994 Nov: 49(3): 643–7.

Chaperon, F., Soubrie, P., Puech, A.J., and Thiebot, M.H. Involvement of central cannabinoid (CB1) receptors in the establishment of place conditioning in rats. *Psychopharmacology (Berl).* 1998 Feb: 135(4): 324–32.

Cheer, J.F., Kendall, D.A., and Marsden, C.A. Cannabinoid receptors and reward in the rat: a conditioned place preference study. *Psychopharmacology (Berl).* 2000 Jul:151(1): 25–30.

Community Epidemiology Work Group, National Institutes of Health, National Institute on Drug Abuse, Epidemiologic Trends in Drug Abuse, Volume I: Highlights and Executive Summary, June 2000, *http://www.nida.nih.gov/CEWG/pubs.html.*

Cone, E.J., Johnson, R.E., Moore, J.D., and Roache, J.D. Acute effects of smoking marijuana on hormones, subjective effects and performance in male human subjects. *Pharmacol Biochem Behav.* 1986 Jun: 24(6): 1749–54.

Croxford, J.L. and Yamamura, T. Cannabinoids and the immune system: potential for the treatment of inflammatory diseases? *J Neuroimmunol.* 2005 Sep: 166(1–2): 3–18. Review.

Dax, E.M., Pilotte, N.S., Adler, W.H., Nagel, J.E., and Lange, W.R. The effects of 9-ene-tetrahydrocannabinol on hormone release and immune function. *J Steroid Biochem.* 1989: 34(1–6): 263–70.

Degenhardt, L., Hall, W., and Lynskey, M. Testing hypotheses about the relationship between cannabis use and psychosis. *Drug Alcohol Depend.* 2003 Jul 20: 71(1): 37–48.

Department of Health and Human Services. Announcement of the Department of Health and Human Services Guidance on Procedures for the Provision of Marijuana for Medical Research. May 21, 1999. (*http://grants.nih.gov/grants/guide/notice-files/not99-091.html*).

Dewey, W. L., Martin, B. R., and May, E. L. Cannabinoid stereoisomers: pharmacological effects. In Smith, D. F. (Ed.) CRC Handbook of stereoisomers: drugs in psychopharmacology, 317–326 (Boca Raton, FL, CRC Press), 1984.

D'Souza, D.C., Abi-Saab, W.M., Madonick, S., Forselius-Bielen, K., Doersch, A., Braley, G., Gueorguieva, R., Cooper, T.B., and Krystal, J.H. Delta-9-tetrahydrocannabinol effects in schizophrenia: implications for cognition, psychosis, and addiction. *Biol Psychiatry.* 2005 Mar 15: 57(6): 594–608.

Drug Enforcement Administration, *Federal-wide Drug Seizure System,* 1989–2002 (October 2002).

Drug Enforcement Administration, *Drugs of Abuse,* 2005.

Drug Enforcement Administration. *Sourcebook of Criminal Justice Statistics,* 2003.

DSM–IV–TR: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision. American Psychiatric Association. Arlington, VA: American Psychiatric Publishing, Inc., 2000.

Ehrenreich, H., Rinn, T., Kunert, H.J., Moeller, M.R., Poser, W., Schilling, L., Gigerenzer, G., and Hoehe, M.R. Specific attentional dysfunction in adults following early start of cannabis use. *Psychopharmacology (Berl).* 1999 Mar: 142(3): 295–301.

Eldreth, D.A., Matochik, J.A., Cadet, J.L., and Bolla, K.I. Abnormal brain activity in prefrontal brain regions in abstinent marijuana users. *Neuroimage.* 2004 Nov: 23(3): 914–20.

Eldridge, J.C., Murphy, L.L., and Landfield, P.W. Cannabinoids and the hippocampal glucocorticoid receptor: recent findings and possible significance. *Steroids.* 1991 May: 56(5): 226–31. Review.

Fant, R.V., Heishman, S.J., Bunker, E.B., and Pickworth, W.B. Acute and residual effects of marijuana in humans. *Pharmacol Biochem Behav.* 1998 Aug: 60(4): 777–84.

Favrat, B., Menetrey, A., Augsburger, M., Rothuizen, L.E., Appenzeller, M., Buclin, T., Pin, M., Mangin, P., and Giroud, C. Two cases of ''cannabis acute psychosis'' following the administration of oral cannabis. *BMC Psychiatry.* 2005 Apr 1: 5(1): 17.

Fergusson, D.M., Horwood, L.J., and Ridder, E.M. Tests of causal linkages between cannabis use and psychotic symptoms. *Addiction.* 2005 Mar: 100(3): 354–66.

Fried, P. A. and Watkinson, B. 36- and 48-month neurobehabioral follow-up of children prenatally exposed to marijuana, cigarettes and alcohol. *J. Dev. Behav. Pediatr.* 1987: 8: 318–326.

Fried, P. A., Watkinson, B., and Gray, R. A follow-up study of attentional behavior in 6-year-old children exposed prenatally to marihuana, cigarettes and alcohol. *Neurotoxicol. Teratol.* 1992: 14: 299–311.

Fried, P. A., Watkinson, B., and Gray, R. Differential effects on cognitive functioning in 9- to 12-year olds prenatally exposed to cigarettes and marihuana. *Neurotoxicol. Teratol.* 1998: 20(3): 293–306.

Fried, P., Watkinson, B., James, D., and Gray, R. Current and former marijuana use: preliminary findings of a longitudinal study of effects on IQ in young adults. *CMAJ.* 2002 Apr 2: 166(7): 887–91.

Fung, M., Gallagher, C., and Machtay, M. Lung and aeo-digestive cancers in young marijuana smokers. *Tumori.* 1999: 85 (2): 140–142.

Galiegue, S., Mary, S., Marchand, J., Dussossoy, D., Carriere, D., Carayon, P., Bouaboula, M., Shire, D., Le Fur, G., and Casellas, P. Expression of central and peripheral cannabinoid receptors in human immune tissues and leukocyte subpopulations. *Eur J Biochem.* 1995 Aug 15: 232(1): 54–61.

Gaoni, Y. and Mechoulam, R. Isolation, structure, and partial synthesis of an active constituent of hashish. *J. Am. Chem. Soc.* 1964: 86: 1646–1947.

Gerard, C. M., Mollereau, C., Vassart, G., and Parmentier, M. Molecular cloning of a human cannabinoid receptor which is also expressed in testis. *Biochem J.* 1991: 279: 129–34.

Ghozland, S., Matthes, H.W., Simonin, F., Filliol, D., Kieffer, B.L., and Maldonado, R. Motivational effects of cannabinoids are mediated by mu-opioid and kappa-opioid receptors. *J Neurosci.* 2002 Feb 1: 22(3): 1146–54.

Gold, L.H., Balster, R.L., Barrett, R.L., Britt, D.T., and Martin, B.R. A comparison of the discriminative stimulus properties of delta 9-tetrahydrocannabinol and CP 55,940 in rats and rhesus monkeys. *J Pharmacol Exp Ther.* 1992 Aug: 262(2): 479–86.

Golub, A. and Johnson, B.D. Variation in youthful risks of progression from alcohol and tobacco to marijuana and to hard drugs across generations. *Am J Public Health.* 2001 Feb: 91(2): 225–32.

Gong, H. Jr., Tashkin, D.P., Simmons, M.S., Calvarese, B., and Shapiro, B.J. Acute and subacute bronchial effects of oral cannabinoids. *Clin Pharmacol Ther.* 1984 Jan: 35(1): 26–32.

Gong, J.P., Onaivi, E.S., Ishiguro, H., Liu, Q.R., Tagliaferro, P.A., Brusco, A., and Uhl, G.R. Cannabinoid CB2 receptors: Immunohistochemical localization in rat brain. *Brain Res.* 2006 Feb 3: 1071(1): 10–23.

Gonsiorek, W., Lunn, C., Fan, X., Narula, S., Lundell, D., and Hipkin, R.W. Endocannabinoid 2-arachidonyl glycerol is a full agonist through human type 2 cannabinoid receptor: antagonism by anandamide. *Mol Pharmacol.* 2000 May: 57(5): 1045–50.

Graham, J.D.P., ed. Cannabis and Health. New York: Academic Press, 1976.

Grant I. Foreword by Igor Grant, M.D., Director, Center for Medicinal Cannabis Research (CMCR). *Neuropharmacology.* 2005 Jun: 48(8): 1067.

Griffith, D. R., Azuma, S. D., and Chasnoff, I. J. Three-year outcome of children exposed prenatally to drugs. *J. Am. Acad. Child Adolesc. Psychiatry.* 1994: 33: 20–27.

Grotenhermen, F. Pharmacokinetics and pharmacodynamics of cannabinoids. *Clin Pharmacokin et.* 2003: 42(4): 327–60.

Gruber, A.J., Pope, H.G., Hudson, J.I., and Yurgelun-Todd, D. Attributes of long-term heavy cannabis users: a case-control study. *Psychological Medicine.* 2003: 33: 1415–1422.

Gruber, S.A. and Yurgelun-Todd, D.A. Neuroimaging of marijuana smokers during inhibitory processing: a pilot investigation. *Brain Res Cogn Brain Res.* 2005 Apr: 23(1): 107–18.

Hall, W., Degenhardt, L., and Teesson, M. Cannabis use and psychotic disorders: an update. *Drug Alcohol Rev.* 2004 Dec: 23(4): 433–43.

Hall, W.D. and Lynskey, M. Is cannabis a gateway drug? Testing hypotheses about the relationship between cannabis use and the use of other illicit drugs. Drug Alcohol Rev. 2005 Jan: 24(1): 39–48.

Haney, M., Ward, A.S., Comer, S.D., Foltin, R.W., and Fischman, M.W. Abstinence symptoms following smoked marijuana in humans. *Psychopharmacology (Berl).* 1999: 141(4): 395–404.

Hanus, L., Breuer, A., Tchilibon, S., Shiloah, S., Goldenberg, D., Horowitz, M., Pertwee, R.G., Roos, R. A., Mechoulam, R., and Fride, E. HU–308: a specific agonist for CB (2), a peripheral Cannabinoid receptor. *Proc. Natl. Acad. Sci. USA.* 1999: 96: 14228–33.

Harrison, G.P. Jr., Gruber, A.J., Hudson, J.I., Huestis, M.A., and Yurgelun-Todd, D. Cognitive measures in long-term cannabis users. *J Clin Pharmacol.* 2002 Nov: 42(11 Suppl): 41S–47S. Review.

Heishman, S.J., Huestis, M.A., Henningfield, J.E., and Cone, E.J. Acute and residual effects of marijuana: profiles of plasma THC levels, physiological, subjective, and performance measures. *Pharmacol Biochem Behav.* 1990 Nov: 37(3): 561–5.

Herkenham, M. Cannabinoid receptor localization in brain: Relationship to motor and reward systems. In: Kalivas, P.W., and Samson, H.H., eds. The neurobiology of drug and alcohol addiction. Ann N Y Acad Sci 1992: 654: 19–32.

Herkenham, M., Lynn, A. B., Little, M. D., Johnson, M. R., Melvin, L. S., de Costa, B. R., and Rice, K. C. Cannabinoid receptor localization in Brain. *Proc. Natl. Acad. Sci. U S A.* 1990: 87: 1932–1936.

Herning, R.I., Hooker, W.D., and Jones, R.T. Tetrahydrocannabinol content and differences in marijuana smoking behavior. *Psychopharmacology.* 1986: 90(2): 160–162.

Hively, R. L., Mosher, W. A., and Hoffman, F. W. Isolation of trans-Δ^9-tetrahydrocannabinol from marihuana. *J. Am. Chem. Soc.* 1966: 88: 1832–1833.

Hollister, L.E. Health aspects of cannabis. *Pharmacological Rev.* 1986: 38: 1–20.

Hollister, L.E. Cannabis. (Literature review). *Acta Psychiatr Scand (Suppl).* 1988: 78: 108–118.

Howlett, A.C., Breivogel, C.S., Childers, S.R., Deadwyler, S.A., Hampson, R.E., and Porrino, L.J. Cannabinoid physiology and pharmacology: 30 years of progress. *Neuropharmacology.* 2004: 47 Suppl 1: 345–58.

Huestis, M. A., Sampson, A. H., Holicky, B. J., Henningfield, J. E., and Cone, E. J. Characterization of the absorption phase of marijuana smoking. *Clin. Pharmacol. Ther.* 1992a: 52: 31–41.

Huestis, M.A., Henningfield, J.E.,; and Cone, E.J. Blood Cannabinoids. 1. Absorption of THC and formation of 11–OH–THC and

THC COOH during and after smoking marijuana. *J Anal Toxicol.* 1992b: 16(5): 276–282.
Hunt, C.A. and Jones, R.T. Tolerance and disposition of tetrahydrocannabinol in man. *J Pharmacol Exp Ther.* 1980 Oct: 215(1): 35–44.
Institute of Medicine. Division of Health Sciences Policy. Marijuana and Health: Report of a Study by a Committee of the Institute of Medicine, Division of Health Sciences Policy. Washington, DC: National Academy Press, 1982.
Institute of Medicine, Division of Neuroscience and Behavioral Health. Marijuana and Medicine: Assessing the Science Base. Washington D.C.: National Academy Press, 1999.
Johansson, E., Halldin, M.M., Agurell, S., Hollister, L.E.; and Gillespie, H.K. Terminal elimination plasma half-life of delta 1-tetrahydrocannabinol (delta 1–THC) in heavy users of marijuana. *Eur J Clin Pharmacol.* 1989: 37(3): 273–277.
Johnston, L. D., O'Malley, P. M., Bachman, J. G., and Schulenberg, J. E. Monitoring the Future national results on adolescent drug use: Overview of key findings, 2005 (*NIH Publication No. 06–5882*). Bethesda, MD: National Institute on Drug Abuse, 2006: 67.
Jones, R.T., Benowitz, N.L., and Herning, R.I. Clinical relevance of cannabis tolerance and dependence. *J Clin Pharmacol.* 1981: 21: 143S–152S.
Jones, R.T. Cardiovascular system effects of marijuana. *J Clin Pharmacol.* 2002 Nov: 42(11 Suppl): 58S–63S.
Justinova, Z., Tanda, G., Redhi, G.H., and Goldberg, S.R. Self-administration of delta9-tetrahydrocannabinol (THC) by drug naive squirrel monkeys. *Psychopharmacology (Berl).* 2003 Sep: 169(2): 135–40.
Kandel, D.B. and Chen, K. Types of marijuana users by longitudinal course. *J Stud Alcohol.* 2000 May: 61(3): 367–78.
Kirk, J.M. and de Wit, H. Responses to oral delta9-tetrahydrocannabinol in frequent and infrequent marijuana users. *Pharmacol Biochem Behav.* 1999 May: 63(1): 137–42.
Kurzthaler, I., Hummer, M., Miller, C., Sperner-Unterweger, B., Gunther, V., Wechdorn, H., Battista, H.J., and Fleischhacker, W.W. Effect of cannabis use on cognitive functions and driving ability. *J Clin Psychiatry.* 1999 Jun: 60(6): 395–9.
Lane, J.D. and Phillips-Bute, B.G. Caffeine deprivation affects vigilance performance and mood. *Physiol Behav.* 1998: 65: 171–5.
Lemberger, L., Silberstein, S. D., Axelrod, J., and Kopin, I. J. Marihuana: studies on the disposition and metabolism of delta-9-tetrahydrocannabinol in man. *Science.* 1970: 170: 1320–1322.
Lemberger, L., Weiss, J. L., Watanabe, A. M., Galanter, I. M., Wyatt, R. J., and Cardon, P. V. Delta-9-tetrahydrocannabinol: temporal correlation of the psychological effects and blood levels after various routes of administration. *New Eng. J. Med.* 1972a: 286(13): 685–688.
Lemberger, L., Crabtree, R. E., and Rowe, H. M. 11-Hydroxy-Δ^9-tetrahydrocannabinol: pharmacology, disposition and metabolism of a major metabolite of marihuana in man. *Science.* 1972b: 177: 62–63.
Lemberger, L. and Rubin, A. The physiologic disposition of marihuana in man. *Life Sci.* 1975: 17: 1637–42.
Liguori, A., Gatto, C.P., and Robinson, J.H. Effects of marijuana on equilibrium, psychomotor performance, and simulated driving. *Behav Pharmacol.* 1998 Nov: 9(7): 599–609.
Lyketsos, C.G., Garrett, E., Liang, K.Y., and Anthony, J.C. Cannabis use and cognitive decline in persons under 65 years of age. *Am J Epidemiol.* 1999 May 1: 149(9): 794–800.
Lyons, M.J., Bar, J.L., Panizzon, M.S., Toomey, R., Eisen, S., Xian, H., and Tsuang, M.T. Neuropsychological consequences of regular marijuana use: a twin study. *Psychol Med.* 2004 Oct: 34(7): 1239–50.
Mackie, K., Lai, Y., Westenbroek, R., and Mitchell, R. Cannabinoids activate an inwardly rectifying potassium conductance and inhibit Q-type calcium currents in AtT20 cells transfected with rat brain cannabinoid receptor. *J Neurosci.* 1995 Oct: 15(10): 6552–61.
Maldonado, R. Study of cannabinoid dependence in animals. *Pharmacol Ther.* 2002 Aug: 95(2): 153–64.
Maremmani, I., Lazzeri, A., Pacini, M., Lovrecic, M., Placidi, G.F., and Perugi, G. Diagnostic and symptomatological features in chronic psychotic patients according to cannabis use status. *J Psychoactive Drugs.* 2004 Jun: 36(2): 235–41.
Martellotta, M.C., Cossu, G., Fattore, L., Gessa, G.L., and Fratta, W. Self-administration of the cannabinoid receptor agonist WIN 55,212–2 in drug-naive mice. *Neuroscience.* 1998 Jul: 85(2): 327–30.
Mathers, D.C. and Ghodse, A.H. Cannabis and psychotic illness. *Br J Psychiatry.* 1992 Nov: 161: 648–53.
Martin, B.R., Mechoulam, R., and Razdan, R.K. Discovery and characterization of endogenous cannabinoids. *Life Sci.* 1999: 65: 573–595.
Matsuda, L. A., Lolait, S. J., Brownstein, M. J., Young, A. C., and Bonner, T.I. Structure of a cannabinoid receptor and functional expression of the cloned cDNA. *Nature.* 1990: 346: 561–564.
Mechoulam, R. Cannabinoid chemistry. In Mechoulam, R. (ED.) Marijuana (New York, NY, Academic Press, Inc.), 1973: 2–88.
Mendelson, J.H. and Mello, N.K. Effects of marijuana on neuroendocrine hormones in human males and females. *NIDA Res Monogr.* 1984: 44: 97–114.
Messinis, L., Kyprianidou, A., Malefaki, S., and Papathanasopoulos, P. Neuropsychological deficits in long-term frequent cannabis users. *Neurology.* 2006: 66: 737–739.
Monitoring the Future. National Results on Adolescent Drug Use. Overview of 1999 Key findings, 1999. Department of Health and Human Services. National Institute on Drug Abuse. Rockville, MD. (*http://monitoringthefuture.org*)
Nace, E.P., Meyers, A.L., Rothberg, J.M., and Maleson, F. Addicted and nonaddicted drug users. A comparison of drug usage patterns. *Arch Gen Psychiatry.* 1975: 32(1): 77–80.
National Institutes of Health (NIH). Workshop on the medical Utility of Marijuana, February 19–20, 1997. (*www.nih.gov/news/medmarijuana/MedicalMarijuana.htm*)
Office of National Drug Control Policy. The National Drug Control Strategy: 2000 Annual Report. Superintendent of Documents, Mail Stop: SSOP, Washington, DC.
Oviedo, A., Glowa, J. and Herkenham, M. Chronic cannabinoid administration alters cannabinoid receptor binding in rat brain: a quantitative autoradiographic study. *Brain Res.* 1993: 616: 293–302.
Pencer, A., Addington, J., and Addington, D. Outcome of a first episode of psychosis in adolescence: a 2-year follow-up. *Psychiatry Res.* 2005 Jan 30: 133(1): 35–43.
Piomelli, D. The endocannabinoid system: a drug discovery perspective. *Curr Opin Investig Drugs.* 2005 Jul: 6(7): 672–9.
Pope, H.G. Jr., Gruber, A.J., Hudson, J.I., Cohane, G., Huestis, M.A., and Yurgelun-Todd, D. Early-onset cannabis use and cognitive deficits: what is the nature of the association? *Drug Alcohol Depend.* 2003 Apr 1: 69(3): 303–10.
Ramaekers, J.G., Berghaus, G., van Laar, M., and Drummer, O.H. Dose related risk of motor vehicle crashes after cannabis use. *Drug Alcohol Depend.* 2004 Feb 7: 73(2): 109–19.
Rodriguez de Fonseca, F., Gorriti, M.A., Fernandez-Ruiz, J.J., Palomo, T., and Ramos, J.A. Downregulation of rat brain cannabinoid binding sites after chronic delta 9-tetrahydrocannabinoil treatment. *Phamacol. Biochem. Behav.* 1994: 47 (1): 33–40.
Ross, S. A. and El Sohly, M. A. Constituents of Cannabis Sativa L. A review of the natural constituents: 1980–1994. *Zagazig J. Pharm.* Sci. 1995: 4 (2): 1–10.
Roth, M.D., Tashkin, D.P., Whittaker, K.M., Choi, R., and Baldwin, G.C. Tetrahydrocannabinol suppresses immune function and enhances HIV replication in the huPBL-SCID mouse. *Life Sci.* 2005 Aug 19: 77(14): 1711–22.
Sarfaraz, S., Afaq, F., Adhami, V.M., and Mukhtar, H. Cannabinoid receptor as a novel target for the treatment of prostate cancer. *Cancer Res.* 2005 Mar 1: 65(5): 1635–41.
Sanudo-Pena, M. C., Tsou, K., Delay, E. R., Hohman, A. G., Force, M., and Walker, J. M. Endogenous cannabinoids as an aversive or counter-rewarding system in the rat. *Neurosci. Lett.* 1997: 223: 125–128.
Schiffman, J., Nakamura, B., Earleywine, M., and LaBrie, J. Symptoms of schizotypy precede cannabis use. *Psychiatry Res.* 2005 Mar 30: 134(1): 37–42.
Sidney, S. Cardiovascular consequences of marijuana use. *J Clin Pharmacol.* 2002 Nov: 42(11 Suppl): 64S–70S.
Solowij, N., Stephens, R.S., Roffman, R.A., Babor, T., Kadden, R., Miller, M., Christiansen, K., McRee, B., and Vendetti, J. Marijuana Treatment Project Research Group. Cognitive functioning of long-term heavy cannabis users seeking treatment. *JAMA.* 2002 Mar 6: 287(9): 1123–31.
Stirling, J., Lewis, S., Hopkins, R., and White, C. Cannabis use prior to first onset psychosis predicts spared neurocognition at 10-year follow-up. *Schizophr Res.* 2005 Jun 1: 75(1): 135–7.

Substance Abuse and Mental Health Services Administration, Office of Applied Studies. *Drug Abuse Warning Network, 2004: National Estimates of Drug-Related Emergency Department Visits.* DAWN Series D–28, HHS Publication No. (SMA) 06–4143, Rockville, MD, 2006.

Substance Abuse and Mental Health Services Administration. *Results from the 2004 National Survey on Drug Use and Health: National Findings* (Office of Applied Studies, NSDUH Series H–28, HHS Publication No. SMA 05–4062). Rockville, MD, 2005.

Substance Abuse and Mental Health Services Administration, Office of Applied Studies. *Treatment Episode Data Set (TEDS). Highlights—2004.* National Admissions to Substance Abuse Treatment Services, DASIS Series: S–31, HHS Publication No. (SMA) 06–4140, Rockville, MD, 2006.

Tanda, G., Munzar, P., and Goldberg, S.R. Self-administration behavior is maintained by the psychoactive ingredient of marijuana in squirrel monkeys. *Nat Neurosci.* 2000 Nov: 3(11): 1073–4.

Tashkin, D.P. Smoked marijuana as a cause of lung injury. *Monaldi Arch Chest Dis.* 2005 Jun: 63(2): 93–100.

Tashkin, D.P., Zhang, Z.F., Greenland, S., Cozen, W., Mack, T.M., and Morgenstern, H. Marijuana Use and Lung Cancer: Results of a Case-Control Study. Abstract #A777, American Thoracic Society meeting, May 24, 2006.

Thornicroft, G. Cannabis and psychosis. Is there epidemiological evidence for an association? *Br J Psychiatry.* 1990 Jul: 157: 25–33.

Twitchell, W., Brown, S., and Mackie, K. Cannabinoids inhibit N- and P/Q-type calcium channels in cultured rat hippocampal neurons. *J Neurophysiol.* 1997 Jul: 78(1): 43–50.

Tzilos, G.K., Cintron, C.B., Wood, J.B., Simpson, N.S., Young, A.D., Pope, H.G. Jr., and Yurgelun-Todd, D.A. Lack of hippocampal volume change in long-term heavy cannabis users. *Am J Addict.* 2005 Jan–Feb: 14(1): 64–72.

Vandrey, R.G., Budney, A.J., Moore, B.A., and Hughes, J.R. A cross-study comparison of cannabis and tobacco withdrawal. *Am J Addict.* 2005 Jan–Feb: 14(1): 54–63.

van Os, J., Bak, M., Hanssen, M., Bijl, R.V., de Graaf, R., and Verdoux, H. Cannabis use and psychosis: a longitudinal population-based study. *Am J Epidemiol.* 2002 Aug 15: 156(4): 319–27.

von Sydow, K., Lieb, R., Pfister, H., Hofler, M., and Wittchen, H.U. What predicts incident use of cannabis and progression to abuse and dependence? A 4-year prospective examination of risk factors in a community sample of adolescents and young adults. *Drug Alcohol Depend.* 2002 Sep 1: 68(1): 49–64.

Wachtel, S.R., El Sohly, M.A., Ross, S.A., Ambre, J., and de Wit, H. Comparison of the subjective effects of Delta (9)-tetrahydrocannabinol and marijuana in humans. *Psychopharmacology (Berl).* 2002 Jun: 161(4): 331–9.

Wagner, J.A., Varga, K., and Kunos, G. Cardiovascular actions of cannabinoids and their generation during shock. *J Mol Med.* 1998 Nov–Dec: 76(12): 824–36.

Wiley, J.L., Barrett, R.L., Britt, D.T., Balster, R.L., and Martin, B.R. Discriminative stimulus effects of delta 9-tetrahydrocannabinol and delta 9-11-tetrahydrocannabinol in rats and rhesus monkeys. *Neuropharmacology.* 1993 Apr: 32(4): 359–65.

Wiley, J.L., Huffman, J.W., Balster, R.L., and Martin, B.R. Pharmacological specificity of the discriminative stimulus effects of delta 9-tetrahydrocannabinol in rhesus monkeys. *Drug Alcohol Depend.* 1995 Nov: 40(1): 81–6.

Wu, X. and French, E.D. Effects of chronic delta9-tetrahydrocannabinol on rat midbrain dopamine neurons: an electrophysiological assessment. *Neuropharmacology.* 2000 Jan 28: 39(3): 391–8.

Yanagita, T. Self-administration studies on psychological dependence. *Trends in Pharmacological Sciences.* 1979–1980: 1:1: 161–164.

Zhang, Z.F., Morgenstern, H., Spitz, M.R., Tashkin, D.P., Yu, G.P., Marshall, J.R., Hsu, T.C., and Schantz, S.P. Marijuana use and increased risk of squamous cell carcinoma of the head and neck. *Cancer Epidemiol Biomarkers Prev.* 1999 Dec: 8(12): 1071–8.

Marijuana

Scheduling Review Document: Eight Factor Analysis

Drug and Chemical Evaluation Section
Office of Diversion Control
Drug Enforcement Administration, April 2011

INTRODUCTION

On October 9, 2002, the Coalition for Rescheduling Cannabis submitted a petition to the Drug Enforcement Administration (DEA) to initiate proceedings for a repeal of the rules or regulations that place marijuana [3] in schedule I of the Controlled Substances Act (CSA). The petition requests that marijuana be rescheduled as ''cannabis'' in either schedule III, IV, or V of the CSA. The petitioner claims that:

1. Cannabis has an accepted medical use in the United States;

2. Cannabis is safe for use under medical supervision;

3. Cannabis has an abuse potential lower than schedule I or II drugs; and

4. Cannabis has a dependence liability that is lower than schedule I or II drugs.

The DEA accepted this petition for filing on April 3, 2003. In accordance with 21 U.S.C. 811(b), after gathering the necessary data, the DEA requested a medical and scientific evaluation and scheduling recommendation for cannabis from the Department of Health and Human Services (DHHS) on July 12, 2004. On December 6, 2006, the DHHS provided its scientific and medical evaluation titled *Basis for the Recommendation for Maintaining Marijuana in Schedule I of the Controlled Substances Act* and recommended that marijuana continue to be controlled in schedule I of the CSA.

The CSA requires DEA to determine whether the DHHS scientific and medical evaluation and scheduling recommendation and ''all other relevant data'' constitute substantial evidence that the drug should be rescheduled as proposed in the petition. 21 U.S.C. 811(b). This document is prepared accordingly.

The Attorney General ''may by rule'' transfer a drug or other substance between schedules if he finds that such drug or other substance has a potential for abuse, and makes with respect to such drug or other substance the findings prescribed by subsection (b) of Section 812 for the schedule in which such drug is to be placed. 21 U.S.C. 811(a)(1). In order for a substance to be placed in schedule I, the Attorney General must find that:

A. The drug or other substance has a high potential for abuse.

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

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

21 U.S.C. 812(b)(1)(A)–(C). To be classified in one of the other schedules (II through V), a drug of abuse must have either a ''currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions.'' 21 U.S.C. 812(b)(2)–(5). If a controlled substance has no such currently accepted medical use, it must be placed in schedule I. *See* Notice of Denial of Petition, 66 FR 20038, 20038 (Apr. 18, 2001) (''Congress established only one schedule—schedule I—for drugs of abuse with 'no currently accepted medical use in treatment in the United States' and 'lack of accepted safety for use . . . under medical supervision.'''').

In deciding whether to grant a petition to initiate rulemaking proceedings with respect to a particular drug, DEA must determine whether there is sufficient evidence to conclude that the drug meets the criteria for placement in another schedule based on the criteria set forth in 21 U.S.C. 812(b). To do so, the CSA requires that DEA and DHHS consider eight factors as specified in 21 U.S.C. 811(c). This document is organized according to these eight factors.

With specific regard to the issue of whether the drug has a currently accepted medical use in treatment in the United States, DHHS states that the FDA has not evaluated nor approved a new drug application (NDA) for marijuana. The long-established factors applied by the DEA for determining whether a drug has a ''currently accepted medical use'' under the CSA are:

[3] The Controlled Substances Act (CSA) defines marijuana as the following:

All parts of the plant Cannabis sativa L., whether growing or not; the seeds thereof; the resin extracted from any part of such plant; and every compound, manufacture, salt, derivative, mixture, or preparation of such plant, its seeds or resin. Such term does not include the mature stalks of such plant, fiber produced from such stalks, oil or cake made from the seeds of such plant, any other compound, manufacture, salt, derivative, mixture, or preparation of such mature stalks (except the resin extracted there from), fiber, oil, or cake, or the sterilized seed of such plant which is incapable of germination. 21 U.S.C. 802(16).

Note that ''marihuana'' is the spelling originally used in the CSA. This document uses the spelling that is more common in current usage, ''marijuana.''

1. The drug's chemistry must be known and reproducible;
2. There must be adequate safety studies;
3. There must be adequate and well-controlled studies proving efficacy;
4. The drug must be accepted by qualified experts; and
5. The scientific evidence must be widely available.

57 FR 10,499, 10,506 (1992); *Alliance for Cannabis Therapeutics v. DEA,* 15 F.3d 1131, 1135 (D.C. Cir. 1994) (*ACT*) (upholding these factors as valid criteria for determining ''accepted medical use''). A drug will be deemed to have a currently accepted medical use for CSA purposes only if all five of the foregoing elements are demonstrated. This test is considered here under the third factor.

Accordingly, as the eight factor analysis sets forth in detail below, the evidence shows:

1. *Actual or relative potential for abuse.* Marijuana has a high abuse potential. It is the most widely used illicit substance in the United States. Preclinical and clinical data show that it has reinforcing effects characteristic of drugs of abuse. National databases on actual abuse show marijuana is the most widely abused drug, including significant numbers of substance abuse treatment admissions. Data on marijuana seizures show widespread availability and trafficking.

2. *Scientific evidence of its pharmacological effect.* The scientific understanding of marijuana, cannabinoid receptors, and the endocannabinoid system has improved. Marijuana produces various pharmacological effects, including subjective (e.g., euphoria, dizziness, disinhibition), cardiovascular, acute and chronic respiratory, immune system, cognitive impairment, and prenatal exposure effects as well as possible increased risk of schizophrenia among those predisposed to psychosis.

3. *Current scientific knowledge.* There is no currently accepted medical use for marijuana in the United States. Under the five-part test for currently accepted medical use approved in *ACT,* 15 F.3d at 1135, there is no complete scientific analysis of marijuana's chemical components; there are no adequate safety studies; there are no adequate and well-controlled efficacy studies; there is not a consensus of medical opinion concerning medical applications of marijuana; and the scientific evidence regarding marijuana's safety and efficacy is not widely available. While a number of states have passed voter referenda or legislative actions authorizing the use of marijuana for medical purposes, this does not establish a currently accepted medical use under federal law. To date, scientific and medical research has not progressed to the point that marijuana has a currently accepted medical use, even under conditions where its use is severely restricted.

4. *History and current pattern of abuse.* Marijuana use has been relatively stable from 2002 to 2009, and it continues to be the most widely used illicit drug. In 2009, there were 16.7 million current users. There were also 2.4 million new users, most of whom were less than 18 years of age. During the same period, marijuana was the most frequently identified drug exhibit in federal, state, and local laboratories. High consumption of marijuana is fueled by increasing amounts of both domestically grown and illegally smuggled foreign source marijuana, and an increasing percentage of seizures involve high potency marijuana.

5. *Scope, duration, and significance of abuse.* Abuse of marijuana is widespread and significant. In 2008, for example, an estimated 3.9 million people aged 12 or older used marijuana on a daily or almost daily basis over a 12-month period. In addition, a significant proportion of all admissions for treatment for substance abuse are for primary marijuana abuse: in 2007, 16 percent of all admissions were for primary marijuana abuse, representing 287,933 individuals. Of individuals under the age of 19 admitted to substance abuse treatment, more than half were treated for primary marijuana abuse.

6. *Risk, if any, to public health.* Together with the health risks outlined in terms of pharmacological effects above, public health risks from acute use of marijuana include impaired psychomotor performance, including impaired driving, and impaired performance on tests of learning and associative processes. Public health risks from chronic use of marijuana include respiratory effects, physical dependence, and psychological problems.

7. *Psychic or physiological dependence liability.* Long-term, regular use of marijuana can lead to physical dependence and withdrawal following discontinuation, as well as psychic addiction or dependence.

8. *Immediate precursor.* Marijuana is not an immediate precursor of any controlled substance.

This review shows, in particular, that the evidence is insufficient with respect to the specific issue of whether marijuana has a currently accepted medical use under the five-part test. The evidence was insufficient in this regard on the prior two occasions when DEA considered petitions to reschedule marijuana in 1992 (57 FR 10499)[4] and in 2001 (66 FR 20038).[5] Little has changed since then with respect to the lack of clinical evidence necessary to establish that marijuana has a currently accepted medical use: only a limited number of FDA-approved Phase 1 clinical investigations have been carried out, and there have been no studies that have scientifically assessed the efficacy and full safety profile of marijuana for any medical condition.[6] The limited existing clinical evidence is not adequate to warrant rescheduling of marijuana under the CSA.

To the contrary, the data in this Scheduling Review document show that marijuana continues to meet the criteria for schedule I control under the CSA for the following reasons:

1. Marijuana has a high potential for abuse.
2. Marijuana has no currently accepted medical use in treatment in the United States.
3. Marijuana lacks accepted safety for use under medical supervision.

FACTOR 1: THE DRUG'S ACTUAL OR RELATIVE POTENTIAL FOR ABUSE

Marijuana is the most commonly abused illegal drug in the United States. It is also the most commonly used illicit drug by American high-schoolers. Marijuana is the most frequently identified drug in state, local and federal forensic laboratories, with increasing amounts both of domestically grown and of illicitly smuggled marijuana. Marijuana's main psychoactive ingredient, Δ^9-THC, is an effective reinforcer in laboratory animals, including primates and rodents. These animal studies both predict and support the observations that Δ^9-THC, whether smoked as marijuana or administered by other routes, produces reinforcing effects in humans. Such reinforcing effects can account for the repeated abuse of marijuana.

A. Indicators of Abuse Potential

DHHS has concluded in its document, ''Basis for the Recommendation for Maintaining Marijuana in Schedule I of the Controlled Substances Act'', that marijuana has a high potential for abuse. The finding of ''abuse potential'' is critical for control under the Controlled Substances Act (CSA). Although the term is not defined in the CSA, guidance in determining abuse potential is provided in the legislative history of the Act (Comprehensive Drug Abuse Prevention and Control Act of 1970, H.R. Rep. No. 91–144, 91st Cong., Sess.1 (1970), reprinted in 1970 U.S.C.C.A.N. 4566, 4603). Accordingly, the following items are indicators that a drug or other substance has potential for abuse:

- There is evidence that individuals are taking the drug or other substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community; or
- There is significant diversion of the drug or other substance from legitimate drug channels; or
- Individuals are taking the drug or substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs; or
- The drug is a new drug so related in its action to a drug or other substance already listed as having a potential for abuse to make it likely that the drug substance will have the same potential for abuse as such drugs, thus

[4] *Petition for review dismissed, Alliance for Cannabis Therapeutics v. DEA,* 15 F.3d 1131 (D.C. Cir. 1994).

[5] *Petition for review dismissed, Gettman v. DEA,* 290 F.3d 430 (D.C. Cir. 2002).

[6] Clinical trials generally proceed in three phases. *See* 21 CFR 312.21 (2010). Phase I trials encompass initial testing in human subjects, generally involving 20 to 80 patients. Id. They are designed primarily to assess initial safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary studies of potential therapeutic benefit. 62 FR 66113, 1997. Phase II and Phase III studies involve successively larger groups of patients: usually no more than several hundred subjects in Phase II, and usually from several hundred to several thousand in Phase III. 21 CFR 312.21. These studies are designed primarily to explore (Phase II) and to demonstrate or confirm (Phase III) therapeutic efficacy and benefit in patients. 62 FR 66113, 1997. *See also Riegel v. Medtronic, Inc.,* 128 S.Ct. 999, 1018–19 n.15 (2008) (Ginsburg, J., dissenting).

making it reasonable to assume that there may be significant diversion 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. Of course, evidence of actual abuse of a substance is indicative that a drug has a potential for abuse.

After considering the above items, DHHS has found that marijuana has a high potential for abuse.

1. There is evidence that individuals are taking the drug or other substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community.

Marijuana is the most highly used illicit substance in the United States. Smoked marijuana exerts a number of cardiovascular and respiratory effects, both acutely and chronically and can cause chronic bronchitis and inflammatory abnormalities of the lung tissue. Marijuana's main psychoactive ingredient Δ^9-THC alters immune function and decreases resistance to microbial infections. The cognitive impairments caused by marijuana use that persist beyond behaviorally detectable intoxication may have significant consequences on workplace performance and safety, academic achievement, and automotive safety, and adolescents may be particularly vulnerable to marijuana's cognitive effects. Prenatal exposure to marijuana was linked to children's poorer performance in a number of cognitive tests. Data on the extent and scope of marijuana abuse are presented under factors 4 and 5 of this analysis. DHHS's discussion of the harmful health effects of marijuana and additional information gathered by DEA are presented under factor 2, and the assessment of risk to the public health posed by acute and chronic marijuana abuse is presented under factor 6 of this analysis.

2. There is significant diversion of the drug or other substance from legitimate drug channels.

DHHS states that at present, marijuana is legally available through legitimate channels for research only and thus has a limited potential for diversion. (DEA notes that while a number of states have passed voter referenda or legislative actions authorizing the use of marijuana for medical purposes, this does not establish a currently accepted medical use under federal law.) In addition, the lack of significant diversion of investigational supplies may result from the ready availability of illicit cannabis of equal or greater quality.

DEA notes that the magnitude of the demand for illicit marijuana is evidenced by information from a number of databases presented under factor 4. Briefly, marijuana is the most commonly abused illegal drug in the United States. It is also the most commonly used illicit drug by American high-schoolers. Marijuana is the most frequently identified drug in state, local, and federal forensic laboratories, with increasing amounts both of domestically grown and of illicitly smuggled marijuana. An observed increase in the potency of seized marijuana also raises concerns.

3. Individuals are taking the drug or substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs.

16.7 million adults over the age of 12 reported having used marijuana in the past month, according to the 2009 National Survey on Drug Use and Health (NSDUH), as further described later in this factor. DHHS states in its 2006 analysis of the petition that the FDA has not evaluated or approved a new drug application (NDA) for marijuana for any therapeutic indication, although several investigational new drug (IND) applications are currently active. Based on the large number of individuals who use marijuana, DHHS concludes that the majority of individuals using cannabis do so on their own initiative, not on the basis of medical advice from a practitioner licensed to administer the drug in the course of professional practice.

4. The drug is a new drug so related in its action to a drug or other substance already listed as having a potential for abuse to make it likely that the drug substance will have the same potential 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. Of course, evidence of actual abuse of a substance is indicative that a drug has a potential for abuse.

Marijuana is not a new drug. Marijuana's primary psychoactive ingredient delta-9-tetrahydrocannabinol (Δ^9-THC) is controlled in schedule I of the CSA. DHHS states that there are two drug products containing cannabinoid compounds that are structurally related to the active components in marijuana. Both are controlled under the CSA. Marinol is a schedule III drug product containing synthetic Δ^9-THC, known generically as dronabinol, formulated in sesame oil in soft gelatin capsules. Marinol was approved by the FDA in 1985 for the treatment of two medical conditions: nausea and vomiting associated with cancer chemotherapy in patients that had failed to respond adequately to conventional anti-emetic treatments, and for the treatment of anorexia associated with weight loss in patients with acquired immunodeficiency syndrome (AIDS). Cesamet is a drug product containing the schedule II substance, nabilone, that was approved for marketing by the FDA in 1985 for the treatment of nausea and vomiting associated with cancer chemotherapy. All other structurally related cannabinoids in marijuana are already listed as Schedule I drugs under the CSA.

In addition, DEA notes that marijuana and its active ingredient Δ^9-THC are related in their action to other controlled drugs of abuse when tested in preclinical and clinical tests of abuse potential. Data showing that marijuana and Δ^9-THC exhibit properties common to other controlled drugs of abuse in those tests are described below in this factor.

In summary, examination of the indicators set forth in the legislative history of the CSA demonstrates that marijuana has a high potential for abuse. Indeed, marijuana is abused in amounts sufficient to create hazards to public health and safety; there is significant trafficking of the substance; individuals are using marijuana on their own initiative, for the vast majority, rather than on the basis of medical advice; and finally, marijuana exhibits several properties common to those of drugs already listed as having abuse potential.

The petitioner states that, ''widespread use of cannabis is not an indication of its abuse potential [...] .'' (Exh. C, Section IV(15), pg. 87).

To the contrary, according to the indicators set forth in the legislative history of the CSA as described above, the fact that ''Individuals are taking the drug or substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs'' is indeed one of several indicators that a drug has high potential for abuse.

B. Abuse Liability Studies

In addition to the indicators suggested by the CSA's legislative history, data as to preclinical and clinical abuse liability studies, as well as actual abuse, including clandestine manufacture, trafficking, and diversion from legitimate sources, are considered in this factor.

Abuse liability evaluations are obtained from studies in the scientific and medical literature. There are many preclinical measures of a drug's effects that when taken together provide an accurate prediction of the human abuse liability. Clinical studies of the subjective and reinforcing effects in humans and epidemiological studies provide quantitative data on abuse liability in humans and some indication of actual abuse trends. Both preclinical and clinical studies have clearly demonstrated that marijuana and Δ^9-THC possess the attributes associated with drugs of abuse: they function as a positive reinforcer to maintain drug-seeking behavior, they function as a discriminative stimulus, and they have dependence potential.

Preclinical and most clinical abuse liability studies have been conducted with the psychoactive constituents of marijuana, primarily Δ^9-THC and its metabolite, 11-OH-Δ^9-THC. Δ^9-THC's subjective effects are considered to be the basis for marijuana's abuse liability. The following studies provide a summary of that data.

1. Preclinical Studies

Delta-9-THC is an effective reinforcer in laboratory animals, including primates and rodents, as these animals will self-administer Δ^9-THC. These animal studies both predict and support the observations that Δ^9-THC, whether smoked as marijuana or administered by other routes, produces reinforcing effects in humans. Such reinforcing effects can account for the repeated abuse of marijuana.

a. Discriminative Stimulus Effects

The drug discrimination paradigm is used as an animal model of human subjective effects (Solinas *et al.*, 2006). This procedure provides a direct measure of stimulus

specificity of a test drug in comparison with a known standard drug or a neutral stimulus (e.g., injection of saline water). The light-headedness and warmth associated with drinking alcohol or the jitteriness and increased heart rate associated with drinking coffee are examples of substance-specific stimulus effects. The drug discrimination paradigm is based on the ability of nonhuman and human subjects to learn to identify the presence or absence of these stimuli and to differentiate among the constellation of stimuli produced by different pharmacological classes. In drug discrimination studies, the drug stimuli function as cues to guide behavioral choice, which is subsequently reinforced with other rewards. Repeated pairing of the reinforcer with only drug-appropriate responses can engender reliable discrimination between drug and no-drug or amongst several drugs. Because some interoceptive stimuli are believed to be associated with the reinforcing effects of drugs, the drug discrimination paradigm is used to evaluate the abuse potential of new substances.

DHHS states that in the drug discrimination test, animals are trained to respond by pressing one bar when they receive the known drug of abuse and another bar when they receive placebo.

DHHS states that cannabinoids appear to provide unique discriminative stimulus effects because stimulants, non-cannabinoid hallucinogens, opioids, benzodiazepines, barbiturates, NMDA antagonists and antipsychotics do not fully substitute for Δ^9-THC (Browne and Weissman, 1981; Balster and Prescott, 1992, Gold *et al.*, 1992; Barrett *et al.*, 1995; Wiley *et al.*, 1995). Animals, including monkeys and rats (Gold et al., 1992), as well as humans (Chait *et al.*, 1988), can discriminate cannabinoids from other drugs or placebo.

DEA notes several studies that show that the discriminative stimulus effects of Δ^9-THC are mediated via a cannabinoid receptor, specifically, the CB_1 receptor subtype, and that the CB_1 antagonist rimonabant (SR 141716A) antagonizes the discriminative stimulus effects of Δ^9-THC in several species (Pério *et al.*, 1996; Mansbach *et al.*, 1996; Järbe *et al.*, 2001). The subjective effects of marijuana and Δ^9-THC are, therefore, mediated by a neurotransmitter system in the brain that is specific to Δ^9-THC and cannabinoids.

b. Self-Administration Studies

Self-administration is a behavioral assay that measures the rewarding effects of a drug that increase the likelihood of continued drug-taking behavior. Drugs that are self-administered by animals are likely to produce rewarding effects in humans. A strong correlation exists between drugs and other substances that are abused by humans and those that maintain self-injection in laboratory animals (Schuster and Thompson, 1969; Griffiths *et al.*, 1980). As a result, intravenous self-injection of psychoactive substances in laboratory animals is considered to be useful for the prediction of human abuse liability of these compounds (Johanson and Balster, 1978; Collins et al., 1984).

DHHS states that self-administration of hallucinogenic-like drugs, such as cannabinoids, lysergic acid diethylamide (LSD), and mescaline, has been difficult to demonstrate in animals (Yanagita, 1980). DHHS further states that an inability to establish self-administration has no practical importance in the assessment of abuse potential, because it is known that humans voluntarily consume a particular drug (such as cannabis) for its pleasurable effects.

DHHS states that the experimental literature generally reports that naïve animals will not self-administer cannabinoids unless they have had previous experience with other drugs of abuse, however, animal research in the past decade has provided several animal models of reinforcement by cannabinoids to allow for pre-clinical research into cannabinoids' reinforcing effects. Squirrel monkeys trained to self-administer intravenous cocaine will continue to respond at the same rate as when Δ^9-THC is substituted for cocaine, at doses that are comparable to those used by humans who smoke marijuana (Tanda *et al.*, 2000). This effect is blocked by the cannabinoid receptor antagonist, SR 141716. Squirrel monkeys without a history of any drug exposure can be successfully trained to self-administer Δ^9-THC intravenously (Justinova *et al.*, 2003). The maximal rate of responding is 4 μg/kg/injection, which is 2–3 times greater than that observed in previous studies using cocaine-experienced monkeys. Rats will self-administer Δ^9-THC when it is applied intracerebroventricularly (i.c.v.), but only at the lowest doses tested (0.01:–0.02/μg/infusion) (Braida *et al.*, 2004). This effect is antagonized by the cannabinoid antagonist SR141716 and by the opioid antagonist naloxone (Braida et al., 2004). Additionally, mice will self-administer WIN 55212, a synthetic CB_1 receptor agonist with a non-cannabinoid structure (Martellotta *et al.*, 1998).

DEA notes a study showing that the opioid antagonist naltrexone reduces the self-administration responding for Δ^9-THC in squirrel monkeys (Justinova *et al.*, 2004). These investigators, using second-order schedules of drug-seeking procedures, also showed that pre-session administration of Δ^9-THC and other cannabinoid agonists, or morphine, but not cocaine, reinstates the Δ^9-THC seeking behavior following a period of abstinence (Justinova *et al.*, 2008). Furthermore, the endogenous cannabinoid anandamide and its synthetic analog methanandamide are self-administered by squirrel monkeys, and CB_1 receptor antagonism blocks the reinforcing effect of both substances (Justinova *et al.*, 2005).

c. Place Conditioning Studies

Conditioned place preference (CPP) is another behavioral assay used to determine if a drug has rewarding properties. In this test, animals in a drug-free state are given the opportunity to spend time in two distinct environments: one where they previously received a drug and one where they received a placebo. If the drug is reinforcing, animals in a drug-free state will choose to spend more time in the environment paired with the drug when both environments are presented simultaneously.

DHHS states that animals exhibit CPP to Δ^9-THC, but only at the lowest doses tested (0.075–0.75 mg/kg, i.p.) (Braida *et al.*, 2004). The effect is antagonized by the cannabinoid antagonist, rimonabant, as well as the opioid antagonist, naloxone. The effect of naloxone on CPP to Δ^9-THC raises the possibility that the opioid system may be involved in the rewarding properties of Δ^9-THC and marijuana. DEA notes a recent review (Murray and Bevins, 2010) that further explores the currently available knowledge on Δ^9-THC's ability to induce CPP and conditioned place aversion (CPA), and further supports that low doses of Δ^9-THC appear to have conditioned rewarding effects, whereas higher doses have aversive effects.

2. Clinical Studies

DHHS states that the physiological, psychological, and behavioral effects of marijuana vary among individuals and presents a list of common responses to cannabinoids, as described in the scientific literature (Adams and Martin, 1996; Hollister, 1986, 1988; Institute of Medicine, 1982):

1. Dizziness, nausea, tachycardia, facial flushing, dry mouth and tremor initially
2. Merriment, happiness and even exhilaration at high doses
3. Disinhibition, relaxation, increased sociability, and talkativeness
4. Enhanced sensory perception, giving rise to increased appreciation of music, art and touch
5. Heightened imagination leading to a subjective sense of increased creativity
6. Time distortions
7. Illusions, delusions and hallucinations are rare except at high doses
8. Impaired judgment, reduced coordination and ataxia, which can impede driving ability or lead to an increase in risk-taking behavior
9. Emotional lability, incongruity of affect, dysphoria, disorganized thinking, inability to converse logically, agitation, paranoia, confusion, restlessness, anxiety, drowsiness and panic attacks may occur, especially in inexperienced users or in those who have taken a large dose
10. Increased appetite and short-term memory impairment are common

These subjective responses to marijuana are pleasurable to many humans and are associated with drug-seeking and drug-taking (Maldonado, 2002). DHHS states that, as with most psychoactive drugs, an individual's response to marijuana can be influenced by a person's medical/psychiatric history as well as their experience with drugs. Frequent marijuana users (used more than 100 times) were better able to identify a drug effect from low-dose Δ^9-THC than infrequent users (used less than 10 times) and were less likely to experience sedative effects from the drug (Kirk and de Wit, 1999). However, dose preferences have been demonstrated for marijuana in which higher doses (1.95 percent Δ^9-THC) are preferred over lower doses (0.63 percent Δ^9-THC) (Chait and Burke, 1994).

DEA notes that an extensive review of the reinforcing effects of marijuana in humans was included in DEA/DHHS's prior review of

marijuana (Notice of Denial of Petition, 66 FR 20038, 2001). While additional studies have been published on the reinforcing effects of marijuana in humans (e.g., see review by Cooper and Haney, 2009), they are consistent with the information provided in DEA/DHHS's prior review of this matter. Excerpts are provided below, with some citations omitted.

Both marijuana and THC can serve as positive reinforcers in humans. Marijuana and Δ^9-THC produced profiles of behavioral and subjective effects that were similar regardless of whether the marijuana was smoked or taken orally, as marijuana in brownies, or orally as THC-containing capsules, although the time course of effects differed substantially. There is a large clinical literature documenting the subjective, reinforcing, discriminative stimulus, and physiological effects of marijuana and THC and relating these effects to the abuse potential of marijuana and THC (e.g., Chait *et al.*, 1988; Lukas *et al.*, 1995; Kamien et al., 1994; Chait and Burke, 1994; Chait and Pierri, 1992; Foltin *et al.*, 1990; Azorlosa *et al.*, 1992; Kelly et al., 1993, 1994; Chait and Zacny, 1992; Cone *et al.*, 1988; Mendelson and Mello, 1984).

These listed studies represent a fraction of the studies performed to evaluate the abuse potential of marijuana and THC. In general, these studies demonstrate that marijuana and THC dose-dependently increases heart rate and ratings of ''high'' and ''drug liking'', and alters behavioral performance measures (e.g., Azorlosa *et al.*, 1992; Kelly et al., 1993, 1994; Chait and Zacny, 1992; Kamien *et al.*, 1994; Chait and Burke, 1994; Chait and Pierri, 1992; Foltin *et al.*, 1990; Cone *et al.*, 1988; Mendelson and Mello, 1984). Marijuana also serves as a discriminative stimulus in humans and produces euphoria and alterations in mood. These subjective changes were used by the subjects as the basis for the discrimination from placebo (Chait *et al.*, 1988).

In addition, smoked marijuana administration resulted in multiple brief episodes of euphoria that were paralleled by rapid transient increases in EEG alpha power (Lukas *et al.*, 1995); these EEG changes are thought to be related to CNS processes of reinforcement (Mello, 1983).

To help elucidate the relationship between the rise and fall of plasma THC and the self-reported psychotropic effects, Harder and Rietbrock (1997) measured both the plasma levels of THC and the psychological ''high'' obtained from smoking a marijuana cigarette containing 1% THC. As can be seen from these data, a rise in plasma THC concentrations results in a corresponding increase in the subjectively reported feelings of being ''high''. However, as THC levels drop the subjectively reported feelings of ''high'' remain elevated. The subjective effects seem to lag behind plasma THC levels. Similarly, Harder and Rietbrock compared lower doses of 0.3% THC-containing and 0.1% THC-containing cigarettes in human subjects.

As can be clearly seen from these data, even low doses of marijuana, containing 1%, 0.3% and even 0.1% THC, typically referred to as ''non-active'', are capable of producing subjective reports and physiological markers of being ''high'.

THC and its major metabolite, 11-OH-THC, have similar psychoactive and pharmacokinetic profiles in man (Wall *et al.*, 1976; DiMarzo *et al.*, 1998; Lemberger *et al.*, 1972). Perez-Reyes *et al.* (1972) reported that THC and 11-OH-THC were equipotent in generating a ''high'' in human volunteers. However, the metabolite, 11-OH-THC, crosses the blood-brain barrier faster than the parent THC compound (Ho *et al.*, 1973; Perez-Reyes et al., 1976). Therefore, the changes in THC plasma concentrations in humans may not be the best predictive marker for the subjective and physiological effects of marijuana in humans. Cocchetto *et al.* (1981) have used hysteresis plots to clearly demonstrate that plasma THC concentration is a poor predictor of simultaneous occurring physiological (heart rate) and psychological (''high'') pharmacological effects. Cocchetto *et al.* demonstrated that the time course of tachycardia and psychological responses lagged behind the plasma THC concentration-time profile. As recently summarized by Martin and Hall (1997, 1998)

''There is no linear relationship between blood [THC] levels and pharmacological effects with respect to time, a situation that hampers the prediction of cannabis-induced impairment based on THC blood levels (p90)''.

Drug craving is an urge or desire to re-experience the drug's effects and is considered to be one component of drug dependence, in part responsible for continued drug use and relapse after treatment or during periods of drug abstinence. DEA notes that Budney and colleagues (1999) reported that 93 percent of marijuana-dependent adults seeking treatment reported experiencing mild craving for marijuana, and 44 percent rated their past craving as severe. Heishman and colleagues developed in 2001 a Marijuana Craving Questionnaire (MCQ). When they administered their MCQ to 217 current marijuana smokers who were not attempting to quit or reduce their marijuana use, they found that marijuana craving can be measured in current smokers that are not seeking treatment. Most subjects (83 percent) reported craving marijuana 1–5 times per day, and 82 percent reported that each craving episode lasted 30 minutes or less. Furthermore, they determined that craving for marijuana can be characterized by four components: (1) compulsivity, an inability to control marijuana use; (2) emotionality, use of marijuana in anticipation of relief from withdrawal or negative mood; (3) expectancy, anticipation of positive outcomes from smoking marijuana; and (4) purposefulness, intention and planning to use marijuana for positive outcomes.

C. Actual Abuse of Marijuana—National Databases Related to Marijuana Abuse and Trafficking

Marijuana use has been relatively stable from 2002 to 2008, and it continues to be the most widely used illicit drug. Evidence of actual abuse can be defined by episodes/mentions in databases indicative of abuse/dependence. DHHS provided in its 2006 documents data relevant to actual abuse of marijuana including data from the National Survey on Drug Use and Health (NSDUH; formally known as the National Household Survey on Drug Abuse), the Drug Abuse Warning Network (DAWN), Monitoring the Future (MTF) survey, and the Treatment Episode Data Set (TEDS). These data collection and reporting systems provide quantitative data on many factors related to abuse of a particular substance, including incidence, pattern, consequence and profile of the abuser of specific substances. DEA provides here updates to these databases as well as additional data on trafficking and illicit availability of marijuana using information from databases it produces, such as the National Forensic Laboratory Information System (NFLIS), the System to Retrieve Information from Drug Evidence (STRIDE) and the Federal-wide Drug Seizure System (FDSS), as well as other sources of data specific to marijuana, including the Potency Monitoring Project and the Domestic Cannabis Eradication and Suppression Program (DCE/SP).

1. National Survey on Drug Use and Health (NSDUH)

The National Survey on Drug Use and Health, formerly known as the National Household Survey on Drug Abuse (NHSDA), is conducted annually by the Department of Health and Human Service's Substance Abuse and Mental Health Services Administration (SAMHSA). It is the primary source of estimates of the prevalence and incidence of pharmaceutical drugs, illicit drugs, alcohol, and tobacco use in the United States. The survey is based on a nationally representative sample of the civilian, non-institutionalized population 12 years of age and older. The survey excludes homeless people who do not use shelters, active military personnel, and residents of institutional group quarters such as jails and hospitals.

According to the 2009 NSDUH report, marijuana was the most commonly used illicit drug (16.7 million past month users) in the United States. (Note that NSDUH figures on marijuana use include hashish use; the relative proportion of hashish use to marijuana use is very low). Marijuana was also the most widely abused drug. The 2009 NSDUH report stated that 4.3 million persons were classified with substance dependence or abuse of marijuana in the past year based on criteria specified in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM–IV). Among persons aged 12 or older, the past month marijuana use in 2009 (6.6 percent) was statistically significantly higher than in 2008 (6.1 percent). In 2008, among adults aged 18 or older who first tried marijuana at age 14 or younger, 13.5 percent were classified with illicit drug dependence or abuse, higher than the 2.2 percent of adults who had first used marijuana at age 18 or older.

In 2008, among past year marijuana users aged 12 or older, 15.0 percent used marijuana on 300 or more days within the previous 12 months. This translates into 3.9 million people using marijuana on a daily or almost

daily basis over a 12-month period, higher than the estimate of 3.6 million (14.2 percent of past year users) in 2007. Among past month marijuana users, 35.7 percent (5.4 million) used the drug on 20 or more days in the past month.

2. Monitoring the Future

Monitoring the Future (MTF) is a national survey conducted by the Institute for Social Research at the University of Michigan under a grant from the National Institute on Drug Abuse (NIDA) that tracks drug use trends among American adolescents in the 8th, 10th, and 12th grades. Marijuana was the most commonly used illicit drug reported in the 2010 MTF report. Approximately 8.0 percent of 8th graders, 16.7 percent of the 10th graders, and 21.4 percent of 12th graders surveyed in 2010 reported marijuana use during the past month prior to the survey. Monitoring the Future participants reported a statistically significant increase of daily use in the past month in 2010, compared to 2009, 1.2 percent, 3.3 percent, and 6.1 percent of eighth, tenth and twelfth graders, respectively.

3. DAWN ED (Emergency Department)

The Drug Abuse Warning Network (DAWN) is a public health surveillance system that monitors drug-related hospital emergency department (ED) visits to track the impact of drug use, misuse, and abuse in the United States. DAWN provides a picture of the impact of drug use, misuse, and abuse on metropolitan areas and across the nation. DAWN gathers data on drug abuse-related ED visits from a representative sample of hospitals in the coterminous United States. DAWN ED gathers data on emergency department visits relating to substance use including, but not limited to, alcohol, illicit drugs, and other substances categorized as psychotherapeutic, central nervous system, respiratory, cardiovascular, alternative medication, anti-infective, hormone, nutritional product and gastrointestinal agents. For the purposes of DAWN, the term ''drug abuse'' applies if the following conditions are met: (1) the case involved at least one of the following: use of an illegal drug; use of a legal drug contrary to directions; or inhalation of a non-pharmaceutical substance and (2) the substance was used for one of the following reasons: because of drug dependence; to commit suicide (or attempt to commit suicide); for recreational purposes; or to achieve other psychic effects.

In 2009, marijuana was involved in 376,467 ED visits, out of 1,948,312 drug-related ED visits, as estimated by DAWN ED for the entire United States. This compares to a higher number of ED visits involving cocaine (422,896), and lower numbers of ED visits involving heroin (213,118) and stimulants (amphetamine, methamphetamine) (93,562). Visits involving the other major illicit drugs, such as MDMA, GHB, LSD and other hallucinogens, PCP, and inhalants, were much less frequent, comparatively.

In young patients, marijuana is the illicit drug most frequently involved in ED visits according to DAWN estimates, with 182.2 per 100,000 population aged 12 to 17, 484.8 per 100,000 population aged 18 to 20, and 360.2 per 100,000 population aged 21 to 24.

4. Treatment Episode Data Set (TEDS) System

Users can become dependent on marijuana to the point that they seek treatment to stop abusing it or are referred to a drug abuse treatment program. The TEDS system is part of the SAMHSA Drug and Alcohol Services Information System. TEDS comprises data on treatment admissions that are routinely collected by states in monitoring their substance abuse treatment systems. The primary goal of the TEDS is to monitor the characteristics of treatment episodes for substances abusers. The TEDS report provides information on both the demographic and substance use characteristics of admissions to treatment for abuse of alcohol and drugs in facilities that report to individual state administrative data systems. TEDS does not include all admissions to substance abuse treatment. It includes admissions to facilities that are licensed or certified by the state substance abuse agency to provide substance abuse treatment (or are administratively tracked by the agency for other reasons). In general, facilities reporting to TEDS are those that receive state alcohol and/or drug agency funds (including federal block grant funds) for the provision of alcohol and/or drug treatment services. The primary substances reported by TEDS are alcohol, cocaine, marijuana (marijuana is considered together with hashish), heroin, other opiates, PCP, hallucinogens, amphetamines, other stimulants, tranquilizers, sedatives, inhalants and other/unknown. TEDS defines Primary Substance of Abuse as the main substance of abuse reported at the time of admission. TEDS also allows for the recording of two other substances of abuse (secondary and tertiary). A client may be abusing more than three substances at the time of admission, but only three are recorded in TEDS.

Admissions for primary abuse of marijuana/hashish accounted for 16 percent of all treatment admissions reported to the TEDS system in 2006 and 2007. In 2006, 2007 and 2008, 1,933,206, 1,920,401 and 2,016,256 people were admitted to drug and alcohol treatment in the United States, respectively. The marijuana/hashish admissions represented 16 percent (308,670), 16 percent (307,123) and 17.2 percent (346,679) of the total drug/alcohol treatment admissions in 2006, 2007 and 2008, respectively. In 2008, 65.8 percent of the individuals admitted for marijuana were aged 12–17, 18–20 and 21–25 (30.5 percent, 15.3 percent and 20.0 percent, respectively). Among the marijuana/hashish admissions in 2007 in which age of first use was reported (286,194), 25.1 percent began using marijuana at age 12 or younger.

5. Forensic Laboratory Data

Marijuana is widely available in the United States, fueled by increasing marijuana production at domestic grow sites as well as increasing production in Mexico and Canada. Data on marijuana seizures from federal, state, and local law enforcement laboratories have indicated that there is significant trafficking of marijuana. The National Forensic Laboratory Information System (NFLIS) is a program sponsored by the Drug Enforcement Administration's Office of Diversion Control. NFLIS compiles information on exhibits analyzed in state and local law enforcement laboratories. The System to Retrieve Information from Drug Evidence (STRIDE) is a DEA database which compiles information on exhibits analyzed in DEA laboratories. NFLIS and STRIDE together capture data for all substances reported by forensic laboratory analyses. More than 1,700 unique substances are reported to these two databases.

NFLIS showed that marijuana was the most frequently identified drug in state and local laboratories from January 2001 through December 2010. Marijuana accounted for between 34 percent and 38 percent of all drug exhibits analyzed during that time frame. Similar to NFLIS, STRIDE data showed that marijuana was the most frequently identified drug in DEA laboratories for the same reporting period. From January 2001 through December 2010, a range of between 17 percent and 21 percent of all exhibits analyzed in DEA laboratories were identified as marijuana (Table 1).

TABLE 1—MARIJUANA (OTHER THAN HASHISH) (EXHIBITS AND CASES) REPORTED BY NFLIS AND STRIDE, 2001–2010, FORENSIC LABORATORY DATA

	NFLIS		STRIDE	
	Exhibits (percent total exhibits)	Cases	Exhibits (percent total exhibits)	Cases
2001	314,002 (37.9%)	261,191	16,523 (20.7%)	13,256
2002	373,497 (36.6%)	312,161	14,010 (19.4%)	11,306
2003	407,046 (36.7%)	339,995	13,946 (19.9%)	10,910
2004	440,964 (35.5%)	371,841	13,657 (18.4%)	10,569
2005	469,186 (33.5%)	394,557	14,004 (18.3%)	10,661

TABLE 1—MARIJUANA (OTHER THAN HASHISH) (EXHIBITS AND CASES) REPORTED BY NFLIS AND STRIDE, 2001–2010, FORENSIC LABORATORY DATA—Continued

	NFLIS		STRIDE	
	Exhibits (percent total exhibits)	Cases	Exhibits (percent total exhibits)	Cases
2006	506,472 (33.6%)	421,943	13,597 (18.5%)	10,277
2007	512,082 (34.7%)	423,787	13,504 (19.2%)	10,413
2008	513,644 (35.1%)	421,782	12,828 (18.8%)	10,109
2009	524,827 (35.6%)	414,006	12,749 (17.7%)	10,531
2010	464,059 (36.3%)	362,739	11,293 (16.7%)	7,158

Data queried 03–04–2011.

TABLE 2—HASHISH (EXHIBITS AND CASES) REPORTED BY NFLIS AND STRIDE, 2001–2010, FORENSIC LABORATORY DATA

	NFLIS		STRIDE	
	Exhibits	Cases	Exhibits	Cases
2001	1,689	1,671	53	50
2002	2,278	2,254	40	38
2003	2,533	2,503	48	42
2004	2,867	2,829	63	51
2005	2,674	2,639	122	90
2006	2,836	2,802	102	76
2007	3,224	3,194	168	122
2008	2,988	2,920	124	102
2009	2,952	2,843	119	96
2010	2,473	2,392	141	84

Data queried 03–04–2011.

Since 2001, the total number of exhibits and cases of marijuana and the amount of marijuana seized federally has remained high and the number of marijuana plants eradicated has considerably increased (see data from Federal-wide Drug Seizure System and Domestic Cannabis Eradication and Suppression Program below).

6. Federal-wide Drug Seizure System

The Federal-wide Drug Seizure System (FDSS) contains information about drug seizures made by the Drug Enforcement Administration, the Federal Bureau of Investigation, United States Customs and Border Protection, and United States Immigration and Customs Enforcement, within the jurisdiction of the United States. It also records maritime seizures made by the United States Coast Guard. Drug seizures made by other Federal agencies are included in the FDSS database when drug evidence custody is transferred to one of the agencies identified above. FDSS is now incorporated into the National Seizure System (NSS), which is a repository for information on clandestine laboratory, contraband (chemicals and precursors, currency, drugs, equipment and weapons). FDSS reports total federal drug seizures (kg) of substances such as cocaine, heroin, MDMA, methamphetamine, and cannabis (marijuana and hashish). The yearly volume of cannabis seized (Table 3), consistently exceeding a thousand metric tons per year, shows that cannabis is very widely trafficked in the United States.

TABLE 3—TOTAL FEDERAL SEIZURES OF CANNABIS

[Expressed in kg]

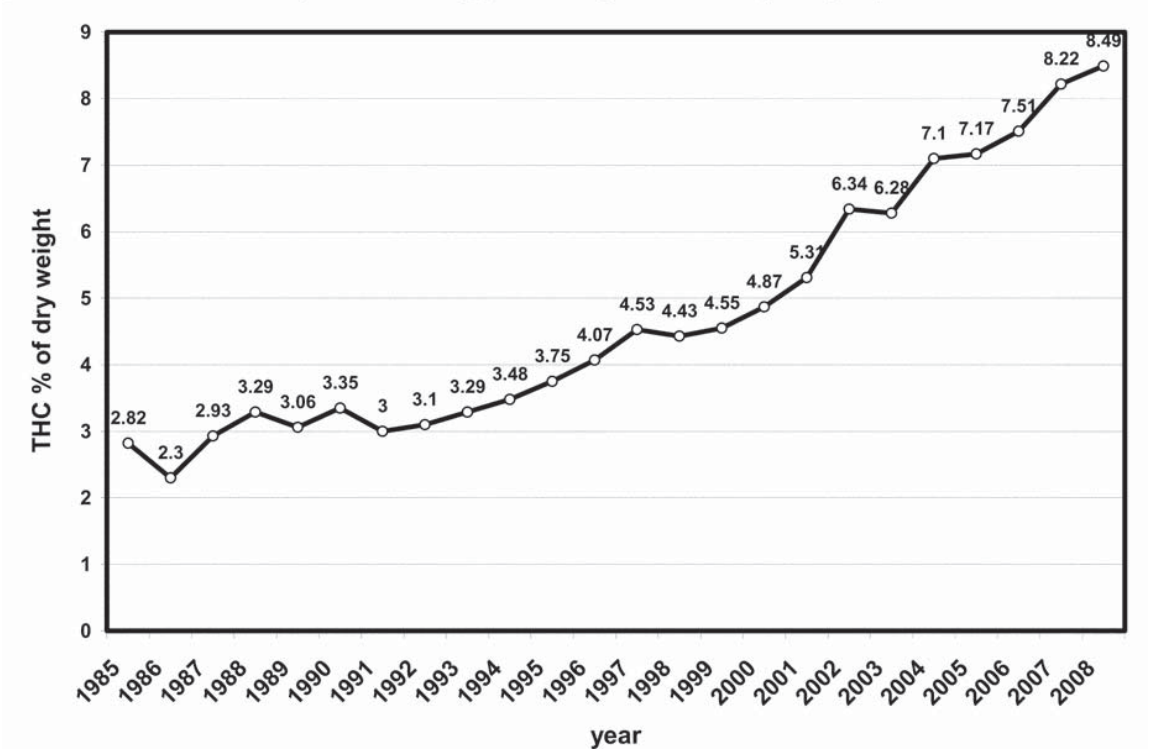
	2002	2003	2004	2005	2006	2007	2008	2009	2009
Cannabis	1,103,173	1,232,711	1,179,230	1,116,977	1,141,915	1,459,220	1,590,793	1,911,758	1,858,808
Marijuana	1,102,556	1,232,556	1,179,064	1,116,589	1,141,737	1,458,883	1,590,505	1,910,775	1,858,422
Hashish	618	155	166	388	178	338	289	983	386

7. Potency Monitoring Project

Rising availability of high potency (i.e., with high Δ^9-THC concentrations) marijuana has pushed the average marijuana potency to its highest recorded level. The University of Mississippi's Potency Monitoring Project (PMP), through a contract with the National Institute on Drug Abuse (NIDA), analyzes and compiles data on the Δ^9-THC concentrations of cannabis, hashish and hash oil samples provided by DEA regional laboratories and by state and local police agencies.

DEA notes studies showing that when given the choice between low- and high-potency marijuana, subjects chose the high-potency marijuana significantly more often than the low-potency marijuana (Chait and Burke, 1994), supporting the hypothesis that the reinforcing effects of marijuana, and possibly its abuse liability, are positively related to THC content.

Figure 1. Average Percentage of Δ^9-THC in Samples of Seized Marijuana (1985 –2008) (Source: The University of Mississippi Potency Monitoring Project)



8. The Domestic Cannabis Eradication and Suppression Program

The Domestic Cannabis Eradication and Suppression Program (DCE/SP) was established in 1979 to reduce the supply of domestically cultivated marijuana in the United States. The program was designed to serve as a partnership between federal, state, and local agencies. Only California and Hawaii were active participants in the program at its inception. However, by 1982 the program had expanded to 25 states and by 1985 all fifty states were participants. Cannabis is cultivated in remote locations and frequently on public lands. Data provided by the DCE/SP (Table 4) shows that in 2009, there were 9,980,038 plants eradicated in outdoor cannabis cultivation areas in the United States. Marijuana is illicitly grown in all states. Major domestic outdoor cannabis cultivation areas were found in California, Kentucky, Tennessee and Hawaii. Significant quantities of marijuana were also eradicated from indoor cultivation operations. There were 414,604 indoor plants eradicated in 2009 compared to 217,105 eradicated in 2000. As indoor cultivation is generally associated with plants that have higher concentrations of Δ^9-THC, the larger numbers of indoor grow facilities may be impacting the higher average Δ^9-THC concentrations of seized materials.

TABLE 4—DOMESTIC CANNABIS ERADICATION, OUTDOOR AND INDOOR PLANTS SEIZED, 2000–2009

[Source: Domestic Cannabis Eradication/Suppression Program]

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Outdoor	2,597,798	3,068,632	3,128,800	3,427,923	2,996,144	3,938,151	4,830,766	6,599,599	7,562,322	9,980,038
Indoor	217,105	236,128	213,040	223,183	203,896	270,935	400,892	434,728	450,986	414,604
Total	2,814,903	3,304,760	3,341,840	3,651,106	3,200,040	4,209,086	5,231,658	7,034,327	8,013,308	10,394,642

The recent statistics from these various surveys and databases show that marijuana continues to be the most commonly used illicit drug, with considerable rates of heavy abuse and dependence. They also show that marijuana is the most readily available illicit drug in the United States.

The petitioner states that, ''The abuse potential of cannabis is insufficient to justify the prohibition of medical use.'' The petitioner also states that, ''[s]everal studies demonstrate that abuse rates for cannabis are lower than rates for other common drugs.'' (Exh. C, Section IV(16), pg. 92).

DHHS states, to the contrary, ''the large number of individuals using marijuana on a regular basis, its widespread use, and the vast amount of marijuana that is available for illicit use are indicative of the high abuse potential for marijuana.'' Indeed, the data presented in this section shows that marijuana has a high potential for abuse as determined using the indicators identified in the CSA's legislative history. Both clinical and preclinical studies have demonstrated that marijuana and its principal psychoactive constituent Δ^9-THC possess the attributes associated with drugs of abuse. They function as positive reinforcers and as discriminative stimuli to maintain drug-seeking behavior.

In addition, marijuana is the most highly abused and trafficked illicit substance in the United States. Chronic abuse has resulted in a considerable number of individuals seeking substance abuse treatment according to national databases such as TEDS. Abuse of marijuana is associated with significant public health and safety risks that are described under factors 2, 6 and 7.

The issue of whether marijuana has a currently accepted medical use is discussed under Factor 3.

The petitioner claims that, ''[…]widespread use of marijuana without dependency supports the argument that marijuana is safe for use under medical supervision.'' (Exh. C, Section IV(15), pg. 87).

Petitioner's claim of widespread use without dependency is not supported by abuse-related data. In particular, this claim disregards the high numbers of admissions to treatment facilities for marijuana abuse. Indeed, TEDS admissions for primary abuse of marijuana/hashish accounted for roughly 17 percent of all treatment admissions in 2008. In 2008, 2,016,256 people were admitted to drug and alcohol treatment in the United States and 346,679 of those admissions were for marijuana/hashish abuse. These drug treatment numbers are not consistent with this claim. Marijuana is not safe for use under medical supervision, and this point is addressed further in Factor 3.

The petitioner also claims that, ''Data on both drug treatment and emergency room admissions also distinguishes the abuse potential of marijuana from that of other drugs and establishes its relative abuse potential as lower than schedule I drugs such as heroin and schedule II drugs such as cocaine.'' (Exh. C, Section IV(17), pg. 99). The petitioner then presents data from TEDS in 1998, in which a larger proportion of all marijuana treatment admissions are referred to by the criminal justice system (54 percent), compared to much smaller percentages for heroin and cocaine. The petitioner argues that the abuse potential of these other drugs is more severe such that addicts seek treatment on their own or through persuasion of their associates, and claims that this difference establishes marijuana's relative abuse potential as lower than the other drugs.

Petitioner's claim is not supported by an examination of the absolute numbers of admissions for treatment for each drug discussed. Regardless of proportions of referrals from the criminal justice systems, the absolute numbers of admissions for treatment for marijuana, heroin, or cocaine dependence are very high. Furthermore, data from TEDS in 2007 (SAMHSA, 2009) show that both primary marijuana and methamphetamine/amphetamine admissions had the largest proportion of admissions referred through the criminal justice system (57 percent each), followed by PCP (54 percent). Both methamphetamine/amphetamine and PCP have very high potential for abuse (Lile, 2006; Crider, 1986). Accordingly, this illustrates that it is not possible to establish or predict relative abuse potentials from the ranking of proportions of treatment admissions referred by the criminal justice system.

FACTOR 2: SCIENTIFIC EVIDENCE OF THE DRUG'S PHARMACOLOGICAL EFFECTS, IF KNOWN

DHHS states that there are abundant scientific data available on the neurochemistry, toxicology, and pharmacology of marijuana. Following is a summary of the current scientific understanding of the endogenous cannabinoid system and of marijuana's pharmacological effects, including its effects on the cardiovascular, respiratory, and immune systems, as well as its effects on mental health and cognitive function and the effect of prenatal exposure to marijuana.

Neurochemistry of the Psychoactive Constituents of Marijuana

DHHS states that of 483 natural constituents identified in marijuana, 66 are classified as cannabinoids (Ross and El Sohly, 1995). Cannabinoids are not known to exist in plants other than marijuana and most of the cannabinoid compounds have been identified chemically. The activity of marijuana is largely attributed to Δ^9-THC (Wachtel *et al.,* 2002).

DEA notes that Δ^9-THC and delta-8-tetrahydrocannabinol (Δ^8-THC) are the only known compounds in the cannabis plant which show all the psychoactive effects of marijuana. Δ^9-THC is more abundant than Δ^8-THC and Δ^9-THC concentrations vary within portions of the cannabis plant (Hanus and Subivá, 1989; Hanus *et al.,* 1975). The pharmacological activity of Δ^9-THC is stereospecific: the (-)-trans isomer is 6–100 times more potent than the (+)-trans isomer (Dewey *et al.,* 1984).

The mechanism of action of Δ^9-THC was verified with the cloning of cannabinoid receptors, first from rat brain tissue (Matsuda *et al.,* 1990) and then from human brain tissue (Gerard *et al.,* 1991). Two cannabinoid receptors have been identified and characterized, CB_1 and CB_2 (Piomelli, 2005). Autoradiographic studies have provided information on the distribution of CB_1 and CB_2 receptors. High densities of CB_1 receptors are found in the basal ganglia, hippocampus, and cerebellum of the brain (Howlett *et al.,* 2004; Herkenham *et al.,* 1990; Herkenham, 1992). These brain regions are associated with movement coordination and cognition and the location of CB_1 receptors in these areas may explain cannabinoid interference with these functions. Although CB_1 receptors are predominantly expressed in the brain, they have also been detected in the immune system (Bouaboula *et al.,* 1993). CB_2 receptors are primarily located in B lymphocytes and natural killer cells of the immune system and it is believed that this receptor is responsible for mediating immunological effects of cannabinoids (Galiegue *et al.,* 1995). Recently, however, CB_2 receptors have been localized in the brain, primarily in the cerebellum and hippocampus (Gong *et al.,* 2006).

Cannabinoid receptors are linked to an inhibitory G-protein (Breivogel and Childers, 2000). When the receptor is activated, adenylate cyclase activity is inhibited, preventing the conversion of adenosine triphosphate (ATP) to the second messenger cyclic adenosine monophosphate (cAMP). Other examples of inhibitory-coupled receptors include opioid, muscarinic cholinergic, alpha$_2$-adrenoreceptors, dopamine and serotonin receptors. However, several studies also suggest a link to stimulatory G-proteins, through which activation of CB_1 stimulates adenylate cyclase activity (Glass and Felder, 1997; Maneuf and Brotchie, 1997; Felder *et al.,* 1998).

Activation of CB_1 receptors inhibits N-and P/Q-type calcium channels and activate inwardly rectifying potassium channels (Mackie *et al.,* 1995; Twitchell *et al.,* 1997). Inhibition of N-type calcium channels decreases neurotransmitter release from a number of tissues and may be the mechanism by which cannabinoids inhibit acetylcholine, norepinephrine, and glutamate release from specific areas of the brain. These effects on G protein-mediated pathways and on calcium and potassium channels may represent potential cellular mechanisms underlying the antinociceptive and psychoactive effects of cannabinoids (Ameri, 1999).

Delta^9-THC displays similar affinity for both cannabinoid receptors but behaves as a weak agonist at CB_2 receptors, based on inhibition of adenylate cyclase. The identification of synthetic cannabinoid ligands that selectively bind to CB_2 receptors but do not have the typical Δ^9-THC-like psychoactive properties, along with the respective anatomical distribution of the two receptor subtypes suggests that the psychoactive effects of cannabinoids are mediated through the activation of CB_1 receptors (Hanus *et al.,* 1999). Naturally occurring cannabinoids and synthetic cannabinoid agonists (such as WIN-55,212-2 and CP-55,940) produce hypothermia, analgesia, hypoactivity, and catalepsy in addition to their psychoactive effects.

In 2000, two endogenous cannabinoid receptor agonists were discovered, anandamide and arachidonyl glycerol (2-AG). Anandamide is a low efficacy agonist (Breivogel and Childers, 2000) and 2-AG is a highly efficacious agonist (Gonsiorek *et al.,* 2000). These endogenous ligands are present in both central and peripheral tissues. The physiological role of these endogenous ligands is an active area of research (Martin *et al.,* 1999).

In summary, two receptors have been cloned, CB_1 (found in the central nervous system) and CB2 (predominantly found in the periphery), that bind Δ^9-THC and other cannabinoids. Activation of these inhibitory G-protein-coupled receptors inhibits calcium channels and adenylate cyclase. Endogenous cannabinoid agonists have been identified, anandamide and arachidonyl glycerol (2-AG).

Pharmacological Effects of Marijuana

Marijuana produces a number of central nervous system effects. Many of these effects are directly related to the abuse potential of marijuana, and are discussed in Factor 1. Other effects are discussed herein.

Cardiovascular and Autonomic Effects

DHHS states that acute use of marijuana causes an increase in heart rate (tachycardia) and may cause a modest increase in blood pressure as well (Capriotti *et al.,* 1988; Benowitz and Jones, 1975). Conversely, chronic exposure to marijuana will produce a decrease in heart rate (bradycardia) and decrease of blood pressure. In heavy smokers of marijuana, the degree of increased heart rate is diminished due to the development of tolerance (Jones, 2002 and Sidney, 2002). These effects are thought to be mediated through peripherally located, presynaptic CB_1 receptor inhibition of norepinephrine release with possible direct activation of vascular cannabinoid receptors (Wagner *et al.,* 1998).

DHHS cites a review (Jones, 2002) of studies showing that smoked marijuana causes orthostatic hypotension (sympathetic insufficiency, a sudden drop in blood pressure upon standing up) often accompanied by dizziness. DHHS states that tolerance can develop to this effect.

Marijuana smoking by older patients, particularly those with some degree of coronary artery or cerebrovascular disease, poses risks related to increased cardiac work, increased catecholamines, carboxyhemoglobin, and postural hypotension (Benowitz and Jones, 1981; Hollister, 1988).

DEA further notes studies in which marijuana has been administered under controlled conditions to marijuana-experienced users that showed that marijuana causes a substantial increase, compared to placebo, in heart rate (tachycardia) ranging from 20 percent to 100 percent above baseline. This effect was seen as usually greatest starting during the 10 minutes or so it takes to smoke a marijuana cigarette and lasting 2 to 3 hours (reviewed in Jones *et al.,* 2002).

DEA also notes a randomized, double-blind, placebo-controlled study by Mathew and colleagues (2003) that examined pulse rate, blood pressure (BP), and plasma Δ^9-THC levels during reclining and standing for 10 minutes before and after smoking one marijuana cigarette (3.55 percent Δ^9-THC) by twenty-nine volunteers. Marijuana induced postural dizziness, with 28 percent of subjects reporting severe symptoms. Intoxication and dizziness peaked immediately after drug intake. The severe dizziness group showed the most marked postural drop in blood pressure and showed a drop in pulse rate after an initial increase during standing.

Respiratory Effects

Both acute and chronic respiratory effects are associated with marijuana smoking.

DHHS states that acute exposure to marijuana produces transient bronchodilation (Gong *et al.,* 1984). DHHS states that long-term use of smoked marijuana can lead to increased frequency of chronic cough, increased sputum, large airway obstruction, as well as cellular inflammatory histopathological abnormalities in bronchial epithelium (Adams and Martin, 1996; Hollister, 1986).

DEA notes a study showing that both smoked marijuana and oral Δ^9-THC increases specific airway conductance in asthmatic subjects (Tashkin *et al.,* 1974). In addition, other studies have suggested that chronic marijuana smoking is also associated with increased incidence of emphysema and asthma (Tashkin *et al.,* 1987).

DHHS states that the evidence that marijuana may lead to cancer is inconsistent, with some studies suggesting a positive correlation while others do not. DHHS cited a large clinical study with 1,650 subjects in which no positive correlation was found between marijuana use and lung cancer (Tashkin *et al.,* 2006). This finding held true regardless of the extent of marijuana use when both tobacco use and other potential confounding factors were controlled. DHHS also cites other studies reporting lung cancer occurrences in young marijuana users with no history of tobacco smoking (Fung *et al.,* 1999), and suggesting a dose-dependent effect of marijuana on the risk of head and neck cancer (Zhang *et al.,* 1999).

DEA notes the publication of a more recent case–control study of lung cancer in adults under 55 years of age, conducted in New Zealand by Aldington and colleagues (2008). Interviewer-administered questionnaires were used to assess possible risk factors, including cannabis use. In total, 79 cases of lung cancer and 324 controls were included in the study. The risk of lung cancer increased 8 percent (95 percent confidence interval (CI) 2–15) for each joint-year of cannabis smoking (one joint-year being equivalent to one joint per day for a year), after adjustment for confounding variables including cigarette smoking; it went up 7 percent (95 percent CI 5–9) for each pack-year of cigarette smoking (one pack-year being equivalent to one pack per day for a year), after adjustment for confounding variables including cannabis smoking. Thus, a major differential risk between cannabis and cigarette smoking was observed, with one joint of cannabis being similar to 20 cigarettes for risk of lung cancer. Users reporting over 10.5 joint-years of exposure had a significantly increased risk of developing lung cancer (relative risk 5.7 (95 percent CI 1.5–21.6)) after adjustment for confounding variables including cigarette smoking. DEA notes that the authors of this study concluded from their results that long-term cannabis use increases the risk of lung cancer in young adults.

Some studies discuss marijuana smoke and tobacco smoke. DHHS states that chronic exposure to marijuana smoke is considered to be comparable to tobacco smoke with respect to increased risk of cancer and lung damage. DEA notes studies showing that marijuana smoke contains several of the same carcinogens and co-carcinogens as tobacco smoke and suggesting that pre-cancerous lesions in bronchial epithelium also seem to be caused by long-term marijuana smoking (Roth *et al.,* 1998).

In summary, studies are still needed to clarify the impact of marijuana on the risk of developing lung cancer as well as head and neck cancer. DHHS states that the evidence that marijuana may lead to cancer is inconsistent, with some studies suggesting a positive correlation while others do not.

Endocrine Effects

DHHS states that Δ^9-THC reduces binding of the corticosteroid dexamethasone in hippocampal tissue from adrenalectomized rats and acute Δ^9-THC releases corticosterone, with tolerance developing to this effect with chronic administration (Eldridge *et al.,* 1991). These data suggest that Δ^9-THC may interact with the glucocorticoid receptor system.

DHHS states that experimental administration of marijuana to humans does not consistently alter the endocrine system. In an early study, four male subjects administered smoked marijuana showed a significant depression in luteinizing hormone and a significant increase in cortisol (Cone *et al.,* 1986). However, later studies in male subjects receiving smoked Δ^9-THC (18 mg/marijuana cigarette) or oral Δ^9-THC (10 mg t.i.d. for 3 days) showed no changes in plasma prolactin, ACTH, cortisol, luteinizing hormone or testosterone levels (Dax *et al.,* 1989). Similarly, a study with 93 males and 56 female subjects showed that chronic marijuana use did not significantly alter concentrations of testosterone, luteinizing hormone, follicle stimulating hormone, prolactin or cortisol (Block *et al.,* 1991).

DHHS cites a study (Sarfaraz *et al.,* 2005) which showed that the cannabinoid agonist WIN 55,212-2 induces apoptosis in prostate cancer cells growth and decreases expression of androgen receptors. DHHS states that this data suggests a potential therapeutic value for cannabinoid agonists in the treatment of prostate cancer, an androgen-stimulated type of carcinoma.

In summary, while animal studies have suggested that cannabinoids can alter multiple hormonal systems, the effects in humans, in particular the consequences of long-term marijuana abuse, remain unclear.

Immune System Effects

DHHS states that cannabinoids alter immune function but that there can be differences between the effects of synthetic, natural, and endogenous cannabinoids (Croxford and Yamamura, 2005).

DHHS cites a study by Roth *et al.* (2005) that examined the effect of Δ^9-THC exposure on immune function and response to HIV infection in immunodeficient mice that were implanted with human blood cells infected with HIV. The study shows that exposure to Δ^9-THC *in vivo* suppresses immune function, increases HIV co-receptor expression and acts as a cofactor to enhance HIV replication. DEA notes that the authors of this study state that their results suggest a dynamic interaction between Δ^9-THC, immunity, and the pathogenesis of HIV and support epidemiologic studies that have identified marijuana use as a risk factor for HIV infection and the progression of AIDS. However, DHHS discusses a recent study by Abrams *et al.* (2003) that investigated the effect of marijuana on immunological functioning in 67 AIDS patients who were taking protease inhibitors. Subjects received one of three treatments, three times a day: smoked marijuana cigarette containing 3.95 percent Δ^9-THC; oral tablet containing Δ^9-THC (2.5 mg oral dronabinol); or oral placebo. There were no changes in HIV-RNA levels between groups, demonstrating no short-term adverse virologic effects from using cannabinoids.

DEA notes a review suggesting that Δ^9-THC and cannabinoids decrease resistance to microbial infections in experimental animal models and *in vitro* (see review by Cabral and Staab, 2005). Various studies have been conducted in drug-abusing human subjects, experimental animals exposed to marijuana smoke or injected with cannabinoids, and in *in vitro* models using immune cell cultures treated with various cannabinoids. DEA notes that for the most part, these studies suggest that cannabinoids modulate the function of various cells of the human immune system, including T- and B-

lymphocytes as well as natural killer (NK) cells and macrophages. Macrophages engulf and destroy foreign matter, NK cells target cells (e.g., cancerous cells) and destroy them, B-lymphocytes produce antibodies against infective organisms, and T-lymphocytes kill cells or trigger the activity of other cells of the immune system.

In addition to studies examining cannabinoid effects on immune cell function, DEA also notes other reports which have documented that cannabinoids modulate resistance to various infectious agents. Viruses such as herpes simplex virus and murine retrovirus have been studied as well as bacterial agents such as members of the genera Staphylococcus, Listeria, Treponema, and Legionella. These studies suggest that cannabinoids modulate host resistance, especially the secondary immune response (reviewed in Cabral and Dove-Pettit, 1998).

Finally, DEA notes a review suggesting that cannabinoids modulate the production and function of cytokines as well as modulate the activity of network cells such as macrophages and T helper cells. Cytokines are the chemicals produced by cells of the immune system in order to communicate and orchestrate the attack. Binding to specific receptors on target cells, cytokines recruit many other cells and substances to the field of action. Cytokines also encourage cell growth, promote cell activation, direct cellular traffic, and destroy target cells (see review by Klein *et al.*, 2000).

In summary, as DHHS states, cannabinoids alter immune function, but there can be differences between the effects of synthetic, natural, and endogenous cannabinoids. While there is a large body of evidence to suggest that Δ^9-THC alters immune function, research is still needed to clarify the effects of cannabinoids and marijuana on the immune system in humans, in particular the risks posed by smoked marijuana in immunocompromized individuals.

Association with Psychosis

The term psychosis is generally used in research as a generic description of severe mental illnesses characterized by the presence of delusions, hallucinations and other associated cognitive and behavioral impairments. Psychosis is measured either by using standardized diagnostic criteria for psychotic conditions such as schizophrenia or by using validated scales that rank the level of psychotic symptoms from none to severe (Fergusson *et al.*, 2006).

DHHS states that extensive research has been conducted recently to investigate whether exposure to marijuana is associated with schizophrenia or other psychoses. DHHS states that, at the time of their review, the data does not suggest a causative link between marijuana use and the development of psychosis.

DHHS discusses an early epidemiological study conducted by Andreasson and colleagues (1987), which examined the link between psychosis and marijuana use. In this study, 45,000 18- and 19-year-old male Swedish subjects provided detailed information on their drug-taking history. The incidence of schizophrenia was then recorded over the next 15 years. Those individuals who claimed, on admission, to have taken marijuana on more than 50 occasions were six times more likely to be diagnosed with schizophrenia in the following 15 years than those who had never consumed the drug. When confounding factors were taken into account, the risk of developing schizophrenia remained statistically significant. The authors concluded that marijuana users who are vulnerable to developing psychoses are at the greatest risk for schizophrenia. DHHS states that therefore marijuana per se does not appear to induce schizophrenia in the majority of individuals who try or continue to use the drug.

DHHS discusses another large longitudinal study in which the prevalence of schizophrenia was modeled against marijuana use across birth cohorts in Australia from 1940 to 1979 (Degenhardt *et al.*, 2003). The authors found that marijuana use may precipitate disorders in vulnerable individuals and worsen the course of the disorder among those that have already developed it. They did not find any causal relationship between marijuana use and increased incidence of schizophrenia.

DEA notes that Degenhardt and colleagues (2003) acknowledged that several environmental risk factors for schizophrenia had been reduced (i.e., poor maternal nutrition, infectious disease and poor antenatal and prenatal care) and that the diagnostic criteria for schizophrenia had changed over the span of this study making the classification of schizophrenia more rigorous. These confounders could reduce the reported prevalence of schizophrenia.

DHHS also discusses several longitudinal studies that found a dose-response relationship between marijuana use and an increasing risk of psychosis among those who are vulnerable to developing psychosis (Fergusson *et al.*, 2005; van Os *et al.*, 2002).

DEA notes several longitudinal studies (Arseneault *et al.*, 2002, Caspi *et al.*, 2005; Henquet *et al.*, 2005) that found increased rates of psychosis or psychotic symptoms in people using cannabis. Finally, DEA notes some studies that observe that individuals with psychotic disorders have higher rates of cannabis use compared to the general population (Regier *et al.*, 1990; Green *et al.*, 2005).

DEA also notes that, more recently, Moore and colleagues (2007) performed a meta-analysis of the longitudinal studies on the link between cannabis use and subsequent psychotic symptoms. Authors observed that there was an increased risk of any psychotic outcome in individuals who had ever used cannabis (pooled adjusted odds ratio=1.41, 95 percent CI 1.20–1.65). Furthermore, findings were consistent with a dose-response effect, with greater risk in people who used cannabis most frequently (2.09, 1.54–2.84). The authors concluded that their results support the view that cannabis increases risk of psychotic outcomes independently of confounding and transient intoxication effects.

DEA also notes another more recent study examining the association between marijuana use and psychosis-related outcome in pairs of young adult siblings in Brisbane, Australia (McGrath *et al.*, 2010). This study found a dose-response relationship where the longer the duration of time since the first cannabis use, the higher the risk of psychosis-related outcome. Those patients with early-onset psychotic symptoms were also likely to report early marijuana use. Authors suggest that their results support the hypothesis that early cannabis use is a risk-modifying factor for psychosis-related outcomes in young adults.

Cognitive Effects

DHHS states that acute administration of smoked marijuana impairs performance on tests of learning, associative processes, and psychomotor behavior (Block *et al.*, 1992; Heishman *et al.*, 1990). Marijuana may therefore considerably interfere with an individual's ability to learn in a classroom or to operate motor vehicles. DHHS cites a study conducted by Kurzthalar and colleagues (1999) with human volunteers, in which the administration of 290 µg/kg of Δ^9-THC in a smoked cigarette resulted in impaired perceptual motor speed and accuracy, skills of paramount importance for safe driving. Similarly, administration of 3.95 percent Δ^9-THC in a smoked cigarette increased disequilibrium measures, as well as the latency in a task of simulated vehicle braking (Liguori *et al.*, 1998).

DHHS states that the effects of marijuana may not be fully resolved until at least one day after the acute psychoactive effects have subsided, following repeated administration. Heishman and colleagues (1988) showed that impairment on memory tasks persists for 24 hours after smoking marijuana cigarettes containing 2.57 percent Δ^9-THC. However, Fant and colleagues (1998) showed minimal residual alterations in subjective or performance measures the day after subjects were exposed to 1.8 percent or 3.6 percent smoked Δ^9-THC.

DHHS discussed a study by Lyons and colleagues (2004) on the neuropsychological consequences of regular marijuana use in fifty-four monozygotic male twin pairs, with one subject being a regular user and its co-twin a non-user, and neither twin having used any other illicit drug regularly. Marijuana-using twins significantly differed from their non-using co-twins on the general intelligence domain. However, only one significant difference was noted between marijuana-using twins and their non-using co-twins on measures of cognitive functioning. Authors of the study proposed that the results indicate an absence of any marked long-term residual effects of marijuana use on cognitive abilities. This conclusion is similar to the results found by Lyketsos and colleagues (1999), who investigated the possible adverse effects of cannabis use on cognitive decline after 12 years in persons under 65 years of age. There were no significant differences in cognitive decline between heavy users, light users, and nonusers of cannabis. The authors conclude that over long time periods, in persons under age 65 years, cognitive decline occurs in all age groups. This decline is closely associated with aging and educational level but does not appear to be associated with cannabis use.

DEA notes that while Lyketsos and colleagues (1999) propose that their results

provide strong evidence of the absence of a long term residual effect of cannabis use on cognition, they also acknowledge a number of limitations to their study. Notably, authors remark that it is possible that some cannabis users in the study may have used cannabis on the day the test was administered. Given the acute effects on cannabis on cognition, this would have tended to reduce their test score on that day. This may have adversely affected accurate measurement of test score changes over time in cannabis users. The authors also noted, as another important limitation, that the test used is not intended for the purpose for which it was used in this study and is not a very sensitive measure of cognitive decline, even though it specifically tests memory and attention. Thus, small or subtle effects of cannabis use on cognition or psychomotor speed may have been missed.

DHHS also discussed a study by Solowij and colleagues (2002) which examined the effects of duration of cannabis use on specific areas of cognitive functioning among users seeking treatment for cannabis dependence. They compared 102 near-daily cannabis users (51 long-term users: mean, 23.9 years of use; 51 shorter-term users: mean, 10.2 years of use) with 33 nonuser controls. They collected measures from nine standard neuropsychological tests that assessed attention, memory, and executive functioning, and that were administered prior to entry to a treatment program and following a median 17-hour abstinence. Authors found that long-term cannabis users performed significantly less well than shorter-term users and controls on tests of memory and attention. Long-term users showed impaired learning, retention, and retrieval compared with controls. Both user groups performed poorly on a time estimation task. Performance measures often correlated significantly with the duration of cannabis use, being worse with increasing years of use, but were unrelated to withdrawal symptoms and persisted after controlling for recent cannabis use and other drug use. Authors of this study state that their results support the hypothesis that long-term heavy cannabis users show impairments in memory and attention that endure beyond the period of intoxication and worsen with increasing years of regular cannabis use.

DHHS cited a study by Messinis and colleagues (2006) which examined neurophysiological functioning for heavy, frequent cannabis users. The study compared 20 long-term (LT) and 20 shorter-term (ST) heavy, frequent cannabis users after abstinence for at least 24 hours prior to testing with 24 non-using controls. LT users performed significantly worse on verbal memory and psychomotor speed. LT and ST users had a higher proportion of deficits on verbal fluency, verbal memory, attention and psychomotor speed. Authors conclude from their study that specific cognitive domains appear to deteriorate with increasing years of heavy frequent cannabis use.

DHHS discussed a study by Pope and colleagues (2003) which reported no differences in neuropsychological performance in early- or late-onset users compared to non-using controls, after adjustment for intelligence quotient (IQ). In another cohort of chronic, heavy marijuana users, some deficits were observed on memory tests up to a week following supervised abstinence but these effects disappeared by day 28 of abstinence (Pope *et al.*, 2002). The authors concluded that ''cannabis-associated cognitive deficits are reversible and related to recent cannabis exposure rather than irreversible and related to cumulative lifetime use.'' Conversely, DHHS notes that other investigators have reported persistent neuropsychological deficits in memory, executive functioning, psychomotor speed, and manual dexterity in heavy marijuana smokers who had been abstinent for 28 days (Bolla *et al.*, 2002). Furthermore, when dividing the group into light, middle, and heavy user groups, Bolla and colleagues (2002) found that the heavy user group performed significantly below the light user group on 5 of 35 measures. A follow-up study of heavy marijuana users noted decision-making deficits after 25 days of abstinence (Bolla *et al.*, 2005). When IQ was contrasted in adolescents 9–12 years of age and at 17–20 years of age, current heavy marijuana users showed a 4-point reduction in IQ in later adolescence compared to those who did not use marijuana (Fried *et al.*, 2002).

DHHS states that age of first use may be a critical factor in persistent impairment from chronic marijuana use. Individuals with a history of marijuana-only use that began before the age of 16 were found to perform more poorly on a visual scanning task measuring attention than individuals who started using marijuana after 16 (Ehrenreich *et al.*, 1999). DHHS's document noted that Kandel and Chen (2000) assert that the majority of early-onset marijuana users do not go on to become heavy users of marijuana, and those that do tend to associate with delinquent social groups.

DEA notes an additional recent study that indicates that because neuromaturation continues through adolescence, results on the long-lasting cognitive effects of marijuana use in adults cannot necessarily generalize to adolescent marijuana users. Medina and colleagues (2007) examined neuropsychological functioning in 31 adolescent abstinent marijuana users, after a period of abstinence from marijuana of 23 to 28 days, and in 34 demographically similar control adolescents, all 16–18 years of age. After controlling for lifetime alcohol use and depressive symptoms, adolescent marijuana users demonstrated slower psychomotor speed (p .05), and poorer complex attention (p .04), story memory (p .04), and planning and sequencing ability (p .001) compared with nonusers. The number of lifetime marijuana use episodes was associated with poorer cognitive function, even after controlling for lifetime alcohol use. The general pattern of results suggested that, even after a month of monitored abstinence, adolescent marijuana users demonstrate subtle neuropsychological deficits compared with nonusers. The authors of this study suggest that frequent marijuana use during adolescence may negatively influence neuromaturation and cognitive development.

In summary, acute administration of marijuana impairs performance on tests of learning, associative processes, and psychomotor behavior. The effects of chronic marijuana use have also been studied. While a few studies did not observe strong persistent neurocognitive consequences of long-term cannabis use (Lyketsos *et al.*, 1999; Lyons *et al.*, 2004), others provide support for the existence of persistent consequences (Bolla *et al.*, 2002, 2005). The cognitive impairments that are observed 12 hours to seven days after marijuana use (Messinis *et al.*, 2006; Solowij *et al.*, 2002; Harrison *et al.*, 2002), and that persist beyond behaviorally detectable intoxication, are noteworthy and may have significant consequences on workplace performance and safety, academic achievement, and automotive safety. In addition, adolescents may be particularly vulnerable to the long-lasting deleterious effects of marijuana on cognition. The overall significant effect on general intelligence as measured by IQ should also not be overlooked.

Behavioral Effects of Prenatal Exposure

The impact of *in utero* marijuana exposure on performance in a series of cognitive tasks has been studied in children of various ages. DHHS concludes in its analysis of the presently examined petition that since many marijuana users have abused other drugs, it is difficult to determine the specific impact of marijuana on prenatal exposure. Fried and Watkinson (1990) found that four year old children of heavy marijuana users have deficits in memory and verbal measures. Maternal marijuana use is predictive of poorer performance on abstract/visual reasoning tasks of three year old children (Griffith *et al.*, 1994) and an increase in omission errors on a vigilance task of six year olds (Fried *et al.*, 1992). When the effect of prenatal exposure in nine to 12 year old children is analyzed, in utero exposure to marijuana is negatively associated with executive function tasks that require impulse control, visual analysis, and hypothesis testing (Fried *et al.*, 1998).

DEA notes studies showing that Δ^9-THC passes the placental barrier (Idanpaan-Heikkila *et al.*, 1969) and that fetal blood concentrations are at least equal to those found in the mother's blood (Grotenhermen, 2003).

In summary, smoked marijuana exerts a number of cardiovascular and respiratory effects, both acutely and chronically. Marijuana's main psychoactive ingredient Δ^9-THC alters immune function. The cognitive impairments caused by marijuana use that persist beyond behaviorally detectable intoxication may have significant consequences on workplace performance and safety, academic achievement, and automotive safety, and adolescents may be particularly vulnerable to marijuana's cognitive effects. Prenatal exposure to marijuana was linked to children's poorer performance in a number of cognitive tests.

FACTOR 3: THE STATE OF THE CURRENT SCIENTIFIC KNOWLEDGE REGARDING THE DRUG OR SUBSTANCE

DHHS states that marijuana is a mixture of the dried leaves and flowering tops of the cannabis plant (Agurell *et al.*, 1984; Graham,

1976; Mechoulam, 1973). These portions of the plant have the highest levels of Δ^9-THC, the primary psychoactive ingredient in marijuana. The most potent product (i.e., that having the highest percentage of Δ^9-THC) of dried material is sinsemilla, derived from the unpollinated flowering tops of the female cannabis plant. Generally, this potent marijuana product is associated with indoor grow sites and may have a Δ^9-THC content of 15 to 20 percent or more. Other, less common forms of marijuana found on the illicit market are hashish and hashish oil. Hashish is a Δ^9-THC-rich resinous material of the cannabis plant which is dried and compressed into a variety of forms (balls, cakes or sticks). Dried pieces are generally broken off and smoked. Δ^9-THC content is usually about five percent. The Middle East, North Africa and Pakistan/Afghanistan are the main sources of hashish. Hashish oil is produced by extracting the cannabinoids from plant material with a solvent. Hashish oil is a light to dark brown viscous liquid with a Δ^9-THC content of about 15 percent. The oil is often sprinkled on cigarettes, allowed to dry, and then smoked.

Chemistry

DHHS states that some 483 natural constituents have been identified in marijuana, including 66 compounds that are classified as cannabinoids (Ross and El Sohly, 1995). Cannabinoids are not known to exist in plants other than marijuana, and most naturally occurring cannabinoids have been identified chemically. The psychoactive properties of cannabis are attributed to one or two of the major cannabinoid substances, namely delta-9- tetrahydrocannabinol (Δ^9-THC) and delta-8-tetrahydrocannabinol (Δ^8-THC). Other natural cannabinoids, such as cannabidiol (CBD) and cannabinol (CBN), have been characterized. CBD does not possess Δ^9-THC-like psychoactivity. Its pharmacological properties appear to include anticonvulsant, anxiolytic and sedative properties (Agurell *et al.*, 1984, 1986; Hollister, 1986).

DHHS states that Δ^9-THC is an optically active resinous substance, extremely lipid soluble, and insoluble in water. Chemically, Δ^9-THC is known as (6aR-trans)-6a,7,8,10a-tetrahydro-6,6,9-trimethyl-3-pentyl-6H-dibenzo-[b,d]pyran-1-ol or (-)Δ^9-(trans)-tetrahydrocannabinol. The pharmacological activity of Δ^9-THC is stereospecific: the (-)-trans isomer is 6–100 times more potent than the (+)-trans isomer (Dewey *et al.*, 1984).

DEA notes a review of the contaminants and adulterants that can be found in marijuana (McPartland, 2002). In particular, DEA notes that many studies have reported contamination of both illicit and NIDA-grown marijuana with microbial contaminants, bacterial or fungal (McLaren *et al.*, 2008; McPartland, 1994, 2002; Ungerleider *et al.*, 1982; Taylor *et al.*, 1982; Kurup *et al.*, 1983). Other microbial contaminants include Klebsiella pneumoniae, salmonella enteritidis, and group D Streptococcus (Ungerlerder *et al.*, 1982; Kagen *et al.*, 1983; Taylor *et al.*, 1982). DEA notes that a review by McLaren and colleagues (2008) discusses studies showing that heavy metals present in soil may also contaminate cannabis, and states that these contaminants have the potential to harm the user without harming the plant. Other sources of contaminants discussed by McLaren and colleagues (2008) include growth enhancers and pest control products related to marijuana cultivation and storage.

Human Pharmacokinetics

DHHS states that marijuana is generally smoked as a cigarette (weighing between 0.5 and 1.0 gm; Jones, 1980) or in a pipe. It can also be taken orally in foods or as extracts of plant material in ethanol or other solvents. The absorption, metabolism, and pharmacokinetic profile of Δ^9-THC (and other cannabinoids) in marijuana or other drug products containing Δ^9-THC vary with route of administration and formulation (Adams and Martin, 1996; Agurell *et al.*, 1984, 1986). When marijuana is administered by smoking, Δ^9-THC in the form of an aerosol is absorbed within seconds. The psychoactive effects of marijuana occur immediately following absorption, with mental and behavioral effects measurable up for to six hours after absorption (Grotenhermen, 2003; Hollister, 1986, 1988). Δ^9-THC is delivered to the brain rapidly and efficiently as would be expected of a highly lipid-soluble drug.

The petitioner provided a discussion of new, or less common, routes and methods of administration being currently explored (pg. 57, line 1). These include vaporization for the inhalation route, as well as rectal, sublingual, and transdermal routes.

DEA notes that respiratory effects are only part of the harmful health effects of prolonged marijuana exposure, as described further under factor 2 of this document. DEA also notes that at this time, the majority of studies exploring the potential therapeutic uses of marijuana use smoked marijuana, and the pharmacokinetics and bioavailability from routes of administration other than smoked and oral are not well-known.

The pharmacokinetics of smoked and orally ingested marijuana are thoroughly reviewed in DHHS's review document.

Medical Utility

The petition filed by the Coalition to Reschedule Cannabis (Marijuana) aims to repeal the rule placing marijuana in schedule I of the CSA, based in part on the proposition that marijuana has an accepted medical use in the United States. However DHHS has concluded in its 2006 analysis that marijuana has no accepted medical use in treatment in the United States. Following is a discussion of the petitioner's specific points and a presentation of DHHS's evaluation and recommendation on the question of accepted medical use for marijuana.

The petitioner states (pg. 48, line 2), ''Results from clinical research demonstrated that both dronabinol and whole plant cannabis can offer a safe and effective treatment for the following illnesses: muscle spasm in multiple sclerosis, Tourette syndrome, chronic pain, nausea and vomiting in HIV/AIDS and cancer chemotherapy, loss of appetite from cancer, hyperactivity of the bladder in patients with multiple sclerosis and spinal cord injury, and dyskinesia caused by levodopa in Parkinson's disease.''

To support its claim that marijuana has an accepted medical use in the United States, the petitioner listed supporting evidence that included the following:

- Evidence from clinical research and reviews of earlier clinical research (Exh. C, Section I (4, 6), pg. 29)
- Acceptance of the medical use of marijuana by eight states since 1996 and state officials in these states establishing that marijuana has an accepted medical use in the United States (Exh. C, Section I (1), pg. 13)
- Increased recognition by health care professionals and the medical community, including the Institute of Medicine (IOM) (Exh. C, Section I (2), pg. 15)
- Patients' experience in which they reported benefits from smoking marijuana (Exh. C, Section I (3), pg. 22)
- *Evidence from clinical research (Exh. C, Section I (4, 6), pg. 29)*

DHHS states that a new drug application (NDA) for marijuana has not been submitted to the FDA for any indication and thus no medicinal product containing botanical cannabis has been approved for marketing. Only small clinical studies published in the current medical literature demonstrate that research with marijuana is being conducted in humans in the United States under FDA-authorized investigational new drug (IND) applications.

There are ongoing clinical studies of the potential utility of marijuana in medical applications. DHHS states that in 2000, the state of California established the Center for Medicinal Cannabis Research (CMCR) which has funded studies on the potential use of cannabinoids for the treatment of multiple sclerosis, neuropathic pain, appetite suppression and cachexia, and severe pain and nausea related to cancer or its treatment by chemotherapy. To date, though, no NDAs utilizing marijuana for these indications have been submitted to the FDA.

To establish accepted medical use, among other criteria, the effectiveness of a drug must be established in well-controlled scientific studies performed in a large number of patients. To date, such studies have not been performed for marijuana. Small clinical trial studies with limited patients and short duration such as those cited by the petitioner are not sufficient to establish medical utility. Larger studies of longer duration are needed to fully characterize the drug's efficacy and safety profile. Anecdotal reports, patients' self-reported effects, and isolated case reports are not adequate evidence to support an accepted medical use of marijuana (57 FR 10499, 1992).

In addition to demonstrating efficacy, adequate safety studies must be performed to show that the drug is safe for treating the targeted disease. DHHS states that safety studies for acute or subchronic administration of marijuana have been carried out through a limited number of Phase 1 clinical investigations approved by the FDA, but there have been no NDA-quality studies that have scientifically assessed the efficacy and full safety profile of marijuana for any medical condition.

DEA further notes that a number of clinical studies from CMCR have been discontinued. Most of these discontinuations were due to

recruitment difficulties (*http://www.cmcr.ucsd.edu/geninfo/research.htm* (last retrieved 07/07/2010) (listing 6 discontinued studies, 5 of which were discontinued because of recruitment issues)).

The petitioner states that the pharmacological effects are well established for marijuana and Δ^9-THC, using the argument that Marinol (containing synthetic Δ^9-THC, known generically as dronabinol) and Cesamet (containing nabilone, a synthetic cannabinoid not found in marijuana) are approved for several therapeutic indications. The approvals of Marinol and Cesamet were based on well-controlled clinical studies that established the efficacy and safety of these drugs as a medicine. Smoked marijuana has not been demonstrated to be safe and effective in treating these medical conditions. Marijuana is a drug substance composed of numerous cannabinoids and other constituents; hence the safety and efficacy of marijuana cannot be evaluated solely on the effects of Δ^9-THC. Adequate and well-controlled studies must be performed with smoked marijuana to establish efficacy and safety. DHHS states that there is a lack of accepted safety for the use of marijuana under medical supervision.

The petitioner has not submitted any new data meeting the requisite scientific standards to support the claim that marijuana has an accepted medical use in the United States. Hence, the new information provided by the petitioner does not change the federal government's evaluation of marijuana's medical use in the United States.

- Petitioner's claim of acceptance of the medical use of marijuana by eight states since 1996 and state officials in these states establishing that marijuana has an accepted medical use in the United States

Petitioner argues that, ''[t]he acceptance of cannabis's medical use by eight states since 1996 and the experiences of patients, doctors, and state officials in these states establish marijuana's accepted medical use in the United States.'' Petition at 10, 13. This argument is contrary to the CSA's statutory scheme. The CSA does not assign to the states the authority to make findings relevant to CSA scheduling determinations. Rather, the CSA expressly delegates the task of making such findings—including whether a substance has any currently accepted medical use in treatment in the United States—to the Attorney General. 21 U.S.C. 811(a). The CSA also expressly tasks the Secretary of DHHS to provide a scientific and medical evaluation and scheduling recommendations to inform the Attorney General's findings. 21 U.S.C. 811(b); *see also* 21 C.F.R. 308.43. That Congress explicitly provided scheduling authority to these two federal entities in this comprehensive and exclusive statutory scheme precludes the argument that state legislative action can establish accepted medical use under the CSA.

The CSA explicitly provides that in making a scheduling determination, the Attorney General shall consider the following eight factors:

1. The drug's actual or relative potential for abuse
2. Scientific evidence of its pharmacological effect, if known;
3. The state of current scientific knowledge regarding the drug;
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. The drug's psychic or physiological dependence liability; and
8. Whether the substance is an immediate precursor of a substance already controlled under the CSA.

21 U.S.C. 811(c). These factors embody Congress's view of the specialized agency expertise required for drug rescheduling decisions. The CSA's statutory text thus further evidences that Congress did not envision such a role for state law in establishing the schedules of controlled substances under the CSA. *See Krumm v. Holder,* 2009 WL 1563381, at *16 (D.N.M. 2009) (''The CSA does not contemplate that state legislatures' determinations about the use of a controlled substance can be used to bypass the CSA's rescheduling process.'').

The long-established factors applied by DEA for determining whether a drug has a ''currently accepted medical use'' under the CSA are:

1. The drug's chemistry must be known and reproducible;
2. There must be adequate safety studies;
3. There must be adequate and well-controlled studies proving efficacy;
4. The drug must be accepted by qualified experts; and
5. The scientific evidence must be widely available.

57 FR 10,499, 10,506 (1992), *ACT,* 15 F.3d at 1135 (upholding these factors as valid criteria for determining ''currently accepted medical use''). A drug will be deemed to have a currently accepted medical use for CSA purposes only if all five of the foregoing elements are demonstrated. The following is a summary of information as it relates to each of these five elements.

1. The drug's chemistry must be known and reproducible

DHHS states that although the structures of many cannabinoids found in marijuana have been characterized, a complete scientific analysis of all the chemical components found in marijuana has not been conducted.

DEA notes that in addition to changes due to its own genetic plasticity, marijuana and its chemistry have been throughout the ages, and continue to be, modified by environmental factors and human manipulation (Paris and Nahas, 1984).

2. There must be adequate safety studies

DHHS states that safety studies for acute or subchronic administration of marijuana have been carried out only through a limited number of Phase 1 clinical investigations approved by the FDA. There have been no NDA-quality studies that have scientifically assessed the safety profile of marijuana for any medical condition. DHHS also states that at this time, the known risks of marijuana use have not been shown to be outweighed by specific benefits in well-controlled clinical trials that scientifically evaluate safety and efficacy.

DHHS further states that it cannot conclude that marijuana has an acceptable level of safety without assurance of a consistent and predictable potency and without proof that the substance is free of contamination.

As discussed in Factors 1 and 2, current data suggest that marijuana use produces adverse effects on the respiratory system, memory and learning. Marijuana use is associated with dependence and addiction. In addition, large epidemiological studies indicate that marijuana use may exacerbate symptoms in individuals with schizophrenia.

Therefore DHHS concludes that, even under medical supervision, marijuana has not been shown to have an accepted level of safety. Furthermore, if marijuana is to be investigated more widely for medical use, information and data regarding the chemistry, manufacturing, and specifications of marijuana must be developed.

3. There must be adequate and well-controlled studies proving efficacy

DHHS states that no studies have been conducted with marijuana showing efficacy for any indication in controlled, large scale, clinical trials.

To establish accepted medical use, the effectiveness of a drug must be established in well-controlled, well-designed, well-conducted, and well-documented scientific studies, including studies performed in a large number of patients (57 FR 10499, 1992). To date, such studies have not been performed. The small clinical trial studies with limited patients and short duration are not sufficient to establish medical utility. Studies of longer duration are needed to fully characterize the drug's efficacy and safety profile. Scientific reliability must be established in multiple clinical studies. Furthermore, anecdotal reports and isolated case reports are not adequate evidence to support an accepted medical use of marijuana (57 FR 10499, 1992). The evidence from clinical research and reviews of earlier clinical research does not meet this standard.

As noted, DHHS states that a limited number of Phase I investigations have been conducted as approved by the FDA. Clinical trials, however, generally proceed in three phases. *See* 21 C.F.R. 312.21 (2010). Phase I trials encompass initial testing in human subjects, generally involving 20 to 80 patients. *Id.* They are designed primarily to assess initial safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary studies of potential therapeutic benefit. (62 FR 66113, 1997). Phase II and Phase III studies involve successively larger groups of patients: usually no more than several hundred subjects in Phase II and usually from several hundred to several thousand in Phase III. 21 C.F.R. 312.21. These studies are designed primarily to explore (Phase II) and to demonstrate or confirm (Phase III) therapeutic efficacy and benefit in patients. (62 FR 66113, 1997). No Phase II or Phase III studies of marijuana have been conducted. Even in 2001, DHHS acknowledged that there is ''suggestive evidence that marijuana may have beneficial

therapeutic effects in relieving spasticity associated with multiple sclerosis, as an analgesic, as an antiemetic, as an appetite stimulant and as a bronchodilator.'' (66 FR 20038, 2001). But there is still no data from adequate and well-controlled clinical trials that meets the requisite standard to warrant rescheduling.

DHHS states in a published guidance that it is committed to providing ''research-grade marijuana for studies that are the most likely to yield usable, essential data'' (DHHS, 1999). DHHS states that the opportunity for scientists to conduct clinical research with botanical marijuana has increased due to changes in the process for obtaining botanical marijuana from NIDA, the only legitimate source of the drug for research in the United States. It further states that in May 1999, DHHS provided guidance on the procedures for providing research-grade marijuana to scientists who intend to study marijuana in scientifically valid investigations and well-controlled clinical trials (DHHS, 1999).

4. The drug must be accepted by qualified experts

A material conflict of opinion among experts precludes a finding that marijuana has been accepted by qualified experts (57 FR 10499, 1992). DHHS states that, at this time, it is clear that there is not a consensus of medical opinion concerning medical applications of marijuana, even under conditions where its use is severely restricted. DHHS also concludes that, to date, research on the medical use of marijuana has not progressed to the point that marijuana can be considered to have a ''currently accepted medical use'' or a ''currently accepted medical use with severe restrictions.''

5. The scientific evidence must be widely available

DHHS states that the scientific evidence regarding the safety or efficacy of marijuana is typically available only in summarized form, such as in a paper published in the medical literature, rather than in a raw data format. As such, there is no opportunity for adequate scientific scrutiny of whether the data demonstrate safety or efficacy. Furthermore, as stated before, there have only been a limited number of small clinical trials and no controlled, large-scale clinical trials have been conducted with marijuana on its efficacy for any indications or its safety.

In summary, from DHHS's statements on the five cited elements required to make a determination of ''currently accepted medical use'' for marijuana, DEA has determined that none has been fulfilled. A complete scientific analysis of all the chemical components found in marijuana is still missing. There has been no NDA-quality study that has assessed the efficacy and full safety profile of marijuana for any medical use. At this time, it is clear that there is not a consensus of medical opinion concerning medical applications of marijuana. To date, research on the medical use of marijuana has not progressed to the point that marijuana can be considered to have a ''currently accepted medical use'' or even a ''currently accepted medical use with severe restrictions.'' 21 U.S.C. 812(b)(2)(B)). Additionally, scientific evidence as to the safety or efficacy of marijuana is not widely available.

• *Petitioner's claim of increased recognition by health care professionals and the medical community, including the Institute of Medicine (IOM)*

The petitioner states (pg. 15 line 2), ''Cannabis's accepted medical use in the United States is increasingly recognized by healthcare professionals and the medical community, including the Institute of Medicine.''

DHHS describes that in February 1997, a National Institutes of Health (NIH)-sponsored workshop analyzed available scientific evidence on the potential utility of marijuana. In March 1999, the Institute of Medicine (IOM) issued a detailed report on the potential medical utility of marijuana. Both reports concluded that there need to be more and better studies to determine potential medical applications of marijuana. The IOM report also recommended that clinical trials should be conducted with the goal of developing safe delivery systems (NIH, 1997; IOM, 1999).

DEA notes that in its recommendations, the 1999 IOM report states,

If there is any future for marijuana as a medicine, it lies in its isolated components, the cannabinoids and their synthetic derivatives. Isolated cannabinoids will provide more reliable effects than crude plant mixtures. Therefore, the purpose of clinical trials of smoked marijuana would not be to develop marijuana as a licensed drug but rather to serve as a first step toward the development of nonsmoked rapid-onset cannabinoid delivery systems.

Thus, while the IOM report did support further research into therapeutic uses of cannabinoids, the IOM report did not *''recognize marijuana's accepted medical use''* but rather the potential therapeutic utility of cannabinoids.

DEA notes that the lists presented by the petitioner (pg. 16–18) of ''Organizations Supporting *Access* to Therapeutic Cannabis'' (emphasis added) and ''[Organizations Supporting] No Criminal Penalty'' contain a majority of organizations that do not specifically represent medical professionals. By contrast, the petitioner also provides a list of ''Organizations Supporting Research on the Therapeutic Use of Cannabis'' (emphasis added), which does contain a majority of organizations specifically representing medical professionals.

The petitioner discusses (pg. 20, line 11) the results of a United States survey presented at the annual meeting of the American Society of Addiction Medicine, and states that the study's results,

indicate that physicians are divided on the medical use of cannabis (Reuters of 23 April 2001). Researchers at Rhode Island Hospital in Providence asked 960 doctors about their attitude towards the statement, ''Doctors should be able to legally prescribe marijuana as medical therapy.'' 36 percent of the responders agreed, 38 percent disagreed and 26 percent were neutral.

DEA notes that the results of the study, later published in full (Charuvastra et al., 2005) show that a slight majority of medical doctors polled were opposed to the legalization of medical prescription of marijuana. This supports the finding that there is a material conflict of opinion among medical professionals.

• *Patients' experience in which they reported benefits from smoking marijuana (Exh. C, Section I(3), pg. 22);*

Under the petition's section C. I. 3., the petitioner proposes both anecdotal self-reported effects by patients and clinical studies. The petitioner states (pg. 22, line 2),

[. . .] an increasing number of patients have collected experience with cannabis. Many reported benefits from its use. Some of this experience has been confirmed in reports and clinical investigations or stimulated clinical research that confirmed these patients' experience on other patients suffering from the same disease.

Anecdotal self-reported effects by patients are not adequate evidence for the determination of a drug's accepted medical use. DEA previously ruled in its final order denying the petition of the National Organization for Reform of Marijuana Laws (NORML) to reschedule marijuana from Schedule I to Schedule II of the Controlled Substances Act (57 FR 10499, 1992) that,

Lay testimonials, impressions of physicians, isolated case studies, random clinical experience, reports so lacking in details they cannot be scientifically evaluated, and all other forms of anecdotal proof are entirely irrelevant.

DEA further explained in the same ruling that,

Scientists call [stories by marijuana users who claim to have been helped by the drug] anecdotes. They do not accept them as reliable proofs. The FDA's regulations, for example, provide that in deciding whether a new drug is a safe and effective medicine, ''isolated case reports will not be considered.'' 21 CFR 314.126(e). Why do scientists consider stories from patients and their doctors to be unreliable?

First, sick people are not objective scientific observers, especially when it comes to their own health. [. . .] Second, most of the stories come from people who took marijuana at the same time they took prescription drugs for their symptoms. [. . .] Third, any mind-altering drug that produces euphoria can make a sick person think he feels better. [. . .] Fourth, long-time abusers of marijuana are not immune to illness. [. . .] Thanks to scientific advances and to the passage of the Federal Food, Drug and Cosmetic Act (FDCA) in 1906, 21 U.S.C. 301 et seq., we now rely on rigorous scientific proof to assure the safety and effectiveness of new drugs. Mere stories are not considered an acceptable way to judge whether dangerous drugs should be used as medicines.

Thus, patients' anecdotal experiences with marijuana are not adequate evidence when evaluating whether marijuana has a currently accepted medical use.

In summary, marijuana contains some 483 natural constituents and exists in several forms, including dried leaves and flowering

tops, hashish and hashish oil. It is generally smoked as a cigarette. Research with marijuana is being conducted in humans in the United States under FDA-authorized IND applications, and using marijuana cigarettes provided by NIDA. Adequate studies have not been published to support the safety and efficacy of marijuana as a medicine. No NDA for marijuana has been submitted to the FDA for any indication and thus no medicinal product containing botanical cannabis has been approved for marketing. DEA notes that state laws do not establish a currently accepted medical use under federal law. Furthermore, DEA previously ruled that anecdotal self-reported effects by patients are not adequate evidence of a currently accepted medical use under federal law. A material conflict of opinion among experts precludes a finding that marijuana has been accepted by qualified experts. At present, there is no consensus of medical opinion concerning medical applications of marijuana. In short, the limited number of clinical trials involving marijuana that have been conducted to date—none of which have progressed beyond phase 1 of the three phases needed to demonstrate safety and efficacy for purposes of FDA approval—fails by a large measure to provide a basis for any alteration of the prior conclusions made by HHS and DEA (in 1992 and in 2001) that marijuana has no currently accepted medical use in treatment in the United States.

FACTOR 4: ITS HISTORY AND CURRENT PATTERN OF ABUSE

Marijuana use has been relatively stable from 2002 to 2009, and it continues to be the most widely used illicit drug. According to the NSDUH, there were 2.4 million new users (6,000 initiates per day) in 2009 and 16.7 million current (past month) users of marijuana aged 12 and older. Past month use of marijuana was statistically significantly higher in 2009 (16.7 million) than in 2008 (15.2 million), according to NSDUH. An estimated 104.4 million Americans age 12 or older had used marijuana or hashish in their lifetime and 28.5 million had used it in the past year. In 2008, most (62.2 percent) of the 2.2 million new users were less than 18 years of age. In 2008, marijuana was used by 75.7 percent of current illicit drug users and was the only drug used by 57.3 percent of these users. In 2008, among past year marijuana users aged 12 or older, 15.0 percent used marijuana on 300 or more days within the previous 12 months. This translates into 3.9 million people using marijuana on a daily or almost daily basis over a 12-month period. In 2008, among past month marijuana users, 35.7 percent (5.4 million) used the drug on 20 or more days in the past month.

Marijuana is also the illicit drug with the highest rate of past year dependence or abuse. According to the 2009 NSDUH report, 4.3 million persons were classified with marijuana dependence or abuse based on criteria specified in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM–IV).

According to the 2010 Monitoring the Future (MTF) survey, marijuana is used by a large percentage of American youths. Among students surveyed in 2010, 17.3 percent of eighth graders, 33.4 percent of tenth graders, and 43.8 percent of twelfth graders reported lifetime use (i.e., any use in their lifetime) of marijuana. In addition, 13.7, 27.5 and 34.8 percent of eighth, tenth and twelfth graders, respectively, reported using marijuana in the past year. A number of high-schoolers reported daily use in the past month, including 1.2, 3.3 and 6.1 percent of eighth, tenth and twelfth graders, respectively.

The prevalence of marijuana use and abuse is also indicated by criminal investigations for which drug evidences were analyzed in DEA and state laboratories. The National Forensic Laboratory System (NFLIS), which compiles information on exhibits analyzed in state and local law enforcement laboratories, showed that marijuana was the most frequently identified drug from January 2001 through December 2010: In 2010, marijuana accounted for 36.3 percent (464,059) of all drug exhibits in NFLIS. Similar findings were reported by the System to Retrieve Information from Drug Evidence (STRIDE), a DEA database which compiles information on exhibits analyzed in DEA laboratories, for the same reporting period. From January 2001 through December 2010, marijuana was the most frequently identified drug. In 2010, there were 11,293 marijuana exhibits associated with 7,158 law enforcement cases representing 16.7 percent of all exhibits in STRIDE.

The high consumption of marijuana is being fueled by increasing amounts of domestically grown marijuana as well as increased amounts of foreign source marijuana being illicitly smuggled into the United States. In 2009, the Domestic Cannabis Eradication and Suppression Program (DCE/SP) reported that 9,980,038 plants were eradicated in outdoor cannabis cultivation areas in the United States. Major domestic outdoor cannabis cultivation areas were found in California, Kentucky, Tennessee and Hawaii. Significant quantities of marijuana were also eradicated from indoor cultivation operations. There were 414,604 indoor plants eradicated in 2009 compared to 217,105 eradicated in 2000. Most foreign-source marijuana smuggled into the United States enters through or between points of entry at the United States-Mexico border. However, drug seizure data show that the amount of marijuana smuggled into the United States from Canada via the United States-Canada border has risen to a significant level. In 2009, the Federal-wide Drug Seizure System (FDSS) reported seizures of 1,910,600 kg of marijuana.

While most of the marijuana available in the domestic drug markets is lower potency commercial-grade marijuana, usually derived from outdoor cannabis grow sites in Mexico and the United States, an increasing percentage of the available marijuana is high potency marijuana derived from indoor, closely controlled cannabis cultivation in Canada and the United States. The rising prevalence of high potency marijuana is evidenced by a nearly two-fold increase in average potency of tested marijuana samples, from 4.87 percent Δ^9-THC in 2000 to 8.49 percent Δ^9-THC in 2008.

In summary, marijuana is the most commonly used illegal drug in the United States, and it is used by a large percentage of American high-schoolers. Marijuana is the most frequently identified drug in state, local and federal forensic laboratories, with increasing amounts both of domestically grown and of illicitly smuggled marijuana. An observed increase in the potency of seized marijuana also raises concerns.

FACTOR 5: THE SCOPE, DURATION, AND SIGNIFICANCE OF ABUSE

Abuse of marijuana is widespread and significant. DHHS presented data from the NSDUH, and DEA has updated this information. As previously noted, according to the NSDUH, in 2009, an estimated 104.4 million Americans age 12 or older had used marijuana or hashish in their lifetime, 28.5 million had used it in the past year, and 16.7 million (6.6 percent) had used it in the past month. In 2008, an estimated 15.0 percent of past year marijuana users aged 12 or older used marijuana on 300 or more days within the past 12 months. This translates into 3.9 million persons using marijuana on a daily or almost daily basis over a 12-month period. In 2008, an estimated 35.7 percent (5.4 million) of past month marijuana users aged 12 or older used the drug on 20 or more days in the past month (SAMHSA, NSDUH and TEDS). Chronic use of marijuana is associated with a number of health risks (see Factors 2 and 6).

Marijuana's widespread availability is being fueled by increasing marijuana production domestically and increased illicit importation from Mexico and Canada. Domestically both indoor and outdoor grow sites have been encountered. In 2009, nearly 10 million marijuana plants were seized from outdoor grow sites and over 410,000 were seized from indoor sites for a total of over 10 million plants in 2009 compared to about 2.8 million plants in 2000 (Domestic Cannabis Eradication/Suppression Program). An increasing percentage of the available marijuana being trafficked in the United States is higher potency marijuana derived from the indoor, closely controlled cultivation of marijuana plants in both the US and Canada (Domestic Cannabis Eradication/Suppression Program) and the average percentage of Δ^9-THC in seized marijuana increased almost two-fold from 2000 to 2008 (The University of Mississippi Potency Monitoring Project). Additional studies are needed to clarify the impact of greater potency, but DEA notes one study showing that higher levels of Δ^9-THC in the body are associated with greater psychoactive effects (Harder and Rietbrock, 1997), which can be correlated with higher abuse potential (Chait and Burke, 1994).

Data from TEDS show that in 2008, 17.2 percent of all admissions were for primary marijuana abuse. In 2007, more than half of the drug-related treatment admissions involving individuals under the age of 15 (60.8 percent) and more than half of the drug-related treatment admissions involving individuals 15 to 19 years of age (55.9 percent), were for primary marijuana abuse. In 2007, among the marijuana/hashish admissions (286,194), 25.1 percent began using marijuana at age 12 or younger.

In summary, the recent statistics from these various surveys and databases show that

marijuana continues to be the most commonly used illicit drug, with significant rates of heavy use and dependence in teenagers and adults.

The petitioner states, ''The use and abuse of cannabis has been widespread in the United States since national drug use surveys began in the 1970s. A considerable number of cannabis users suffer from problems that meet the criteria for abuse. However, the large majority of cannabis users do not experience any relevant problems related to their use.'' (pg. 4, line 31).

Petitioner acknowledges that a considerable number of cannabis users suffer from problems that meet the criteria for abuse. DEA provides data under this Factor, as well as Factors 1, 2, and 7, that support this undisputed issue. Briefly, current data suggest that marijuana use produces adverse effects on the respiratory system, memory and learning. Marijuana use is associated with dependence and addiction. In addition, large epidemiological studies indicate that marijuana use may exacerbate symptoms in individuals with schizophrenia, and may precipitate schizophrenic disorders in those individuals who are vulnerable to developing psychosis.

FACTOR 6: WHAT, IF ANY, RISK THERE IS TO THE PUBLIC HEALTH

The risk marijuana poses to the public health may manifest itself in many ways. Marijuana use may affect the physical and/or psychological functioning of an individual user, but may also have broader public impacts, for example, from a marijuana-impaired driver. The impacts of marijuana abuse and dependence are more disruptive for an abuser, but also for the abuser's family, friends, work environment, and society in general. Data regarding marijuana health risks are available from many sources, including forensic laboratory analyses, crime laboratories, medical examiners, poison control centers, substance abuse treatment centers, and the scientific and medical literature. Risks have been associated with both acute and chronic marijuana use, including risks for the cardiovascular and respiratory systems, as well as risks for mental health and cognitive function and risks related to prenatal exposure to marijuana. The risks of marijuana use and abuse have previously been discussed in terms of the scientific evidence of its pharmacological effects on physical systems under Factor 2. Below, some of the risks of marijuana use and abuse are discussed in broader terms of the effects on the individual user and the public from acute and chronic use of the drug.

Risks Associated with Acute Use of Marijuana

DHHS states that acute use of marijuana impairs psychomotor performance, including performance of complex tasks, which makes it inadvisable to operate motor vehicles or heavy equipment after using marijuana (Ramaekers *et al.*, 2004). DHHS further describes a study showing that acute administration of smoked marijuana impairs performance on tests of learning, associative processes, and psychomotor behavior (Block *et al.*, 1992). DHHS also describes studies showing that administration to human volunteers of Δ^9-THC in a smoked marijuana cigarette produced impaired perceptual motor speed and accuracy, two skills that are critical to driving ability (Kurzthaler *et al.*, 1999) and produced increases in disequilibrium measures, as well as in the latency in a task of simulated vehicle braking, at a rate comparable to an increase in stopping distance of 5 feet at 60 mph (Liguori *et al.*, 1998).

The petitioner states that (pg., 65, line 10), ''Although the ability to perform complex cognitive operations is assumed to be impaired following acute marijuana smoking, complex cognitive performance after acute marijuana use has not been adequately assessed under experimental conditions.'' As described above, DHHS presents evidence of marijuana's acute effects on complex cognitive tasks.

DHHS states that dysphoria and psychological distress, including prolonged anxiety reactions, are potential responses in a minority of individuals who use marijuana (Haney *et al.*, 1999). DEA notes reviews of studies describing that some users report unpleasant psychological reactions. Acute anxiety reactions to cannabis may include restlessness, depersonalization, derealization, sense of loss of control, fear of dying, panic and paranoid ideas (see reviews by Thomas, 1993 and Weil, 1970).

DEA notes a review of studies showing that the general depressant effect of moderate to high doses of cannabis might contribute to slowed reaction times, inability to maintain concentration and lapses in attention (see review by Chait and Pierri, 1992). The review suggests that fine motor control and manual dexterity are generally adversely affected although simple reaction time may or may not be. DEA also notes studies showing that choice or complex reaction time is more likely to be affected, with reaction time consistently increasing with the difficulty of the task (e.g., Block and Wittenborn, 1985).

DEA also notes additional studies showing marijuana use interferes with the ability to operate motor vehicles. Studies show that marijuana use can cause impairment in driving (Robbe and O'Hanlon, 1999). The National Highway Traffic Safety Administration (NHTSA) conducted a study with the Institute for Human Psychopharmacology at Maastricht University in the Netherlands (Robbe and O'Hanlon, 1999) to evaluate the effects of low and high doses of smoked Δ^9-THC alone and in combination with alcohol on the following tests: 1) the Road Tracking Test, which measures the driver's ability to maintain a constant speed of 62 mph and a steady lateral position between the boundaries of the right traffic lane; and 2) the Car Following Test, which measures a driver's reaction times and ability to maintain distance between vehicles while driving 164 ft behind a vehicle that executes a series of alternating accelerations and decelerations. Mild to moderate impairment of driving was observed in the subjects after treatment with marijuana. The study found that marijuana in combination with alcohol had an additive effect resulting in severe driving impairment.

DEA also notes a study by Bedard and colleagues (2007), which used a cross-sectional, case-control design with drivers aged 20–49 who were involved in a fatal crash in the United States from 1993 to 2003. Drivers were included if they had been tested for the presence of cannabis and had a confirmed blood alcohol concentration of zero. Cases were drivers who had at least one potentially unsafe driving action recorded in relation to the crash (e.g., speeding); controls were drivers who had no such driving action recorded. Authors calculated the crude and adjusted odds ratios (ORs) of any potentially unsafe driving action in drivers who tested positive for cannabis but negative for alcohol consumption. Five percent of drivers tested positive for cannabis. The crude OR of a potentially unsafe action was 1.39 (99 percent CI = 1.21–1.59) for drivers who tested positive for cannabis. Even after controlling for age, sex, and prior driving record, the presence of cannabis remained associated with a higher risk of a potentially unsafe driving action (1.29, 99 percent CI = 1.11–1.50). Authors of the study concluded that cannabis had a negative effect on driving, as predicted from various human performance studies.

In 2001, estimates derived from the United States Census Bureau and Monitoring the Future show that approximately 600,000 of the nearly 4 million United States high-school seniors drive under the influence of marijuana. Approximately 38,000 seniors reported that they had crashed while driving under the influence of marijuana in 2001 (MTF, 2001).

DEA further notes studies suggesting that marijuana can affect the performance of pilots. Yeswavage and colleagues (1985) evaluated the acute and delayed effects of smoking one marijuana cigarette containing 1.9 percent Δ^9-THC (19 mg of Δ^9-THC) on the performance of aircraft pilots. Ten subjects were trained in a flight simulator prior to marijuana exposure. Flight simulator performance was measured by the number of aileron (lateral control) and elevator (vertical control) and throttle changes, the size of these control changes, the distance off the center of the runaway on landing, and the average lateral and vertical deviation from an ideal glideslope and center line over the final mile of the approach. Compared to the baseline performance, significant differences occurred at 4 hours. Most importantly, at 24 hours after a single marijuana cigarette, there were significant impairments in the number and size of aileron changes, size of elevator changes, distance off-center on landing, and vertical and lateral deviations on approach to landing. Interestingly, despite these performance deficits, the pilots reported no significant subjective awareness of their impairments at 24 hours.

DEA notes a review of the contaminants and adulterants that can be found in marijuana (McPartland, 2002). In particular, DEA notes that many studies have reported contamination of both illicit and NIDA-grown marijuana with microbial contaminants, bacterial or fungal (McLaren *et al.*, 2008; McPartland, 1994, 2002; Ungerleider *et al.*, 1982; Taylor *et al.*, 1982; Kurup *et al.*, 1983). In a study by Kagen and

colleagues (1983), fungi was found in 13 of the 14 samples, and evidence of exposure to Aspergillus fungi was found in the majority of marijuana smokers (13 of 23), but only one of the 10 control participants. Aspergillus can cause aspergillosis, a fatal lung disease and DEA notes studies suggesting an association between this disease and cannabis smoking among patients with compromised immune systems (reviewed in McLaren *et al.*, 2008). Other microbial contaminants include bacteria such as *Klebsiella pneumoniae, salmonella enteritidis,* and group *D Streptococcus* (Ungerlerder *et al.*, 1982; Kagen *et al.*, 1983; Taylor *et al.*, 1982). DEA notes reports that *Salmonella* outbreaks have been linked to marijuana (Taylor *et al.*, 1982, CDC, 1981).

Risks Associated with Chronic Use of Marijuana

DHHS states that chronic exposure to marijuana smoke is considered to be comparable to tobacco smoke with respect to increased risk of cancer and lung damage. DEA notes studies showing that marijuana smoke contains several of the same carcinogens and co-carcinogens as tobacco smoke and suggesting that pre-cancerous lesions in bronchial epithelium also seem to be caused by long-term marijuana smoking (Roth *et al.*, 1998). DEA also notes the publication of a recent case-control study of lung cancer in adults (Aldington *et al.*, 2008), in which users reporting over 10.5 joint-years of exposure had a significantly increased risk of developing lung cancer, leading the study's authors to conclude that long-term cannabis use increases the risk of lung cancer in young adults. In addition, a distinctive marijuana withdrawal syndrome has been identified, indicating that marijuana produces physical dependence (Budney *et al.*, 2004), as described in Factor 7.

DHHS further quotes the Diagnostic and Statistical Manual (DSM–IV–TR, 2000) of the American Psychiatric Association, which states that the consequences of cannabis abuse are as follows:

[P]eriodic cannabis use and intoxication can interfere with performance at work or school and may be physically hazardous in situations such as driving a car. Legal problems may occur as a consequence of arrests for cannabis possession. There may be arguments with spouses or parents over the possession of cannabis in the home or its use in the presence of children. When psychological or physical problems are associated with cannabis in the context of compulsive use, a diagnosis of Cannabis Dependence, rather than Cannabis Abuse, should be considered.

Individuals with Cannabis Dependence have compulsive use and associated problems. Tolerance to most of the effects of cannabis has been reported in individuals who use cannabis chronically. There have also been some reports of withdrawal symptoms, but their clinical significance is uncertain. There is some evidence that a majority of chronic users of cannabinoids report histories of tolerance or withdrawal and that these individuals evidence more severe drug-related problems overall. Individuals with Cannabis Dependence may use very potent cannabis throughout the day over a period of months or years, and they may spend several hours a day acquiring and using the substance. This often interferes with family, school, work, or recreational activities. Individuals with Cannabis Dependence may also persist in their use despite knowledge of physical problems (e.g., chronic cough related to smoking) or psychological problems (e.g., excessive sedation and a decrease in goal-oriented activities resulting from repeated use of high doses).

In addition, DHHS states that marijuana use produces acute and chronic adverse effects on the respiratory system, memory and learning. Regular marijuana smoking produces a number of long-term pulmonary consequences, including chronic cough and sputum (Adams and Martin, 1996), and histopathologic abnormalities in bronchial epithelium (Adams and Martin, 1996). DEA also notes studies suggesting marijuana use leads to evidence of widespread airway inflammation and injury (Roth *et al.*, 1998, Fligiel *et al.*, 1997) and immunohistochemical evidence of dysregulated growth of respiratory epithelial cells that may be precursors to lung cancer (Baldwin *et al.*, 1997). In addition, very large epidemiological studies indicate that marijuana may increase risk of psychosis in vulnerable populations, i.e., individuals predisposed to develop psychosis (Andreasson *et al.*, 1987) and exacerbate psychotic symptoms in individuals with schizophrenia (Schiffman *et al.*, 2005; Hall *et al.*, 2004; Mathers and Ghodse, 1992; Thornicroft, 1990; see Factor 2).

The petitioner cited ''The Missoula Chronic Clinical Cannabis Use Study'' as evidence that long-term use of marijuana does not cause significant harm in patients (Russo *et al.*, 2002). DEA notes that this article describes the case histories and clinical examination of only four patients that were receiving marijuana cigarettes from the National Institute on Drug Abuse for a variety of medical conditions. The number of patients included in the study is not adequate for this evaluation.

The petitioner states, ''Studies have shown the long-term use of cannabis to be safe. In contrast to many other medicinal drugs, the long-term use of cannabis does not harm stomach, liver, kidneys and heart.'' (Exh. C, Section II (10), pg. 66).

However, DHHS states that marijuana has not been shown to have an accepted level of safety for medical use. There have been no NDA-quality studies that have scientifically assessed the full safety profile of marijuana for any medical condition. DEA notes in addition, as described above, the risks associated with chronic marijuana use, including, as described in Factor 2, risks for the cardiovascular and respiratory systems, as well as risks for mental health and cognitive function and risks related to prenatal exposure to marijuana.

Marijuana as a ''Gateway Drug''

A number of studies have examined the widely held premise that marijuana use leads to subsequent abuse of other illicit drugs, thus functioning as a ''gateway drug.'' DHHS discussed a 25-year study of 1,256 New Zealand children, Fergusson *et al.* (2005), which concluded that the use of marijuana correlates to an increased risk of abuse of other drugs. Other studies, however, do not support a direct causal relationship between regular marijuana use and other illicit drug abuse. DHHS cited the IOM report (1999), which states that marijuana is a ''gateway drug'' in the sense that its use typically precedes rather than follows initiation of other illicit drug use. However, as cited by DHHS, the IOM states that, ''[t]here is no conclusive evidence that the drug effects of marijuana are causally linked to the subsequent abuse of other illicit drugs.'' DHHS noted that for most studies that test the hypothesis that marijuana causes abuse of harder drugs, the determinative measure for testing this hypothesis is whether marijuana leads to ''any drug use'' rather than that marijuana leads to ''drug abuse and dependence'' as defined by DSM–IV criteria.

FACTOR 7: ITS PSYCHIC OR PHYSIOLOGICAL DEPENDENCE LIABILITY

DHHS states that many medications that are not associated with abuse or addiction, such as antidepressants, beta-blockers, and centrally acting antihypertensive drugs, can produce physical dependence and withdrawal symptoms after chronic use. However, psychological and physical dependence of drugs that have abuse potential are important factors contributing to increased or continued drug taking. This section provides scientific evidence that marijuana causes physical and psychological dependence.

Physiological (Physical) Dependence in Humans

Physical dependence is a state of adaptation manifested by a drug class-specific withdrawal syndrome produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist (American Academy of Pain Medicine, American Pain Society and American Society of Addiction Medicine consensus document, 2001).

DHHS states that long-term, regular use of marijuana can lead to physical dependence and withdrawal following discontinuation as well as psychic addiction or dependence. The marijuana withdrawal syndrome consists of symptoms such as restlessness, irritability, mild agitation, insomnia, EEG disturbances, nausea, cramping and decrease in mood and appetite that may resolve after 4 days, and may require in-hospital treatment (Haney *et al.*, 1999). It is distinct and mild compared to the withdrawal syndromes associated with alcohol and heroin use (Budney *et al.*, 1999; Haney *et al.*, 1999). DEA notes that Budney *et al.* (1999) examined the withdrawal symptomatology in 54 chronic marijuana abusers seeking treatment for their dependence. The majority of the subjects (85 percent) reported that they had experienced symptoms of at least moderate severity. Fifty seven percent (57 percent) reported having six or more symptoms of a least moderate severity while 47 percent experienced four or more symptoms rated as severe. The most reported mood symptoms associated with the

withdrawal were irritability, nervousness, depression, and anger. Some of the other behavioral characteristics of the marijuana withdrawal syndrome were craving, restlessness, sleep disruptions, strange dreams, changes in appetite, and violent outbursts.

DHHS discusses a study by Lane and Phillips-Bute (1998) which describes milder cases of dependence including symptoms that are comparable to those from caffeine withdrawal, including decreased vigor, increased fatigue, sleepiness, headache, and reduced ability to work. The marijuana withdrawal syndrome has been reported in adolescents who were admitted for substance abuse treatment or in individuals who had been given marijuana on a daily basis during research conditions. Withdrawal symptoms can also be induced in animals following administration of a cannabinoid antagonist after chronic Δ^9-THC administration (Maldonado, 2002; Breivogel *et al.*, 2003). DHHS also discusses a study comparing marijuana and tobacco withdrawal symptoms in humans (Vandrey *et al.*, 2005) which demonstrated that the magnitude and time course of the two withdrawal syndromes are similar.

DHHS states that a review by Budney and colleagues (2004) of studies of cannabinoid withdrawal, with a particular emphasis on human studies, led to the recommendation that the Diagnostic and Statistical Manual of Mental Disorders (DSM) introduce a listing for cannabis withdrawal. In this listing, common symptoms would include anger or aggression, decreased appetite or weight loss, irritability, nervousness/anxiety, restlessness and sleep difficulties including strange dreams. Less common symptoms/equivocal symptoms would include chills, depressed mood, stomach pain, shakiness and sweating.

Psychological Dependence in Humans

In addition to physical dependence, DHHS states that long-term, regular use of marijuana can lead to psychic addiction or dependence. Psychological dependence on marijuana is defined by the American Psychiatric Association in the DSM–IV and cited by DHHS.

The Diagnostic and Statistical Manual of Mental Disorders (DSM–IV) is published by the American Psychiatric Association (2000), and provides diagnostic criteria to improve the reliability of diagnostic judgment of mental disorders by mental health professionals. DSM–IV currently defines ''Cannabis Dependence'' (DSM–IV diagnostic category 304.30) as follows:

Cannabis dependence: A destructive pattern of cannabis use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring when the cannabis use was at its worst:

1. Cannabis tolerance, as defined by either of the following:

a. A need for markedly increased amounts of cannabis to achieve intoxication,

b. Markedly diminished effect with continued use of the same amount of cannabis.

2. Greater use of cannabis than intended: Cannabis was often taken in larger amounts or over a longer period than was intended.

3. Unsuccessful efforts to cut down or control cannabis use: Persistent desire or unsuccessful efforts to cut down or control cannabis use.

4. Great deal of time spent in using cannabis, or recovering from hangovers.

5. Cannabis caused reduction in social, occupational or recreational activities: Important social, occupational, or recreational activities given up or reduced because of cannabis use.

6. Continued using cannabis despite knowing it caused significant problems: Cannabis use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been worsened by cannabis.

In addition, the DSM–IV added a specifier to this diagnostic by which it can be with or without physiological (physical) dependence.

DEA notes additional clinical studies showing that frequency of Δ^9-THC use (most often as marijuana) escalates over time. Individuals increase the number, doses, and potency of marijuana cigarettes. Several studies have reported that patterns of marijuana smoking and increased quantity of marijuana smoked were related to social context and drug availability (Kelly *et al.*, 1994; Mendelson and Mello, 1984; Mello, 1989).

DEA further notes that Budney *et al.* (1999) reported that 93 percent of marijuana-dependent adults seeking treatment reported experiencing mild craving for marijuana, and 44 percent rated their past craving as severe. Craving for marijuana has also been documented in marijuana users not seeking treatment (Heishman *et al.*, 2001). Two hundred seventeen marijuana users completed a 47-item Marijuana Craving Questionnaire and forms assessing demographics, drug use history, marijuana-quit attempts and current mood. The results indicate that craving for marijuana was characterized by 1) the inability to control marijuana use (compulsivity); 2) the use of marijuana in anticipation of relief from withdrawal or negative mood (emotionality); 3) anticipation of positive outcomes from smoking marijuana (expectancy); and 4) intention and planning to use marijuana for positive outcomes (purposefulness).

In summary, long-term, regular use of marijuana can lead to physical dependence and withdrawal following discontinuation as well as psychic addiction or dependence.

FACTOR 8: WHETHER THE SUBSTANCE IS AN IMMEDIATE PRECURSOR OF A SUBSTANCE ALREADY CONTROLLED UNDER THE CSA

Marijuana is not an immediate precursor of any controlled substance.

DETERMINATION

After consideration of the eight factors discussed above and of DHHS's recommendation, DEA finds that marijuana meets the three criteria for placing a substance in Schedule I of the CSA under 21 U.S.C. 812(b)(1):

1. Marijuana has a high potential for abuse

Marijuana is the most highly abused and trafficked illicit substance in the United States. Approximately 16.7 million individuals in the United States (6.6 percent of the United States population) used marijuana monthly in 2009. A 2009 national survey that tracks drug use trends among high school students showed that by 12th grade, 32.8 percent of students reported having used marijuana in the past year, 20.6 percent reported using it in the past month, and 5.2 percent reported having used it daily in the past month. Its widespread availability is being fueled by increasing marijuana production domestically and increased trafficking from Mexico and Canada.

Marijuana has dose-dependent reinforcing effects that encourage its abuse. Both clinical and preclinical studies have clearly demonstrated that marijuana and its principle psychoactive constituent, Δ^9-THC, possess the pharmacological attributes associated with drugs of abuse. They function as discriminative stimuli and as positive reinforcers to maintain drug use and drug-seeking behavior.

Significant numbers of chronic users of marijuana seek substance abuse treatment. Compared to all other specific drugs included in the 2008 NSDUH survey, marijuana had the highest levels of past year dependence and abuse.

2. Marijuana has no currently accepted medical use in treatment in the United States

DHHS states that the FDA has not evaluated nor approved an NDA for marijuana. The long-established factors applied by DEA for determining whether a drug has a ''currently accepted medical use'' under the CSA are as follows. A drug will be deemed to have a currently accepted medical use for CSA purposes only if all of the following five elements have been satisfied. As set forth below, none of these elements has been fulfilled:

i. The drug's chemistry must be known and reproducible

Although the structures of many cannabinoids found in marijuana have been characterized, a complete scientific analysis of all the chemical components found in marijuana has not been conducted. Furthermore, many variants of the marijuana plant are found due to its own genetic plasticity and human manipulation.

ii. There must be adequate safety studies

Safety studies for acute or sub-chronic administration of marijuana have been carried out through a limited number of Phase I clinical investigations approved by the FDA, but there have been no NDA-quality studies that have scientifically assessed the full safety profile of marijuana for any medical condition. Large, controlled studies have not been conducted to evaluate the risk-benefit ratio of marijuana use, and any potential benefits attributed to marijuana use currently do not outweigh the known risks.

iii. There must be adequate and well-controlled studies proving efficacy

DHHS states that there have been no NDA-quality studies that have scientifically assessed the efficacy of marijuana for any medical condition. To establish accepted medical use, the effectiveness of a drug must be established in well-controlled, well-

designed, well-conducted, and well-documented scientific studies, including studies performed in a large number of patients. To date, such studies have not been performed for any indications.

Small clinical trial studies with limited patients and short duration are not sufficient to establish medical utility. Studies of longer duration are needed to fully characterize the drug's efficacy and safety profile. Scientific reliability must be established in multiple clinical studies. Anecdotal reports and isolated case reports are not sufficient evidence to support an accepted medical use of marijuana. The evidence from clinical research and reviews of earlier clinical research does not meet the requisite standards.

iv. The drug must be accepted by qualified experts

At this time, it is clear that there is no consensus of opinion among experts concerning medical applications of marijuana. To date, research on the medical use of marijuana has not progressed to the point that marijuana can be considered to have a ''currently accepted medical use'' or a ''currently accepted medical use with severe restrictions.

v. The scientific evidence must be widely available

DHHS states that the scientific evidence regarding the safety and efficacy of marijuana is typically available only in summarized form, such as in a paper published in the medical literature, rather than in a raw data format. In addition, as noted, there have only been a limited number of small clinical trials and no controlled, large scale, clinical trials have been conducted with marijuana on its efficacy for any indications or its safety.

3. There is a lack of accepted safety for use of marijuana under medical supervision

At present, there are no FDA-approved marijuana products, nor is marijuana under NDA evaluation at the FDA for any indication. Marijuana does not have a currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions. The Center for Medicinal Cannabis Research in California, among others, is conducting research with marijuana at the IND level, but these studies have not yet progressed to the stage of submitting an NDA. Current data suggest that marijuana use produces adverse effects on the respiratory system, memory and learning. Marijuana use is associated with dependence and addiction. In addition, very large epidemiological studies indicate that marijuana use may be a causal factor for the development of psychosis in individuals predisposed to develop psychosis and may exacerbate psychotic symptoms in individuals with schizophrenia. Thus, at this time, the known risks of marijuana use have not been shown to be outweighed by specific benefits in well-controlled clinical trials that scientifically evaluate safety and efficacy. In sum, at present, marijuana lacks an acceptable level of safety even under medical supervision.

REFERENCES

Abrams, D.I., Hilton, J.F., Leiser, R.J., Shade, S.B., Elbeik, T.A., Aweeka, F.T., Benowitz, N.L., Bredt, B.M., Kosel, B., Aberg, J.A., Deeks, S.G., Mitchell, T.F., Mulligan, K., Bacchetti, P., McCune, J.M., and Schambelan, M. (2003). Short-term effects of cannabinoids in patients with HIV–1 infection: a randomized, placebo-controlled clinical trial. *Annals of Internal Medicine*. 139(4):258–266.

Adams, I.B. and Martin, B.R. (1996). Cannabis: Pharmacology and toxicology in animals and humans. *Addiction*. 91:1585–1614.

Agurell, S., Dewey, W., and Willett, R.E., eds. (1984). The Cannabinoids: Chemical, Pharmacologic, and Therapeutic Aspects. New York: Academic Press.

Agurell, S., Halldin, M., Lindgren, J.E., Ohlsson, A., Widman, M., Gillespie, H., and Hollister, L. (1986). Pharmacokinetics and metabolism of delta-1-tetrahydrocannabinol and other cannabinoids with an emphasis on man. *Pharmacological Reviews*. 38(1):21–43.

Aldington S, Harwood M, Cox B, Weatherall M, Beckert L, Hansell A, Pritchard A, Robinson G, Beasley R; Cannabis and Respiratory Disease Research Group (2008). Cannabis use and risk of lung cancer: a case-control study. *European Respiratory Journal*. 31(2):280–6.

Ameri, A. The effects of cannabinoids on the brain. *Progress in Neurobiology*. 1999: 58 (4): 315–348.

Andreasson, S., Allebeck, P., Engström, A., and Rydberg, U. (1987). Cannabis and schizophrenia: A longitudinal study of Swedish conscripts. *Lancet*. 1: 483–1483.

Arseneault, L., Cannon, M., Poulton, R., Murray R., Caspi. A., and Moffitt, T.E. (2002). Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. *British Medical Journal*. 325 (7374):1212–1213.

Azorlosa, J., Heishman, S., Stitzer, M., and Mahaffey, J.M. (1992). Marijuana smoking: effect of varying delta-9-tetrahydrocannabinol content and number of puffs. Journal of *Pharmacology and Experimental Therapeutics*. 261:114–122.

Baldwin, G.C., Tashkin, D.P., Buckley, D.M., Park, A.N., Dubinett, S.M., and Roth, M.D. (1997). Marijuana and cocaine impair alveolar macrophage function and cytokine production. *American Journal of Respiratory and Critical Care Medicine*. 156:1606–1613.

Balster, R.L. and Prescott, W.R. (1992). Δ9-tetrahydrocannabinol discrimination in rats as a model for cannabis intoxication. *Neuroscience and Biobehavioral Reviews*. 16: 55–62.

Barrett, R.L., Wiley, J.L., Balster, R.L. and Martin, B.R. (1995). Pharmacological specificity of Δ9-tetrahydrocannabinol discrimination in rats. *Psychopharmacology*. 118: 419–424.

Bedard, M., Dubois, S., Weaver, B. (2007). The impact of cannabis on driving. *Canadian Journal of Public Health*. 98(1):6–11.

Benowitz, N.L. and Jones, R T. (1975). Cardiovascular effects of prolonged delta-tetrahydrocannabinol ingestion. *Clinical Pharmacology and Therapeutics*. 18(3): 287–97,

Benowitz, N.L. and Jones, R T. (1981). Cardiovascular and metabolic considerations in prolonged cannabinoid administration in man. *Journal of Clinical Pharmacology*. 21 (8–9 Supp): 214S–223S.

Block, R.I. and Wittenborn, J.R. (1985). Marijuana effects on associative processes. *Psychopharmacology (Berl)*. 85(4):426–430.

Block, R.I., Farinpour, R., and Braverman, K. (1992). Acute effects of marijuana on cognition: relationships to chronic effects and smoking techniques. *Pharmacology, Biochemistry and Behavior*. 43(3):907–917.

Block, R.I., Farinpour, R., and Schlechte, J.A. (1991). Effects of chronic marijuana use on testosterone, luteinizing hormone, follicle stimulating hormone, prolactin and cortisol in men and women. *Drug and Alcohol Dependence*. 28(2):121–128.

Bolla, K.I., Brown, K., Eldreth, D., Tate, K., and Cadet, J.L. (2002). Dose-related neurocognitive effects of marijuana use. *Neurology*. 59:1337–1343.

Bolla, K.I., Eldreth, D.A., Matochik, J.A., and Cadet, J.L. (2005). Neural substrates of faulty decision-making in abstinent marijuana users. *NeuroImage*. 26:480–492.

Bouaboula, M., Rinaldi, M., Carayon, P., Carillon, C., Delpech, B., Shire, D., Le Fur, G., and Casellas, P.(1993). Cannabinoid-receptor expression in human leukocytes. *European Journal of Biochemistry*. 214(1):173–180.

Braida, D., Iosue, S., Pegorini, S., and Sala, M. (2004). Delta9-tetrahydrocannabinol-induced conditioned place preference and intracerebroventricular self-administration in rats. *European Journal of Pharmacology*. 506(1):63–69.

Breivogel, C.S. and Childers, S.R. (2000). Cannabinoid agonist signal transduction in rat brain: comparison of cannabinoid agonists in receptor binding, G-protein activation, and adenylate cyclase inhibition. *Journal of Pharmacology and Experimental Therapeutics*. 295(1):328–336.

Breivogel, C.S., Griffin, G., Di Marzo, V., Martin, B.R. (2001). Evidence for a new G protein-coupled cannabinoid receptor in mouse brain. *Molecular Pharmacology*. 60(1):155–63.

Breivogel, C.S., Scates, S.M., Beletskaya, I.O., Lowery, O.B., Aceto, M.D., and Martin, B.R. (2003). The effects of delta9-tetrahydrocannabinol physical dependence on brain cannabinoid receptors. *European Journal of Pharmacology*. 459(2–3):139–150.

Browne, R.G., and Weissman, A. (1981). Discriminative stimulus properties of Δ9-tetrahydrocannabinol: Mechanistic studies. *Journal of Clinical Pharmacology*. 21: 227S–234S.

Budney, A.J., Hughes, J.R., Moore, B.A., and Vandrey, R. (2004). Review of the validity and significance of cannabis withdrawal syndrome. *American Journal of Psychiatry*. 161(11):1967–1977.

Budney, A.J., Novy, P.L., and Hughes, J.R. (1999). Marijuana withdrawal among adults seeking treatment for marijuana dependence. *Addiction*. 94:1311–1322.

Cabral, G.A. and Dove-Pettit, D.A. (1998). Drugs and immunity: cannabinoids and

their role in decreased resistance to infectious disease. *Journal of Neuroimmunology*. 83(1–2):116–123.
Cabral, G.A. and Staab, A. (2005). Effects on the immune system. *Handbook of Experimental Pharmacology*. 168:385–423.
Capriotti, RM., Foltin, R.W., Brady, J.V. and Fischman, M.W. (1988). Effects of marijuana on the task elicited physiological response. *Drug and Alcohol Dependence*. 21(3): 183–7.
Caspi, A., Moffitt, T.E., Cannon, M., McClay, J., Murray, R., Harrington, H., Taylor, A., Arseneault, L., Williams, B., Braithwaite, A., Poulton, R., and Craig, I.W. (2005). Moderation of the effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the catechol-O-methyltransferase gene: longitudinal evidence of a gene X environment interaction. *Biological Psychiatry*. 57(10):1117–1127.
Centers for Disease Control (CDC). (1981). Salmonellosis traced to marijuana—Ohio, Michigan. *Morbidity and Mortality Weekly Report*. 30(7):77–9.
Chait L.D. and Burke, K.A. (1994). Preference for ''high'' versus low-potency marijuana. *Pharmacology, Biochemistry, and Behavior*. 49:643–646.
Chait, L.D. and Pierri, J. (1992). Effects of smoked marijuana on human performance. *In: Marijuana/Cannabinoids. Neurobiology and Neurophysiology*. Murphy, L., and Bartke, A. (Eds). CRC Press, Boca Raton, FL. Pp. 387–423.
Chait, L.D. and Zacny, J.P. (1992). Reinforcing and subjective effects of oral Δ^9-THC and smoked marijuana in humans. *Psychopharmacology*. 107:255–262.
Chait, L.D., Evans, S.M., Grant, K.A., Kamien, J.B., Johanson, C.E., and Schuster, C.R. (1988). Discriminative stimulus and subjective effects of smoked marijuana in humans. *Psychopharmacology*. 94: 206–212.
Charuvastra, A., Friedmann, P.D., Stein, M.D. (2005). Physician attitudes regarding the prescription of medical marijuana. *Journal of Addiction Diseases*. 24(3):87–93.
Cocchetto, D.M., Owens, S.M., Perez-Reyes, M., DiGuiseppi, S., and Miller, L.L. (1981). Relationship between delta-9-tetrahydrocannabinol concentration and pharmacologic effects in man. *Psychopharmacology*. 75:158–164.
Collins, R.J., Weeks, J.R., Cooper, M.M., Good, P.I., and Russell, R.R. (1984). Prediction of abuse liability of drugs using IV self-administration by rats. *Psychopharmacology*, 82: 6–13.
Cone, E.J., Johnson, R.E., Moore, J.D., and Roache, J.D. (1986). Acute effects of smoking marijuana on hormones, subjective effects and performance in male human subjects. *Pharmacology, Biochemistry and Behavior*. 24(6):1749–1754.
Cone, E.J., Johnson, R.E., Paul, B.D., Mell, L.D., and Mitchell, J. (1988). Marijuana-laced brownies: Behavioral effects, physiological effects and urinalysis in humans following ingestion. *Journal of Analytical Toxicology*. 12:169–175.
Crider, R. (1986). Phencyclidine: changing abuse patterns. *NIDA Research Monograph*. 64:163–173.
Croxford, J.L. and Yamamura, T. (2005). Cannabinoids and the immune system: potential for the treatment of inflammatory diseases? *Journal of Neuroimmunology*. 166(1–2): 3–18.
Dax, E.M., Pilotte, N.S., Adler, W.H., Nagel, J.E., and Lange, W.R. (1989). The effects of 9-ene-tetrahydrocannabinol on hormone release and immune function. *Journal of Steroid Biochemistry*. 34:263–70.
Degenhardt, L., Hall, W., Lynskey, M. (2003). Testing hypotheses about the relationship between cannabis use and psychosis. *Drug and Alcohol Dependence*. 71(1): 37–48.
Department of Health and Human Services (2006). Basis For The Recommendation For Maintaining Marijuana In Schedule I Of The Controlled Substances Act.
Department of Health and Human Services. Announcement of the Department of Health and Human Services Guidance on Procedures for the Provision of Marijuana for Medical Research. May 21, 1999. (*http://grants.nih.gov/grants/guide/notice-files/not99-091.html*).
Dewey, W.L., Martin, B.R., and May, E.L. (1984). Cannabinoid stereoisomers: pharmacological effects. In Smith, D.F. (Ed.) CRC Handbook of Stereoisomers: Drugs in Psychopharmacology, 317–326 (Boca Raton, FL, CRC Press).
Ehrenreich, H., Rinn, T., Kunert, H.J., Moeller, M.R., Poser, W., Schilling, L., Gigerenzer, G., and Hoehe, M.R. (1999). Specific attentional dysfunction in adults following early start of cannabis use. *Psychopharmacology (Berl)*. 142(3):295–301.
Eldridge, J.C., Murphy, L.L., and Landfield, P.W. (1991). Cannabinoids and the hippocampal glucocorticoid receptor: recent findings and possible significance. *Steroids*. 56(5): 226–231.
Fant, R.V., Heishman, S.J., Bunker, E.B., and Pickworth, W.B. (1998). Acute and residual effects of marijuana in humans. *Pharmacology Biochemistry and Behavior*. 60(4):777–784.
Felder, C.C., Joyce, K.E., Briley, E.M., Glass, M., Mackie, K.P., Fahey, K.J., Cullinan, G.J., Hunden, D.C., Johnson, D.W., Chaney, M.O., Koppel, G.A. and Brownstein, M. (1998). LY320135, a novel cannabinoid CB1 receptor antagonist, unmasks coupling of the CB1 receptor to stimulation of cAMP accumulation. *Journal of Pharmacology and Experimental Therapeutics*. 284: 291–297
Fergusson, D.M., Horwood, L.J., and Ridder, E.M. (2005). Tests of causal linkages between cannabis use and psychotic symptoms. *Addiction*. 100(3):354–366.
Fergusson, D.M., Poulton, R., Smith, P.F., Boden, J.M. (2006). Cannabis and psychosis. *British Medical Journal*. 332(7534):172–5.
Fligiel, S.E., Roth, M.D., Kleerup, E.C., Barsky, S.H., Simmons, M., and Tashkin, D.P. (1997). Tracheobronchial histopathology in habitual smokers of cocaine, marijuana, and/or tobacco. Chest. 112:319–326.
Foltin, R.W., Fischman M.W., Brady J.V., Bernstein D.J., Capriotti, R.M., Nellis, M.J., and Kelly, T.H. (1990). Motivational effects of smoked marijuana: behavioral contingencies and low probability activities. *Journal of the Experiment Analysis of Behavior*. 53:5–19.
Fried, P. A. and Watkinson, B. (1990). 36- and 48-month neurobehavioral follow-up of children prenatally exposed to marijuana, cigarettes and alcohol. *Journal of Developmental and Behavioral Pediatrics*. 11:49–58.
Fried, P. A., Watkinson, B., and Gray, R. (1992). A follow-up study of attentional behavior in 6-year-old children exposed prenatally to marihuana, cigarettes and alcohol. *Neurotoxicology and Teratology*. 14:299–311.
Fried, P. A., Watkinson, B., Gray, R. (1998). Differential effects on cognitive functioning in 9- to 12-year olds prenatally exposed to cigarettes and marihuana. *Neurotoxicology and Teratology*. 20(3):293–306.
Fried, P., Watkinson, B., James, D., and Gray, R. (2002). Current and former marijuana use: preliminary findings of a longitudinal study of effects on IQ in young adults. *Canadian Medical Association Journal*. 166(7):887–891.
Fung, M., Gallagher, C., and Machtay, M. (1999). Lung and aeo-digestive cancers in young marijuana smokers. *Tumori*. 85 (2): 140–142.
Galiegue, S., Mary, S., Marchand, J., Dussossoy, D., Carriere, D., Carayon, P., Bouaboula, M., Shire, D., Le Fur, G., and Casellas, P. (1995). Expression of central and peripheral cannabinoid receptors in human immune tissues and leukocyte subpopulations. *European Journal of Biochemistry*. 232(1):54–61.
Gerard, C.M., Mollereau, C., Vassart, G., and Parmentier, M. (1991). Molecular cloning of a human cannabinoid receptor which is also expressed in testis. *Biochemistry Journal*. 279:129–134.
Glass, M. and Felder, C.C. (1997). Concurrent stimulation of cannabinoid CB1 and dopamine D2 receptors augments cAMP accumulation in striatal neurons: Evidence for a Gs linkage to the CB1 receptor. *Journal of Neuroscience*. 17: 5327–5333
Gold, L.H., Balster, R.L., Barrett, R.L., Britt, D.T., and Martin, B.R. (1992). A comparison of the discriminative stimulus properties of delta 9-tetrahydrocannabinol and CP 55,940 in rats and rhesus monkeys. *Journal of Pharmacology and Experimental Therapeutics*. 262(2):479–486.
Gong, H. Jr., Tashkin, D.P., Simmons, M.S., Calvarese, B., and Shapiro, B.J. (1984). Acute and subacute bronchial effects of oral cannabinoids. *Clinical Pharmacalology and Therapeutics*. 35(1): 26–32.
Gong, J.P., Onaivi, E.S., Ishiguro, H., Liu, Q.R., Tagliaferro, P.A., Brusco, A., and Uhl, G.R. (2006). Cannabinoid CB2 receptors: Immunohistochemical localization in rat brain. *Brain Research*. 1071(1):10–23.
Gonsiorek, W., Lunn, C., Fan, X., Narula, S., Lundell, D., and Hipkin, R.W. (2000). Endocannabinoid 2-arachidonyl glycerol is a full agonist through human type 2 cannabinoid receptor: antagonism by anandamide. *Molecular Pharmacology*. 57(5): 1045–1050
Graham, J.D.P., ed. (1976). Cannabis and Health. New York: Academic Press. Green,

B., Young, R., and Kavanagh, D. (2005). Cannabis use and misuse prevalence among people with psychosis. *British Journal of Psychiatry.* 187:306–313.
Griffith, D.R., Azuma, S.D., and Chasnoff, I.J. (1994). Three-year outcome of children exposed prenatally to drugs. *Journal of the American Academy of Child and Adolescent Psychiatry.* 33:20–27.
Griffiths, R.R., Bigelow, G.E. and Henningfield, J.E. (1980). Similarities in animal and human drug-taking behavior. In: ''Advances in substance abuse, vol 1''. (Ed. N.K. Mello). pp. 1–90. JAI Press, Greenwich, CT.
Grotenhermen, F. (2003). Pharmacokinetics and pharmacodynamics of cannabinoids. *Clinical Pharmacokinetics.* 42(4):327–60
Hall, W., Degenhardt, L., Teesson, M. (2004). Cannabis use and psychotic disorders: an update. *Drug and Alcohol Reviews.* 23(4):433–43.
Haney, M., Ward, A.S., Comer, S.D., Foltin, R.W., and Fischman, M.W. (1999). Abstinence symptoms following smoked marijuana in humans. *Psychopharmacology.* 141:395–404.
Hanus, L. and Subivá, D. (1989). The amount of main cannabinoid substances in hemp cultivated for industrial fibre production and their changes in the course of one vegetation period. *Acta Universitatis Palackianae Olomucensis Facultatis Medicae.* 122:11–23.
Hanus, L., Breuer, A., Tchilibon, S., Shiloah, S., Goldenberg, D., Horowitz, M., Pertwee, R.G., Roos, R.A., Mechoulam, R., and Fride, E. (1999). HU–308: a specific agonist for CB (2), a peripheral Cannabinoid receptor. *Proceedings of the National Academy of Science.* 96:14228–14233.
Hanus, L., Yoshida, T., and Kreji. (1975). Production of Δ^9-tetrahydrocannabinol from hemp cultivated in climatic conditions of Czechoslovakia. *Acta Universitatis Palackianae Olomucensis Facultatis Medicae.* 74:173–180.
Harder, S. and Rietbrock, S. (1997). Concentration-effect relationship of delta-9-tetrahydrocannabinol and prediction of psychotropic effects after smoking marijuana. *International Journal of Clinical Pharmacology and Therapeutics.* 35(4):155–159.
Heishman, S.J., Huestis, M.A., Henningfield, J.E., and Cone, E.J. (1990). Acute and residual effects of marijuana: profiles of plasma THC levels, physiological, subjective, and performance measures. *Pharmacology, Biochemistry and Behavior.* 37(3):561–565.
Heishman, S.J., Singleton, E.G., and Ligouri, A. (2001). Marijuana craving questionnaire: development and initial validation of a self-report instrument. *Addiction.* 96(7):1023–1034.
Heishman, S.J., Stitzer, M.L., and Bigelow, G.E. (1988). Alcohol and marijuana: Comparative dose effect profiles in humans. *Pharmacology, Biochemistry and Behavior.* 31:649–655.
Henquet, C., Krabbendam, L., Spauwen, J., Kaplan, C., Lieb, R., Wittchen, H.U., and van Os, J. (2005). Prospective cohort study of cannabis use, predisposition for psychosis, and psychotic symptoms in young people. *British Medical Journal.* 330(7481):11.
Herkenham, M. (1992). Cannabinoid receptor localization in brain: Relationship to motor and reward systems. *Annals of the New York Academy of Sciences.* 654:19–32.
Herkenham, M., Lynn, A. B., Little, M. D., Johnson, M. R., Melvin, L. S., de Costa, B. R., and Rice, K. C. (1990). Cannabinoid receptor localization in Brain. *Proceedings of the National Academy of Sciences USA.* 87:1932–1936.
Hollister, L.E. (1986). Health aspects of cannabis. *Pharmacological Reviews.* 3:1–20.
Hollister, L.E. (1988). Cannabis—1988 (Literature Review). *Acta Psychiatrica Scandinavica.* 78:108–118.
Howlett, A.C., Breivogel, C.S., Childers, S.R., Deadwyler, S.A., Hampson, R.E., and Porrino, L.J. (2004). Cannabinoid physiology and pharmacology: 30 years of progress. *Neuropharmacology.* 47 (Suppl 1):345–358.
Idanpaan-Heikkila, J., Fritchie, G.E., Englert, L.F., Ho, B.T. and McIsaac, W.M. (1969). Placental transfer of tritiated-1-delta-9-tetrhydrocannabinol. *New England Journal of Medicine.* 281(6):330.
Institute of Medicine, Division of Neuroscience and Behavioral Health. (1999). Marijuana and Medicine: Assessing the Science Base. National Academy Press. Washington D.C.
Järbe, T.U., Lamb, R.J., Lin, S., and Makriyannis, A. (2001). (R)-methandamide and delta-9–THC as discriminative stimuli in rats: tests with the cannabinoid antagonist SR–141716 and the endogenous ligand anandamide. *Psychopharmacology.* 156(4):369–380.
Johanson, C.E. and Balster, R.L. (1978). A summary of the results of a drug self-administration study using substitution procedures in rhesus monkeys. *Bulletin of Narcotics,* 30:43–54.
Jones, R.T. (1980). Human Effects: An Overview. In *NIDA Research Monograph 31, Marijuana Research Findings:* 1980. 31:54–80.
Jones, R.T. (2002). Cardiovascular system effects of marijuana. *The Journal of Clinical Pharmacology.* 42:58S–63S.
Justinova, Z., Goldberg, S.R., Heishman, S.J., Tanda, G. (2005). Self-administration of cannabinoids by experimental animals and human marijuana smokers. *Pharmacology Biochemistry and Behavior.* 81(2):285–99.
Justinova, Z., Munzar, P., Panlilio, L.V., Yasar, S., Redhi, G.H., Tanda, G., Goldberg, S.R. (2008). Blockade of THC-seeking behavior and relapse in monkeys by the cannabinoid CB(1)-receptor antagonist rimonabant. *Neuropsychopharmacology.* 33(12):2870–7.
Justinova, Z., Tanda, G., Munzar, P., Goldberg, S.R. (2004). The opioid antagonist naltrexone reduces the reinforcing effects of Delta 9 tetrahydrocannabinol (THC) in squirrel monkeys. *Psychopharmacology* (Berl). 173(1–2):186–94.
Justinova, Z., Tanda, G., Redhi, G.H., and Goldberg, S.R. (2003). Self-administration of delta9-tetrahydrocannabinol (THC) by drug naive squirrel monkeys. *Psychopharmacology.* 169(2):135–140.
Kagen, S.L., Kurup, V.P., Sohnle, P.G., Fink, J.N. (1983). Marijuana smoking and fungal sensitization. *The Journal of Allergy and Clinical Immunology.* 71(4):389–93.
Kamien, J.B., Bickel, W.K., Higgins, S.T., and Hughes, J.R. (1994). The effects of Δ9-tetrahydrocannabinol on repeated acquisition and performance of response sequences and on self-reports in humans. *Behavioural Pharmacology.* 5: 71–78.
Kandel, D.B. and Chen, K. (2000). Types of marijuana users by longitudinal course. *Journal on Studies on Alcohol.* 61(3): 367–378.
Kelly, T.H., Foltin, R.W., and Fischman, M.W. (1993). Effects of smoked marijuana on heart rate, drug ratings and task performance by humans. *Behavioural Pharmacology.* 4:167–178.
Kelly, T.H., Foltin, R.W., Mayr, M.T., and Fischman, M.W. (1994). Effects of Δ9-tetrahydrocannabinol and social context on marijuana self-administration by humans. *Pharmacology, Biochemistry and Behavior.* 49:763–768.
Kirk, J.M. and de Wit, H. (1999). Responses to oral delta9-tetrahydrocannabinol in frequent and infrequent marijuana users. *Pharmacology, Biochemistry and Behavior.* 63(1):137–142.
Klein, T.W., Lane, B., Newton, C.A. and Friedman, H. (2000). The cannabinoid system and cytokine network. *Proceedings of the Society for Experimental Biology and Medicine.* 225(1):1–8.
Kurup, V.P., Resnick, A., Kagen, S.L., Cohen, S.H., Fink, J.N. (1983). Allergenic fungi and actinomycetes in smoking materials and their health implications. *Mycopathologia.* 82(1):61–4.
Kurzthaler, I., Hummer, M., Miller, C., Spemer-Unterweger, R, Gunther, V., Wechdom, H., Battista, H.J., and Fleischhacker, W.W. (1999). Effect of cannabis use on cognitive functions and driving ability. *Journal of Clinical Psychiatry.* 60(6): 395–9.
Lane, J.D. and Phillips-Bute, R.G. (1998). Caffeine deprivation affects vigilance performance and mood. *Physiology and Behaviour,* 65: 171–5.
Lemberger, L., Crabtree, R.E., and Rowe, H.M. (1972). 11-hydroxy-9-tetrahydrocannabinol: pharmacology, disposition, and metabolism of a major metabolite of marihuana in man. *Science.* 177(43):62–64.
Liguori, A., Gatto, C.P., and Robinson, J.H. (1998). Effects of marijuana on equilibrium, psychomotor performance, and simulated driving. *Behavioral Pharmacology.* 9(7):599–609.
Lile, J.A. (2006). Pharmacological determinants of the reinforcing effects of psychostimulants: relation to agonist substitution treatment. *Experimental Clinical Psychopharmacology.* 14(1):20–33.
Lukas, S.E., Mendelson, J.H., and Benedikt, R. (1995). Electroencephalographic correlates of marijuana-induced euphoria. *Drug and Alcohol Dependence.* 37:131–140.
Lyketsos, C.G., Garrett, E., Liang, K.Y., and Anthony, J.C. (1999). Cannabis use and cognitive decline in persons under 65 years of age. *American Journal of Epidemiology.* 149(9):794–800.

Lyons, M.J., Bar, J.L., Panizzon, M.S., Toomey, R., Eisen, S., Xian, H., and Tsuang, M.T. (2004). Neuropsychological consequences of regular marijuana use: a twin study. *Psychological Medicine*. 34(7):1239–1250.

Mackie, K., Lai, Y., Westenbroek, R., and Mitchell, R. (1995). Cannabinoids activate an inwardly rectifying potassium conductance and inhibit Q-type calcium currents in AtT20 cells transfected with rat brain cannabinoid receptor. *Journal of Neuroscience*. 15(10):6552–6561.

Maldonado, R. (2002). Study of cannabinoid dependence in animals. *Pharmacology and Therapeutics*. 95(2):153–64.

Maneuf, Y.P., and Brotchie, J.M. (1997). Paradoxical action of the cannabinoid WIN 55212–2 in stimulated and basal cyclic AMP accumulation in rat globus pallidus slices. *British Journal of Pharmacology*. 120: 1397–1398.

Mansbach, R.S., Rovetti, C.C., Winston, E.N., and Lowe J.A. (1996). Effects of the cannabinoid CB1 receptor antagonist SE14176A on the behavior of pigeons and rats. *Psychopharmacology*. 124(4):315–322.

Martellotta, M.C., Cossu, G., Fattore, L., Gessa, G.L., and Fratta, W. (1998). Self-administration of the cannabinoid receptor agonist WIN 55,212–2 in drug-naive mice. *Neuroscience*. 85(2):327–330.

Martin, B.R. and Hall, W. (1997, 1998). The health effects of cannabis: key issues of policy relevance. *Bulletin on Narcotics* XLIX & L (1 &2): 85–116.

Martin, B.R., Mechoulam, R., and Razdan, R.K. (1999). Discovery and characterization of endogenous cannabinoids. *Life Science*. 65:573–595.

Mathers, D.C., Ghodse, A.H. (1992). Cannabis and psychotic illness. *British Journal of Psychiatry*. 61:648–53.

Mathew, R.J., Wilson, W.H., Davis, R. (2003). Postural syncope after marijuana: a transcranial Doppler study of the hemodynamics. *Pharmacology, Biochemistry and Behavior*. 75:309–318.

Matsuda, L. A., Lolait, S. J., Brownstein, M. J., Young, A. C., and Bonner, T.I. (1990). Structure of a cannabinoid receptor and functional expression of the cloned cDNA. *Nature*. 346:561–564.

McGrath, J., Welham, J., Scott, J., Varghese, D., Degenhardt, L., Hayatbakhsh, M.R., Alati, R., Williams, G.M., Bor, W., Najman, J.M. (2010). Association between cannabis use and psychosis-related outcomes using sibling pair analysis in a cohort of young adults. *Archives of General Psychiatry*. 67(5):440–7

McLaren, J., Swift, W., Dillon, P., Allsop, S. (2008). Cannabis potency and contamination: a review of the literature. *Addiction*. 103(7):1100–9.

McPartland, J.M. (1994). Microbiological contaminants of marijuana. *Journal of the International Hemp Association*. 1: 41–44.

McPartland, J.M. (2002). Contaminants and adulterants in herbal cannabis. In In: Grotenhermen F, Russo E, editors. Cannabis and cannabinoids. Pharmacology, toxicology, and therapeutic potential. Binghamton (NY): Haworth Press.

Mechoulam, R. (1973). Marijuana: Chemistry, pharmacology, metabolism, and clinical effects. NY: Academic Press.

Medina, K.L., Hanson, K.L., Schweinsburg, A.D., Cohen-Zion, M., Nagel, B.J., Tapert, S.F. (2007). Neuropsychological functioning in adolescent marijuana users: subtle deficits detectable after a month of abstinence. *Journal of the International Neuropsychology Society*. 13(5):807–20.

Mello, N. K. (1983). A behavioral analysis of the reinforcing properties of alcohol and other drugs in man. In B. Kissin & H. Begleiter (Eds.), The pathogenesis of alcoholism, biological factors (Vol. 7, pp. 133–198). New York: Plenum Press.

Mello, N.K. (1989). Drug self-administration procedures: Alcohol and marijuana. In NIDA Research Monograph 92: *Testing for Abuse Liability of Drugs in Humans*. 92:147–170.

Mendelson, J.H. and Mello, N.K. (1984). Reinforcing properties of oral Δ^9-tetrahydrocannabinol, smoked marijuana and nabilone: Influence of previous marijuana use. *Psychopharmacology*. 83:351–356.

Messinis, L., Kyprianidou, A., Malefaki, S., and Papathanasopoulos, P. (2006). Neuropsychological deficits in long-term frequent cannabis users. *Neurology*. 66: 737–739.

Moore, T.H., Zammit, S., Lingford-Hughes, A., Barnes, T.R., Jones, P.B., Burke, M., Lewis, G. (2007). Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. *Lancet*. 370(9584):319–28.

Murray, J.E., Bevins, R.A. (2010). Cannabinoid conditioned reward and aversion: behavioral and neural processes. *ACS Chemical Neuroscience*. 1(4):265–278.

National Institutes of Health (NIH). Workshop on the medical Utility of Marijuana, February 19–20, 1997. (www.nih.gov/news/medmarijuana/MedicalMarijuana.htm)

Paris, M. and Nahas, G.G. (1984). Botany: the unstabilized species. In: Nahas G.G. (Ed.) Marihuana in science and medicine. NY: Raven Press, pp. 3–36.

Perez-Reyes, M., Simmons, J., Brine, D., Kiel, G.L., Davis, K.H., Wall, M.E. (1976). Rate of penetration of delta-tetrahydrocannabinol to the brain of mice. In: Nahas G, Paton WDM, Idänpään-Heikkilä JE (Eds), Marihuana: Chemistry, biochemistry, and cellular effects. Springer-Verlag: New York, pp 179–185.

Perez-Reyes, M., Timmons, M.C., Lipton, M.A., Davis, K.H., and Wall, M.E. (1972). Intravenous injection in man of 9-tetrahydrocannabinol and 11-OH-9-tetrahydrocannabinol. *Science*. 177(49):633–635.

Pério, A., Rinaldi-Carmona, M., Maruani, J., Barth, F., LeFur, G., and Soubrié, P. (1996). Central mediation of the cannabinoid cue: activity of a selective CB1 antagonist, SR 141716A. *Behavioural Pharmacology*. 7: 65–71.

Piomelli, D. (2005). The endocannabinoid system: a drug discovery perspective. *Current Opinion in Investigational Drugs*. 6(7): 672–9.

Pope, G.H. Jr., Gruber, A.J., Hudson, J.I., Huestis, M.A., and Yurgelun-Todd, D. (2002). Cognitive measures in long-term cannabis users. *Journal of Clinical Pharmacology*. 42(11 Suppl):41S–47S.

Pope, G.H. Jr., Gruber, A.J., Hudson, J.I., Cohane, G., Huestis, M.A., and Yurgelun-Todd, D. (2003). Early-onset cannabis use and cognitive deficits: what is the nature of the association? *Drug and Alcohol Dependence*. 69(3):303–310.

Ramaekers, J.G., Berghaus, G., van Laar, M., Drummer, O.H. (2004). Dose related risk of motor vehicle crashes after cannabis use. *Drug and Alcohol Dependence*. 73(2):109–119.

Regier, D.A., Farmer, M.E., Rae, D.S., Locke, B.Z., Keith, S.J., Judd, L.L., and Goodwin, F.K. (1990). Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. *Journal of the American Medical Association*. 264(19):2511–2518.

Robbe, H.W.J., and O'Hanlon, J.F., (1999). Marijuana, alcohol and actual driving performance. Dot HS 808 939. US Department of Transportation National Highway Traffic Safety Administration, Maastrict, The Netherlands.

Ross, S.A. and El Sohly, M.A. (1995). Constituents of Cannabis Sativa L. A review of the natural constituents: 1980–1994. *Zagazig Journal of Pharmaceutical Sciences*. 4 (2):1–10.

Roth, M.D., Arora, A., Barsky, S.H., Kleerup, E.C., Simmons, M. and Tashkin, D.P. (1998). Airway inflammation in young marijuana and tobacco smokers. *American Journal of Respiratory and Critical Care Medicine*. 157:928–937.

Roth, M.D., Tashkin, D.P., Whittaker, K.M., Choi, R., and Baldwin, G.C. (2005). Tetrahydrocannabinol suppresses immune function and enhances HIV replication in the huPBL–SCID mouse. *Life Science*. 77(14):1711–22.

Russo, E., Mathre, M.L., Byrne, A., Velin, R., Bach, P.J., Sanchez-Ramos, J., Kirlin, K.A. (2002). Chronic Cannabis Use in the Compassionate Investigational New Drug Program: An Examination of Benefits and Adverse Effects of Legal Clinical Cannabis. *Journal of Cannabis Therapeutics*. 2(1):3–58.

Sarfaraz, S., Afaq, F., Adhami, V.M., Mukhtar, H. (2005). Cannabinoid receptor as a novel target for the treatment of prostate cancer. *Cancer Research*. 65(5):1635–41.

Schiffman, J., Nakamura, B., Earleywine, M., LaBrie, J. (2005). Symptoms of schizotypy precede cannabis use. *Psychiatry Research*. 134(1):37–42.

Schuster, C.R. and Thompson, T. (1969). Administration of and behavioral dependence on drugs. *Annual Review of Pharmacology*. 9: 483–502.

Sidney, S. (2002). Cardiovascular consequences of marijuana use. *Journal of Clinical Pharmacology*. 42:64S–70S.

Solinas, M., Panlilio, L.V., Justinova, Z., Yasar, S., Goldberg, S.R. (2006). Using drug-discrimination techniques to study the abuse-related effects of psychoactive drugs in rats. *Nature Protocols*. 1(3):1194–206.

Solowij, N., Stephens, R.S., Roffman, R.A., Babor, T., Kadden, R., Miller, M., Christiansen, K., McRee, B. and Vendetti, J. (2002). Marijuana Treatment Project Research Group. Cognitive functioning of long-term heavy cannabis users seeking treatment. *Journal of the American Medical Association*, 287(9):1123–31.

Substance Abuse and Mental Health Services Administration, Office of Applied Studies (2009). Results from the 2008 National Survey on Drug Use and Health: National Findings (NSDUH Series: H–34, DHHS Publication No. SMA 08–4343). Rockville, MD.

Substance Abuse and Mental Health Services Administration, Office of Applied Studies (2009). Treatment Episode Data Set (TEDS). Highlights—2007. National Admissions to Substance Abuse Treatment Services, DASIS Series: S–45, DHHS Publication No. (SMA) 09–4360, Rockville, MD.

Tanda, G., Munzar, P., Goldberg, S.R. (2000). Self-administration behavior is maintained by the psychoactive ingredient of marijuana in squirrel monkeys. *Nature Neuroscience*. 3(11): 1073–1074.

Tashkin, D.P., Coulson, A.H., Clark, V.A., Simmons, M., Bourque, L.B., Duann, S., Spivey, G.H., and Gong, H. (1987). Respiratory symptoms and lung function in habitual, heavy smokers of marijuana alone, smokers of marijuana and tobacco, smokers of tobacco alone, and nonsmokers. *American Review of Respiratory Disease*. 135:209–216.

Tashkin, D.P., Shapiro, B.J., and Frank, I.M. (1974). Acute effects of smoked marijuana and oral Δ9-tetrahydrocannabinol on specific airway conductance in asthmatic subjects. *American Review of Respiratory Disease*. 109(4):420–428.

Tashkin, D.P., Zhang, Z.F., Greenland, S., Cozen, W., Mack, T.M., and Morgenstern, H. (2006). Marijuana use and lung cancer: results of a case-control study. Abstract #A777, American Thoracic Society.

Taylor, D.N., Wachsmuth, I.K., Shangkuan, Y.H., Schmidt, E.V., Barrett, T.J., Schrader, J.S., Scherach, C.S., McGee, H.B., Feldman, R.A., Brenner, D.J. (1982). Salmonellosis associated with marijuana: a multistate outbreak traced by plasmid fingerprinting. *New England Journal of Medici*ne. 306(21):1249–53.

Thomas, H. (1993). Psychiatric symptoms in cannabis users. *British Journal of Psychiatry*. 163:141–149.

Thornicroft, G. (1990). Cannabis and psychosis. Is there epidemiological evidence for an association? *British Journal of Psychiatry*. 157:25–33.

Twitchell, W., Brown, S., and Mackie, K. (1997). Cannabinoids inhibit N- and P/Q-type calcium channels in cultured rat hippocampal neurons. *Journal of Neurophysiology*. 78(1):43–50.

Ungerleider, J.T., Andrysiak, T., Tashkin, D.P., Gale, R.P. (1982). Contamination of marihuana cigarettes with pathogenic bacteria-possible source of infection in cancer patients. *Cancer Treatment Reports*. 66(3):589–91.

van Os, J., Bak, M., Hanssen, M., Bijl, R.V., de Graaf, R., and Verdoux, H. (2002). Cannabis use and psychosis: a longitudinal population-based study. *American Journal of Epidemiology*. 156(4):319–327.

Vandrey, R.G., Budney, A.J., Moore, B.A., and Hughes, J.R. (2005). A cross-study comparison of cannabis and tobacco withdrawal. *American Journal of Addiction*. 14(1): 54–63.

Wachtel, S.R., El Sohly, M.A., Ross, S.A., Ambre, J., and de Wit, H. (2002). Comparison of the subjective effects of delta (9)-tetrahydrocannabinol and marijuana in humans. *Psychopharmacology*. 161(4):331–339.

Wagner, J.A., Varga, K., and Kunos, G. (1998). Cardiovascular actions of cannabinoids and their generation during shock. *Journal of Molecular Medicine*. 76(12):824–36.

Weil, A.T. (1970). Adverse reactions to marihuana. Classification and suggested treatment. *New England Journal of Medicine*. 282 (18):997–1000.

Wiley, J.L., Huffman, J.W., Balster, R.L., and Martin, B.R. (1995). Pharmacological specificity of the discriminative stimulus effects of Δ9-tetrahydrocannabinol in rhesus monkeys. *Drug and Alcohol Dependence*. 40:81–86.

Yanagita, T. (1980). Self-administration studies on psychological dependence. *Trends in Pharmacological Sciences*. 1:161–164.

Zhang, Z.F., Morgenstern, H., Spitz, M.R, Tashkin, D.P., Yu, G.P., Marshall, J.R, Hsu, T.C., and Schantz, S.P. (1999). Marijuana use and increased risk of squamous cell carcinoma of the head and neck. *Cancer Epidemiology, Biomarkers and Prevention*. 8(12): 1071–8.

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53846 **Federal Register** / Vol. 81, No. 156 / Friday, August 12, 2016 / Rules and Regulations

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1301

[Docket No. DEA–447]

Applications To Become Registered Under the Controlled Substances Act To Manufacture Marijuana To Supply Researchers in the United States

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Policy statement.

SUMMARY: To facilitate research involving marijuana and its chemical constituents, DEA is adopting a new policy that is designed to increase the number of entities registered under the Controlled Substances Act (CSA) to grow (manufacture) marijuana to supply legitimate researchers in the United States. This policy statement explains how DEA will evaluate applications for such registration consistent with the CSA and the obligations of the United States under the applicable international drug control treaty.

DATES: August 12, 2016.

FOR FURTHER INFORMATION CONTACT: Michael J. Lewis, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 598–6812.

SUPPLEMENTARY INFORMATION:

Background

Reasons for This Policy Statement

There is growing public interest in exploring the possibility that marijuana or its chemical constituents may be used as potential treatments for certain medical conditions. The Federal Food, Drug and Cosmetic Act requires that before a new drug is allowed to enter the U.S. market, it must be demonstrated through adequate and well-controlled clinical trials to be both safe and effective for its intended uses. Congress long ago established this process, recognizing that it was essential to protect the health and welfare of the American people.

Although no drug product made from marijuana has yet been shown to be safe and effective in such clinical trials, DEA—along with the Food and Drug Administration (FDA) and the National Institutes of Health (NIH)—fully supports expanding research into the potential medical utility of marijuana and its chemical constituents.[1]

There are a variety of factors that influence whether and to what extent such research takes place. Some of the key factors—such as funding—are beyond DEA's control.[2] However, one of the ways DEA can help to facilitate research involving marijuana is to take steps, within the framework of the CSA and U.S. treaty obligations, to increase the lawful supply of marijuana available to researchers.

For nearly 50 years, the United States has relied on a single grower to produce marijuana used in research. This grower operates under a contract with the National Institute on Drug Abuse (NIDA). This longstanding arrangement has historically been considered by the U.S. Government to be the best way to satisfy our nation's obligations under the applicable international drug control treaty, as discussed in more detail below. For most of the nearly 50 years that this single marijuana grower arrangement has been in existence, the demand for research-grade marijuana in the United States was relatively limited—and the single grower was able to meet such limited demand. However, in recent years, there has been greater public interest in expanding marijuana-related research, particularly with regard to certain chemical constituents in the plant known as cannabinoids.

The term ''cannabinoids'' generally refers to those chemicals unique to the cannabis plant (marijuana).[3] To date, more than 100 different cannabinoids have been found in the plant. One such cannabinoid—known as cannabidiol or CBD—has received increased attention in recent years. Although the effects of CBD are not yet fully understood by scientists, and research is ongoing in this area, some studies suggest that CBD may have uses in the treatment of seizures and other neurological disorders. A growing number of researchers have expressed interest in conducting research with extracts of marijuana that have a particular percentage of CBD and other cannabinoids. DEA fully supports research in this area. Based on discussions with NIDA and FDA, DEA has concluded that the best way to satisfy the current researcher demand for a variety of strains of marijuana and cannabinoid extracts is to increase the number of federally authorized marijuana growers. To achieve this result, DEA, in consultation with NIDA and FDA, has developed a new approach to allow additional marijuana growers to apply to become registered with DEA, while upholding U.S. treaty obligations and the CSA. This policy statement explains the new approach, provides details about the process by which potential growers may apply for a DEA registration, and describes the steps they must take to ensure their activity will be carried out in conformity with U.S. treaty obligations and the CSA.

The historical system, under which NIDA relied on one grower to supply marijuana on a contract basis, was designed primarily to supply marijuana for use in federally funded research—not for commercial product development. Thus, under the historical system, there was no clear legal pathway for commercial enterprises to produce marijuana for product development. In contrast, under the new approach explained in this policy statement, persons may become registered with DEA to grow marijuana not only to supply federally funded or other academic researchers, but also for strictly commercial endeavors funded by the private sector and aimed at drug product development. Likewise, under the new approach, should the state of scientific knowledge advance in the future such that a marijuana-derived drug is shown to be safe and effective for medical use, pharmaceutical firms will have a legal means of producing such drugs in the United States—independent of the NIDA contract process.

Legal Considerations

Applicable CSA Provisions

Under the CSA, all persons who seek to manufacture or distribute a controlled substance must apply for a DEA registration. 21 U.S.C. 822(a)(1). Applications by persons seeking to grow

[1] There are two FDA-approved drugs that contain a synthetic form of dronabinol, which is one of the chemicals found in marijuana. These drugs are Marinol (which the FDA approved for the treatment of nausea and vomiting associated with cancer chemotherapy, and for the treatment of anorexia associated with weight loss in patients with AIDS) and Syndros (which was approved for the same indications as Marinol).

[2] Funding may actually be the most important factor in whether research with marijuana (or any other experimental drug) takes place. What appears to have been the greatest spike in marijuana research in the United States occurred shortly after the State of California enacted legislation in 1999 to fund such research. Specifically, in 1999, California enacted a law that established the ''California Marijuana Research Program'' to develop and conduct studies on the potential medical utility of marijuana. Cal. Health & Safety Code § 11362.9. The state legislature appropriated a total of $9 million for the marijuana research studies. Over the next five years, DEA received applications for registration in connection with at least 17 State-sponsored pre-clinical or clinical studies of marijuana (all of which DEA granted). 74 FR 2101, 2105 (2009). However, it appears that once the State stopped funding the research, the studies ended.

[3] An acceptable and broader definition of ''cannabinoids'' includes not only those chemicals unique to the cannabis plant but also their derivatives and transformation products.

marijuana to supply researchers are governed by 21 U.S.C. 823(a); s*ee generally* 76 FR 51403 (2011); 74 FR 2101 (2009). Under section 823(a), for DEA to grant a registration, two conditions must be satisfied: (1) The registration must be consistent with the public interest (based on the enumerated criteria listed in section 823(a)) and (2) the registration must be consistent with U.S. obligations under the Single Convention on Narcotic Drugs, 1961 (Single Convention). An applicant seeking registration under section 823(a) has ''the burden of proving that the requirements for such registration pursuant to [this section] are satisfied.'' 21 CFR 1301.44(a). Although each application for registration that DEA receives will be evaluated individually based on its own merit, some general considerations warrant mention here.

First, while it is DEA's intention to increase the number of registered marijuana growers who will be supplying U.S. researchers, the CSA does not authorize DEA to register an unlimited number of manufacturers. As subsection 823(a)(1) provides, DEA is obligated to register only the number of bulk manufacturers of a given schedule I or II controlled substance that is necessary to ''produce an adequate and uninterrupted supply of these substances under adequately competitive conditions for legitimate medical, scientific, research, and industrial purposes.'' *See* 74 FR at 2127–2130 (discussing meaning of subsection 823(a)(1)). This provision is based on the long-established principle that having fewer registrants of a given controlled substances tends to decrease the likelihood of diversion.

Consistent with subsection 823(a)(1), DEA will evaluate each application it receives to determine whether adding such applicant to the list of registered growers is necessary to provide an adequate and uninterrupted supply of marijuana (including extracts and other derivatives thereof) to researchers in the United States.[4]

Second, as with any application submitted pursuant to section 823(a), in determining whether the proposed registration would be consistent with the public interest, among the factors to be considered are whether the applicant has previous experience handling controlled substances in a lawful manner and whether the applicant has engaged in illegal activity involving controlled substances. In this context, illegal activity includes any activity in violation of the CSA (regardless of whether such activity is permissible under State law) as well as activity in violation of State or local law. While past illegal conduct involving controlled substances does not automatically disqualify an applicant, it may weigh heavily against granting the registration.

Third, given the in-depth nature of the analysis that the CSA requires DEA to conduct in evaluating these applications, applicants should anticipate that, in addition to the information requested in the application itself, they will be asked to submit other information germane to the application in accordance with 21 CFR 1301.15. This will include, among other things, detailed information regarding an applicant's past experience in the manufacture of controlled substances. In addition, applicants will be asked to provide a written explanation of how they believe they would be able to augment the nation's supply of research-grade marijuana within the meaning of subsection 823(a)(1). Applicants may be asked to provide additional written support for their application and other information that DEA deems relevant in evaluating the application under section 823(a).

Treaty Considerations

As stated above, DEA may only issue a registration to grow marijuana to supply researchers if the registration is consistent with U.S. obligations under the Single Convention. Although this policy document will not list all of the applicable requirements of the Single Convention,[5] the following is a summary of some of the key considerations.

Under articles 23 and 28 of the Single Convention, a party (*i.e.,* a country that is a signatory to the treaty) that allows the cultivation of cannabis for lawful uses (*e.g.,* FDA-authorized clinical trials) must:

(a) Designate the areas in which, and the plots of land on which, cultivation of the cannabis plant for the purpose of producing cannabis shall be permitted;

(b) License cultivators authorized to cultivate cannabis;

(c) Specify through such licensing the extent of the land on which the cultivation is permitted;

(d) Purchase and take physical possession of all cannabis crops from all cultivators as soon as possible, but not later than four months after the end of the harvest; and

(e) Have the exclusive right of importing, exporting, wholesale trading and maintaining stocks of cannabis.

As DEA has stated in a prior publication, DEA carries out those functions of article 23, paragraph 2, that are encompassed by the DEA registration system (paragraphs (a) through (c) above), and NIDA carries out those functions relating to purchasing the marijuana and maintaining a monopoly over the wholesale distribution (paragraphs (d) and (e) above).[6] 76 FR at 51409.

As indicated, DEA's historical approach to ensuring compliance with the foregoing treaty requirements was to limit the registration of marijuana growers who supply researchers to those entities that operate under a contract with NIDA. Under this historical approach, the grower could be considered an extension of NIDA and thus all marijuana produced by the grower was effectively owned by NIDA, with NIDA controlling all distribution to researchers.

However, as further indicated, DEA has concluded, based on discussions with NIDA and FDA, that it would be beneficial for research to allow additional marijuana growers outside the NIDA-contract system, provided this could be accomplished in a manner consistent with the CSA and the treaty. Toward this end, DEA took into account the following statement contained in the official commentary to the Single Convention:

> Countries . . . which produce . . . cannabis . . . , [i]n so far as they permit private farmers to cultivate the plants . . . , cannot establish with sufficient exactitude the quantities harvested by individual producers. If they allowed the sale of the crops to private traders, they would not be in a position to ascertain with reasonable exactitude the amounts which enter their controlled trade. The effectiveness of their control régime would thus be considerably weakened. In fact, experience has shown that permitting licensed private traders to purchase the crops results in diversion of large quantities of drugs into illicit channels. . . . [T]he acquisition of the crops and the wholesale and international trade in these agricultural products cannot be entrusted to private traders, but must be undertaken by governmental authorities in the producing countries. Article 23 . . . and article 28 . . . therefore require a government monopoly of the wholesale and international trade in the agricultural product in question in the country which authorizes its production.
>
> Commentary at 278

[4] In making this determination, DEA will consult with NIH and FDA, as warranted.

[5] A detailed explanation of the relevant Single Convention requirements can be found in 74 FR at 2114–2118.

[6] In accordance with the CSA, DEA carries out functions that are indirectly related to those specified in article 23, paragraph 2(e). For example, DEA controls imports and exports of cannabis through the CSA registration and permitting system.

Given the foregoing considerations, DEA believes it would be consistent with the purposes of articles 23 and 28 of the Single Convention for DEA to register marijuana growers outside of the NIDA-contract system to supply researchers, *provided the growers agree that they may only distribute marijuana with prior, written approval from DEA.* In other words, in lieu of requiring the growers to operate under a contract with NIDA, a registered grower will be permitted to operate independently, provided the grower agrees (through a written memorandum of agreement with DEA) that it will only distribute marijuana with prior, written approval from DEA. DEA believes this new approach will succeed in avoiding one of the scenarios the treaty is designed to prevent: Private parties trading in marijuana outside the supervision or direction of the federal government.

Also, consistent with the purposes and structure of the CSA, persons who become registered to grow marijuana to supply researchers will only be authorized to supply DEA-registered researchers whose protocols have been determined by the Department of Health and Human Services (HHS) to be scientifically meritorious. *See* 21 U.S.C. 823(f). In 2015, HHS announced the details of its current policy for evaluating the merits of research protocols involving marijuana. 80 FR 35960 (2015).

Finally, potential applicants should note that any entity granted a registration to manufacture marijuana to supply researchers will be subject to all applicable requirements of the CSA and DEA regulations, including those relating to quotas, record keeping, order forms, security, and diversion control.

How To Apply for a Registration

Persons interested in applying for a registration to become a bulk manufacturer of marijuana to supply legitimate researchers can find instructions and the application form by going to the DEA Office of Diversion Control Web site registration page at *www.deadiversion.usdoj.gov/drugreg/index.html#regapps.* Applicants will need to submit Form 225.

Note Regarding the Nature of This Document

This document is a general statement of DEA policy. While this document reflects how DEA intends to implement the relevant statutory and regulatory provisions, it does not establish a rule that is binding on any member of the public. Any person who applies for a registration to grow marijuana (as with any other applicant for registration under the CSA) is entitled to due process in the consideration of the application by the Agency. To ensure such due process, the CSA provides that, before taking action to deny an application for registration, DEA must serve upon the applicant an order to show cause why the application should not be denied, which shall provide the applicant with an opportunity to request a hearing on the application in accordance with the Administrative Procedure Act. 21 U.S.C. 824(c).

Dated: July 25, 2016.

Chuck Rosenberg,

Acting Administrator.

[FR Doc. 2016–17955 Filed 8–11–16; 8:45 am]

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FAA Order 7400.11, Airspace Designations and Reporting Points, is published yearly and effective on September 15.

Regulatory Notices and Analyses

The FAA has determined that this proposed regulation only involves an established body of technical regulations for which frequent and routine amendments are necessary to keep them operationally current. It, therefore: (1) Is not a ''significant regulatory action'' under Executive Order 12866; (2) is not a ''significant rule'' under Department of Transportation (DOT) Regulatory Policies and Procedures (44 FR 11034; February 26, 1979); and (3) does not warrant preparation of a regulatory evaluation as the anticipated impact is so minimal. Since this is a routine matter that will only affect air traffic procedures and air navigation, it is certified that this proposed rule, when promulgated, will not have a significant economic impact on a substantial number of small entities under the criteria of the Regulatory Flexibility Act.

Environmental Review

This proposal will be subject to an environmental analysis in accordance with FAA Order 1050.1F, ''Environmental Impacts: Policies and Procedures'' prior to any FAA final regulatory action.

List of Subjects in 14 CFR Part 71

Airspace, Incorporation by reference, Navigation (air).

The Proposed Amendment

In consideration of the foregoing, the Federal Aviation Administration proposes to amend 14 CFR part 71 as follows:

PART 71—DESIGNATION OF CLASS A, B, C, D, AND E AIRSPACE AREAS; AIR TRAFFIC SERVICE ROUTES; AND REPORTING POINTS

■ 1. The authority citation for part 71 continues to read as follows:

Authority: 49 U.S.C. 106(f), 106(g); 40103, 40113, 40120; E.O. 10854, 24 FR 9565, 3 CFR, 1959–1963 Comp., p. 389.

§ 71.1 [Amended]

■ 2. The incorporation by reference in 14 CFR 71.1 of FAA Order 7400.11D, Airspace Designations and Reporting Points, dated August 8, 2019, and effective September 15, 2019, is amended as follows:

Paragraph 2004 Jet Routes

J–2

From Mission Bay, CA; Imperial, CA; Bard, AZ; INT Bard 089° and Gila Bend, AZ, 261°radials; Gila Bend; Tucson, AZ; El Paso, TX; Fort Stockton, TX; Junction, TX; San Antonio, TX; Humble, TX; Lake Charles, LA; Fighting Tiger, LA; Semmes, AL; Crestview, FL; to INT Crestview 091°and Seminole, FL, 290°radials.

J–14

From Panhandle, TX; via Will Rogers, OK; Little Rock, AR; to Vulcan, AL.

J–24

From Myton, UT, to Hayden, CO. From Hugo, CO, Hays, KS; via Salina, KS; Kansas City, MO; St. Louis, MO; Brickyard, IN; Falmouth, KY; Charleston, WV; to Montebello, VA.

J–37

From Hobby, TX, via INT of the Hobby 090° and Harvey, LA, 266° radials; Harvey; Semmes, AL; to Montgomery, AL.

J–39

From Montgomery, AL; Vulcan, AL, Nashville, TN; Louisville, KY, to Rosewood, OH.

J–42

From Delicias, Mexico, via Fort Stockton, TX; Abilene, TX; Ranger, TX; Texarkana, AR; Memphis, TN; Nashville, TN; Beckley, WV; Montebello, VA; to Gordonsville, VA.

J–52

From Vancouver, BC, Canada; via Spokane, WA; Salmon, ID; Dubois, ID; Rock Springs, WY; Falcon, CO; Hugo, CO; Lamar, CO; Liberal, KS; INT Liberal 137° and Ardmor, OK 309° radials; Ardmore; Texarkana, AR; Sidon, MS; Bigbee, MS; to Vulcan, AL.

J–55 [Remove]

J–61

From Westminster, MD; to Philipsburg, PA.

J–62 [Remove]

J–68

From Gopher, MN, INT Gopher 109° and Dells, WI, 310° radials; Dells; Badger, WI; INT Badger 086° and Flint, MI, 278° radials; to Flint.

J–79 [Remove]

J–109 [Remove]

J–121 [Remove]

J–150 [Remove]

J–165 [Remove]

J–174 [Remove]

J–191 [Remove]

J–193 [Remove]

J–222 [Remove]

J–225 [Remove]

J–230 [Remove]

J–506 [Remove]

J–561 [Remove]

J–563 [Remove]

J–570 [Remove]

J–573 [Remove]

J–582 [Remove]

J–585 [Remove]

Paragraph 2006 United States Area Navigation Routes.

Q–108 [Remove]

Issued in Washington, DC, on March 11, 2020.

Scott M. Rosenbloom,

Acting Manager, Airspace Policy Group.

[FR Doc. 2020–05857 Filed 3–20–20; 8:45 am]

BILLING CODE 4910–13–P

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Parts 1301 and 1318

[Docket No. DEA–506]

RIN 1117–AB54

Controls To Enhance the Cultivation of Marihuana for Research in the United States

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Drug Enforcement Administration is proposing to amend its regulations to comply with the requirements of the Controlled Substances Act, including consistency with treaty obligations, in order to facilitate the cultivation of marihuana for research purposes and other licit purposes. Specifically, this proposed rule would amend the provisions of the regulations governing applications by persons seeking to become registered with DEA to grow marihuana as bulk manufacturers and add provisions related to the purchase and sale of this marihuana by DEA.

DATES: Comments must be submitted electronically or postmarked on or before May 22, 2020.

ADDRESSES: To ensure proper handling of comments, please reference ''[RIN 1117–AB54/Docket No. DEA–506]'' on all electronic and written correspondence, including any attachments.

• *Electronic Comments:* DEA encourages that all comments be submitted electronically through the Federal eRulemaking Portal, which provides the ability to type short comments directly into the comment field on the web page or attach a file for lengthier comments. Please go to *http://www.regulations.gov* and follow the

online instructions at that site for submitting comments. Upon completion of your submission, you will receive a Comment Tracking Number for your comment. Please be aware that submitted comments are not instantaneously available for public view on *Regulations.gov.* If you have received a Comment Tracking Number, your comment has been successfully submitted and there is no need to resubmit the same comment. Commenters should be aware that the electronic Federal Docket Management System will not accept any comments after 11:59 p.m. Eastern Time on the last day of the comment period.

• *Paper Comments:* Paper comments that duplicate electronic submissions are not necessary. Should you wish to mail a paper comment *in lieu of* an electronic comment, it should be sent via regular or express mail to: Drug Enforcement Administration, Attn: DEA **Federal Register** Representative/DPW, 8701 Morrissette Drive, Springfield, Virginia 22152–2639.

• *Paperwork Reduction Act Comments:* All comments concerning collections of information under the Paperwork Reduction Act must be submitted to the Office of Information and Regulatory Affairs, Office of Management and Budget, Attention: Desk Officer for DOJ, Washington, DC 20503. Please state that your comment refers to RIN 1117–AB54/Docket No. DEA–506.

FOR FURTHER INFORMATION CONTACT: Scott A. Brinks, Regulatory Drafting and Policy Support Section (DPW), Diversion Control Division, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152–2639; Telephone: (571) 362–3261.

SUPPLEMENTARY INFORMATION:

Posting of Public Comments

Please note that all comments received in response to this docket are considered part of the public record. They will, unless reasonable cause is given, be made available by DEA for public inspection online at *http://www.regulations.gov.* Such information includes personal identifying information (such as your name, address, etc.) that you voluntarily submit. The Freedom of Information Act applies to all comments received. If you want to submit personal identifying information (such as your name, address, etc.) as part of your comment, but do not want it to be made publicly available, you must include the phrase ''PERSONAL IDENTIFYING INFORMATION'' in the first paragraph of your comment. You must also place all of the personal identifying information you do not want made publicly available in the first paragraph of your comment and identify what information you want redacted.

If you want to submit confidential business information as part of your comment, but do not want it to be made publicly available, you must include the phrase ''CONFIDENTIAL BUSINESS INFORMATION'' in the first paragraph of your comment. You must also prominently identify the confidential business information to be redacted within the comment.

Comments containing personal identifying information or confidential business information identified as directed above will be made publicly available in redacted form. If a comment has so much confidential business information that it cannot be effectively redacted, all or part of that comment may not be made publicly available. Comments posted to *http://www.regulations.gov* may include any personal identifying information (such as your name, address, etc.) included in the text of your electronic submission that is not identified as directed above as confidential.

An electronic copy of this proposed rule is available at *http://www.regulations.gov* for ease of reference.

Background and Purpose of This Proposed Rule

Under the Controlled Substances Act (CSA), all persons who seek to manufacture a controlled substance must apply for and obtain a DEA registration.[1] 21 U.S.C. 822(a)(1). The CSA defines ''manufacture'' to include the ''production'' of a controlled substance, which includes, among other things, the planting, cultivation, growing, or harvesting of a controlled substance. 21 U.S.C. 802(15), (22). Thus, any person who seeks to plant, cultivate, grow, or harvest marihuana[2] to supply researchers or for other uses permissible under the CSA (such as product development) must obtain a DEA manufacturing registration. Because marihuana is a schedule I controlled substance, applications by persons seeking to become registered to manufacture marihuana are governed by 21 U.S.C. 823(a). *See generally* 76 FR 51403 (2011); 74 FR 2101 (2009), *pet. for rev. denied, Craker* v. *DEA,* 714 F.3d 17 (1st Cir. 2013). Under section 823(a), for DEA to grant a registration, the DEA Administrator must determine that two conditions are satisfied: (1) The registration is consistent with the public interest (based on the enumerated criteria in section 823(a)), and (2) the registration is consistent with U.S. obligations under the Single Convention on Narcotic Drugs, 1961 (''Single Convention'' or ''Treaty''), 18 U.S.T. 1407.[3]

In 2016, DEA issued a policy statement aimed at expanding the number of manufacturers who could produce marihuana for research purposes. *See* Applications to Become Registered under the Controlled Substances Act to Manufacture Marijuana to Supply Researchers in the United States, 81 FR 53846 (Aug. 12, 2016). Subsequently, the Department of Justice (DOJ) undertook a review of the CSA, including the provisions requiring consistency with obligations under international treaties such as the Single Convention, and determined that certain changes to its 2016 policy were needed. The pertinent Treaty provisions are found in articles 23 and 28 of the Single Convention, which are summarized below. Additionally, DEA believes that these changes will enhance and improve research with marihuana and facilitate research that could result in the development of marihuana-based medicines approved by the Food and Drug Administration (FDA).

This proposed rule is being issued pursuant to the Administrator's authority under the CSA ''to promulgate rules and regulations and to charge reasonable fees relating to the registration and control of the manufacture, distribution, and dispensing of controlled substances,'' 21 U.S.C. 821, and to ''promulgate and enforce any rules, regulations, and procedures which he may deem necessary and appropriate for the efficient execution of his functions under [the CSA],'' 21 U.S.C. 871(b).

A. Relevant Provisions of the Single Convention

Because the terminology used in the Single Convention is somewhat different from that in the CSA, a brief explanation is warranted. The Single Convention uses the terms ''cannabis,'' ''cannabis plant,'' and ''cannabis

[1] All functions vested in the Attorney General by the CSA have been delegated to the Administrator of DEA. 28 CFR 0.100(b).

[2] This document uses both the CSA spelling ''marihuana'' and the modern spelling ''marijuana'' interchangeably.

[3] Section 823(a) provides that the registrations to manufacture controlled substances in schedule I or II must be ''consistent with the public interest and with United States obligations under international treaties, conventions, or protocols in effect on May 1, 1971.'' The Single Convention entered into force for the United States on June 24, 1967. *See* Single Convention, 18 U.S.T. 1407.

resin''—all of which are generally encompassed by the CSA definition of ''marihuana'' in 21 U.S.C. 802(16)).[4] The Single Convention defines ''cannabis plant'' as ''any plant of the genus Cannabis.'' Single Convention art. 1(1)(c). The Single Convention defines ''cannabis'' as the ''flowering or fruiting tops of the cannabis plant (excluding the seeds and leaves when not accompanied by the tops) from which the resin has not been extracted.'' *Id.* art. 1(1)(b). The Single Convention defines ''cannabis resin'' as the ''separated resin, whether crude or purified, obtained from the cannabis plant.'' *Id.* art. 1(1)(d).

Article 28 of the Single Convention states in paragraph 1: ''If a Party permits the cultivation of the cannabis plant for the production of cannabis or cannabis resin, it shall apply thereto the system of controls as provided in article 23 respecting the control of the opium poppy.'' Paragraph 2 of that article excludes from the Convention the cultivation of cannabis for industrial or horticultural purposes. Because the United States permits the cultivation of marihuana for the production of cannabis and cannabis resin currently only for research purposes, it is obligated under the Treaty to apply to the marihuana plant cultivated for these purposes the ''system of controls'' provided in article 23 respecting the control of the opium poppy.

The Commentary to the Single Convention contains the following explanation of articles 23 and 28 within the overall framework of the Treaty:

> The system of control over all stages of the drug economy which the Single Convention provides has two basic features: Limitation of narcotic supplies of each country . . . to the quantities that it needs for medical and scientific purposes, and authorization of each form of participation in the drug economy, that is, licensing of producers, manufacturers and traders . . . . *In the case of the production of opium, coca leaves, cannabis and cannabis resin, this régime is supplemented by the requirement of maintaining government monopolies for the wholesale and international trade in these drugs in countries which produce them* . . . .
>
> Secretary-General of the United Nations, Commentary on the Single Convention on Narcotic Drugs, 1961, 263 (1973) (emphasis added) (footnotes omitted).[5]

Article 23(2) of the Single Convention, made applicable to marijuana cultivation by Article 28, contains five requirements for the supervision, licensing, and distribution of marijuana.[6]

(a) Designate the areas in which, and the plots of land on which, cultivation of the cannabis plant for the purpose of producing cannabis or cannabis resin shall be permitted.

(b) Ensure that only cultivators licensed by the agency shall be authorized to engage in such cultivation.

(c) Ensure that each license shall specify the extent of the land on which the cultivation is permitted.

(d) Require all cultivators of the cannabis plant to deliver their total crops of cannabis and cannabis resin to the agency and ensure that the agency purchases and takes physical possession of such crops as soon as possible, but not later than four months after the end of the harvest.

(e) Have the exclusive right of importing, exporting, wholesale trading, and maintaining stocks of cannabis and cannabis resin, except that this exclusive right need not extend to medicinal cannabis, cannabis preparations, or the stocks of cannabis and cannabis resin held by manufacturers of such medicinal cannabis and cannabis preparations.[7]

DEA already directly performs functions (a), (b), and (c) by virtue of the CSA registration system as applied to manufacturers of marihuana. In order to ensure that DEA complies with the CSA and grants registrations that are consistent with relevant treaty provisions, namely articles 23 and 28 of the Single Convention, DEA proposes to directly perform functions (d) and (e) as well. This proposed rule would amend DEA's regulations so that DEA directly carries out these remaining two functions.

DEA also recognizes that the Department of Health and Human Services (HHS) has, for nearly 50 years, maintained an essential program aimed at ensuring that marihuana is available to meet the research and scientific needs of the United States. The regulations proposed here, if finalized, will require some changes to this program, but DEA is committed to ensuring that the National Institute on Drug Abuse (NIDA) program continues with minimal disruption and there is no impact on the availability of marihuana through the NIDA Drug Supply Program (DSP).

After the publication of the 2016 policy statement, DOJ advised DEA that it must adjust its policies and practices to ensure compliance with the CSA, including the CSA's requirement that registrations be consistent with the Single Convention. Therefore, the regulations being proposed herein, if finalized, would ensure that DEA regulations comply with applicable law. Within that framework, DEA is proposing changes to support using marihuana (including extracts and substances derived therefrom) cultivated in the United States to perform research which, among other things, may lead to the approval of FDA-approved medicines. Thus, the proposed rule, if adopted, would supersede the 2016 policy statement.

To address the foregoing considerations, the proposed rule would add regulations stating:

(1) All registered manufacturers who cultivate cannabis shall deliver their total crops of cannabis to DEA. DEA shall purchase and take physical possession of such crops as soon as possible, but not later than four months after the end of the harvest. DEA may accept delivery and maintain possession of such crops at the registered location of the registered manufacturer authorized to cultivate cannabis consistent with the maintenance of effective controls against diversion. In such cases, DEA shall designate a secure storage mechanism at the registered location in which DEA may maintain possession of the cannabis, and DEA will control access to the stored cannabis. If DEA determines that no suitable location exists at the registered location of the registered manufacturer authorized to cultivate cannabis, then DEA shall designate a location for the

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[4] As discussed below, the Agriculture Improvement Act of 2018, Public Law 115–334, removed hemp from the CSA definition of marihuana. This proposed rule applies only to cannabis that is included in the CSA definition of marihuana.

[5] The United Nations' Economic and Social Council requested that the Secretary-General prepare the Commentary ''in the light of the relevant conference proceedings and other material'' in order to aid governments in applying the Single Convention. The Commentary (1973) is not binding on Parties to the Convention. Economic and Social Council Resolution 1962/914(XXXIV) D (Aug. 3, 1962).

[6] The Single Convention provides that the five functions of article 23, paragraph 2 ''shall be discharged by a single government agency if the constitution of the Party concerned permits it.'' Single Convention art. 23(3). Nothing in the Constitution would preclude the United States from discharging all of those controls through one government agency. The Commentary to the Single Convention notes that this is in order to facilitate national planning and coordinated management of the various tasks imposed upon a country by Article 23, and that in countries where more than one agency is needed on constitutional grounds, administrative arrangements should be made to ensure the required coordination.

[7] The meanings of the terms ''medicinal cannabis'' and ''cannabis preparations'' are addressed later in this document. Article 23, paragraph 2(e) also refers to ''opium alkaloids.'' However, due to distinctions between the opiates derived from the opium poppy and the cannabinoids derived from the cannabis plant, the notion of ''cannabis alkaloids'' is inapplicable.

authorized grower to deliver the crop as soon as possible, but not later than four months after the end of the harvest. However, in all cases the registrant must comply with the security requirements specified in 21 CFR part 1301.

(2) DEA shall, with respect to cannabis, have the exclusive right of importing, exporting, wholesale trading, and maintaining stocks other than those held by registered manufacturers and distributors of medicinal cannabis or cannabis preparations. Such exclusive right shall not extend to medicinal cannabis or cannabis preparations. DEA may exercise its exclusive right by authorizing the performance of such activities by appropriately registered persons. DEA will require prior written notice of each proposed importation, exportation, or distribution of cannabis that specifies the quantity of cannabis to be imported, exported, or distributed and the name, address, and registration number of the registered manufacturer or researcher to receive the cannabis before authorizing the importation, exportation, or distribution. All importation and exportation shall be performed in compliance with 21 CFR part 1312, as applicable. Under no circumstance shall a registered manufacturer authorized to grow cannabis import, export, or distribute cannabis without the express written authorization of DEA.

(3) A registered manufacturer authorized to grow cannabis shall notify DEA in writing of its proposed date of harvest at least fifteen days before the commencement of the harvest.

It should be noted that the timing of when DEA would take physical possession of the crops, if delayed, would not only increase the risk of diversion, but would also adversely impact the quality of the crop. Whereas DEA is proposing to take physical possession not later than four months from the time of harvest, it is DEA's intent to take physical possession as soon as possible and to distribute marihuana as soon as is practical to those who are authorized to receive it.

The exceptions made for ''medicinal cannabis or cannabis preparations'' also warrant explanation. In view of the text of the Single Convention, and taking into account the current wording of Federal law,[8] the regulations being proposed would define these terms as follows:

- Medicinal cannabis means a drug product made from the cannabis plant, or derivatives thereof that can be legally marketed under the Federal Food, Drug, and Cosmetic Act. However, such term does not include any material, compound, mixture, or preparation that falls outside the CSA definition of marihuana.
- Cannabis preparation means cannabis that was delivered to DEA and subsequently converted by a registered manufacturer into a mixture (solid or liquid) containing cannabis, cannabis resin, or extracts of cannabis. However, such term does not include any material, compound, mixture, or preparation that falls outside the CSA definition of marihuana.

Thus, under the proposed rule, DEA would have the exclusive right of importing, exporting, wholesale trading, and maintaining stocks of marihuana other than those held by DEA-registered manufacturers and distributors of medicinal cannabis or cannabis preparations. Further, this exclusive right would not apply to medicinal cannabis or cannabis preparations.

To summarize those provisions of the proposed rule that are intended to ensure that registrations are granted in compliance with the CSA as the number of registered manufacturers increases, all marihuana grown by DEA-registered manufacturers in the United States would be delivered by such registrants to DEA no later than four months after the end of the harvest. Thereafter, DEA would authorize exportation, distribution, and maintenance of stocks of such marihuana with two important exceptions:

(1) DEA-registered manufacturers of (a) an FDA-approved marihuana-derived drug (*i.e.,* ''medicinal cannabis''), and (b) ''cannabis preparations'' would be permitted to maintain stocks of cannabis materials obtained from DEA for the purpose of producing such drugs or preparations; [9] and

(2) Once marihuana material that was previously purchased by DEA is subsequently converted by a DEA-registered manufacturer into (a) an FDA-approved drug (''medicinal cannabis'') or (b) a ''cannabis preparation,'' the material no longer would be subject to the foregoing exclusive right and could be further distributed or dispensed by a DEA registrant in any manner authorized under the CSA. DEA is committed to ensuring this new requirement is implemented in a manner that supports the policy goal of facilitating research involving marijuana and its chemical constituents.

B. Activities Performed by Bulk Manufacturers of Marihuana and the Application of These Proposed Regulations on Those Activities

Based on approximately 35 pending applications resulting from publication of its 2016 policy statement, DEA anticipates that those bulk manufacturers who would obtain a registration from DEA to grow marihuana would be one (or more) of three different types. In this section, DEA describes each type and how the proposed regulations, if finalized as proposed, would impact those registrants with regard to functions (1) and (2) described in the previous section.

(1) A Bulk Manufacturer Who Grows Marihuana for Its Own Research or Drug Development Purposes

A number of applicants seek to grow marihuana for their own research endeavors, including some who wish to develop an FDA-approved medicine from extracts or derivatives of the marihuana plant. Based on the accompanying information supplied by the applicant to DEA in connection with their application, these applicants would list themselves as a ''purchaser,'' meaning that once their crop was harvested, they would seek to use the marihuana for their internal research purposes. Applicants must obtain a separate schedule I research registration from DEA to perform research with marihuana in accordance with 21 CFR 1301.13 and 1301.32. However, bulk marihuana growers may manufacture marihuana for use by other researchers under a manufacturing registration (and pursuant to a quota granted to them by DEA for that purpose under 21 CFR 1303.21(a)).

For applicants within this category, within four months of harvest, DEA would travel to the DEA-registered location, purchase, and take title to the crop by issuing the grower a DEA Form 222.[10] Once DEA has taken title to the

[8] Among other things, these definitions take into account the current CSA definition of marihuana (21 U.S.C. 802(16)), which was amended in 2018 to exclude ''hemp'' as defined in section 297A of the Agricultural Marketing Act of 1946 (7 U.S.C. 1639*o*(1)).

[9] As indicated above, the requirement that registered growers deliver all cannabis to DEA no later than four months after the end of the harvest applies in *all* situations—even where the cannabis will later be distributed by DEA back to the grower for further use. Thus, the above exception that allows DEA-registered manufacturers of medicinal cannabis and cannabis preparations to maintain stocks of cannabis materials for the purpose of producing such drugs or preparations only applies where the raw cannabis material was previously delivered to DEA.

[10] DEA would take title to an amount up to the applicant's manufacturing quota. Growing marihuana in excess of a manufacturing quota is a violation of federal law. 21 U.S.C. 842(b). Thus, any marihuana grown in excess of a manufacturing

Continued

crop, it would then distribute a quantity of marihuana that does not exceed the company's DEA-issued procurement quota back to that same manufacturer. In this way, DEA would take physical possession of the crop and control its distribution. Additionally, the material owned by the government will be maintained at the DEA-registered manufacturer's location and DEA would maintain its ability to access the storage location at which such crops are located as it deemed necessary.

(2) A Bulk manufacturer Who Supplies Marihuana to Other DEA Registrants, Including National Institutes of Health Funded and Non-National Institutes of Health Funded Researchers

Some applicants are seeking to grow marihuana for use by other DEA registrants including ''non-bulk'' manufacturers and schedule I researchers, including National Institutes of Health (NIH) funded and non-NIH funded researchers. This sub-set of bulk manufacturers would be required to obtain from each customer a bona fide supply agreement, listing the name and address of the end user, the end user's DEA registration number, the quantity of marihuana to be supplied, and the price that the end user and grower have mutually agreed upon. DEA will consider this information, along with additional information, when establishing an individual manufacturing quota for the grower.

For applicants that fall within this sub-set, within four months of harvest, DEA would travel to the DEA-registered location, purchase, and take title to the crop by issuing the grower a DEA Form 222.[11] For this reason, each grower must provide written notice to DEA of its proposed date of harvest at least fifteen days prior to the commencement of the harvest. Once DEA has purchased and taken title to the crop, the material would be maintained, under seal, in DEA's possession in the manufacturer's schedule I vault until such time that a distribution is necessary. In this scenario, DEA may distribute (or export) the marihuana directly or may choose to authorize the grower to distribute marihuana on the government's behalf. Again, marihuana owned by the government is maintained at the DEA-registered manufacturer's site where DEA would maintain its ability to access the storage location at which such crops are located as it deemed necessary.

(3) A Bulk Manufacturer Who Supplies Marihuana To Support NIDA's Drug Supply Program

Over the last several decades, NIDA has administered a contract to produce high quality marihuana for use by researchers who have obtained federal funding (grants) for such research.[12] This contract has been awarded to the National Center for Natural Products Research at the University of Mississippi (National Center). In accordance with that contract and DEA regulations, NIDA assesses the quantity of marihuana that is necessary to be grown for research purposes in a given year and communicates that information to both the National Center and DEA. The National Center applies for, and must first obtain, a manufacturing quota from DEA and is then authorized to grow marihuana up to the limit established by their DEA-issued quota. At the time of harvest, a portion of that material is held in inventory at the National Center while other portions are distributed to another DEA registrant, Research Triangle Institute (RTI). Currently, at the direction of NIDA, both RTI and the National Center may prepare marihuana in a manner which is suitable for research studies and ship it to researchers. In these instances, marihuana held in inventory at the National Center and RTI are the property of NIDA. The regulations proposed in this notice of proposed rulemaking (NPRM) are intended to enhance and improve upon existing DEA regulations that supported the NIDA DSP and will facilitate research that may lead to the development of FDA-approved medicines.

This regulation, if finalized, would require changes to the current scheme described above. Although NIDA can, and would, continue to administer the contract in support of its DSP and the National Center (or other NIDA contract holder) could continue to grow and produce marihuana in support of research pursuant to that contract (for as long as that contract is renewed), within four months of harvest, DEA would travel to the National Center at the time of harvest and take title and possession to the crop by issuing the National Center a DEA Form 222.[13] Once DEA has taken title and possession of the crop, the material would be maintained, under seal, in DEA's possession in the National Center's schedule I vault until such time that a distribution to another DEA registrant is authorized. In this scenario, DEA may distribute (or export) the marijuana directly or may choose to authorize the National Center to distribute marihuana on the government's behalf. In both situations, DEA's distributions would be in accordance with NIDA's recommendation. And, as such, DEA does not envision a scenario in which it would deny or delay a distribution to a duly registered schedule I researcher authorized to handle marihuana. Marihuana owned by DEA would be maintained at the National Center, where DEA would maintain its ability to access the storage location at which its crops are located.

C. Application of the Public Interest Factors

As indicated, in addition to the foregoing treaty considerations, DEA may grant a registration to manufacture a schedule I or II controlled substance only where the Administrator determines that the registration is consistent with the public interest, based on the criteria listed in 21 U.S.C. 823(a). The first of those criteria, set forth in subsection 823(a)(1), provides that, for the purpose of maintaining effective controls against diversion, the number of registered bulk manufacturers of a given schedule I or II controlled substance should be limited to that which can produce an adequate and uninterrupted supply of marihuana under adequately competitive conditions.[14]

The proposed rule would explain how DEA will evaluate whether a particular application is consistent with the public interest factors of 21 U.S.C. 823(a), including factor 823(a)(1). As discussed above, a bona fide supply agreement between a grower and a duly registered schedule I researcher or manufacturer provides evidence that an applicant's registration is necessary to produce an adequate and uninterrupted supply of marihuana under adequately competitive conditions. An applicant proposing to grow marihuana to supply its own research may also be deemed to have satisfied the public interest factor of 823(a)(1) upon the presentation of evidence that it possesses a registration to conduct research with marihuana under 21 CFR 1301.32. Such a researcher will only be granted quota to

quota would be subject to seizure and destruction. *See id.* 881(g).

[11] As in the first scenario, DEA only would take title to an amount up to the applicant's manufacturing quota. Any marihuana grown in excess of a manufacturing quota would be subject to seizure and destruction. *See* 21 U.S.C. 842(b), 881(g).

[12] The Department of Health and Human Services maintains procedures for providing this same marihuana to non-NIH funded researchers as well.

[13] As above, DEA only would take title to an amount up to the National Center's manufacturing quota, with amount grown in excess of the manufacturing quota subject to seizure and destruction. *See* 21 U.S.C. 842(b), 881(g).

[14] For a detailed explanation of subsection 823(a)(1), see 74 FR at 2127–33.

the extent authorized by its approved research protocol.

The proposed rule further provides that the Administrator's determination of which applicants to select will be consistent with the public interest factors in section 823(a), with particular emphasis on the criteria discussed in the preceding paragraph as well as the following:

(1) The applicant's ability to consistently produce and supply marihuana of a high quality and defined chemical composition; and

(2) Whether the applicant has demonstrated prior compliance with the CSA and DEA regulations.

The preceding criteria are designed to result in registration of those manufacturers of marihuana that can most efficiently supply the lawful needs of the U.S. market in terms of quantity and quality.[15] These criteria are further aimed at selecting applicants that can be entrusted with the responsibility of a DEA registration and complying with the corresponding obligations under the CSA and DEA regulations.

As indicated above, following the publication of the 2016 policy statement, DEA received numerous applications by persons seeking to become registered as bulk manufacturers of marihuana. There are approximately 35 such applications currently pending. As explained above, the CSA requires DEA to limit the total number of registered bulk manufacturers of a given schedule I or II controlled substance to that necessary to produce an adequate and uninterrupted supply under adequately competitive conditions. In consultation with HHS, DEA wishes to avoid a situation in which the agency is in the midst of evaluating these applications and has to begin an evaluation anew each time it accepts a new marihuana grower application for filing. Thus, the proposed rule provides that, with a limited exception, applications accepted for filing after the date the final rule becomes effective will not be considered pending until all applications accepted for filing on or before the date the final rule becomes effective have been granted or denied by the Administrator.

D. Consideration of the Amendments to the CSA Made by the Hemp Provisions of the Agriculture Improvement Act of 2018

The Agriculture Improvement Act of 2018 (AIA), Public Law 115–334, which became effective December 20, 2018, contained various provisions regarding the cultivation of hemp. The AIA definitions hemp as the plant Cannabis sativa L. and any part of that plant, including the seeds thereof and all derivatives, extracts, cannabinoids, isomers, acids, salts, and salts of isomers, whether growing or not, with a delta-9 tetrahydrocannabinol concentration of not more than 0.3 percent on a dry weight basis. 7 U.S.C. 1639*o*(1). The AIA amended the CSA definition of marihuana to exclude hemp. Thus, anything that falls within the foregoing definition of hemp is no longer a controlled substance, and the CSA's requirements no longer apply to such substances. Accordingly, this proposed rule would apply only to persons seeking authorization under the CSA (*i.e.,* seeking a DEA registration) to manufacture marihuana that involves the planting, cultivation, growing, or harvesting of marihuana as that term is currently defined in the CSA (21 U.S.C. 802(16)).[16]

E. Factors Affecting Prices for the Purchase and Sale of Marihuana by DEA

As stated above, under articles 23 and 28 of the Single Convention, the government agency must—in addition to taking physical possession—*purchase* all lawfully grown cannabis crops within four months of harvest. Thus, under the proposed rule, DEA will purchase marihuana grown by DEA-registered manufacturers and subsequently sell the marihuana to DEA registrants who seek to acquire it for research, product development, or other lawful purposes under the CSA.

In purchasing such marihuana, DEA intends to use the Diversion Control Fee Account, as established in 21 U.S.C. 886a. Thus, DEA would, under the proposed rule, need to take into account its obligation under 21 U.S.C. 886a(1)(C) to charge fees under its diversion control program ''at a level that ensures the recovery of the full costs of operating the various aspects of that program.'' There are two potential categories of fees that could be used to recover the costs of carrying out the proposed new aspects of the diversion control program relating to cannabis: (1) Fees charged to persons who apply for, and seek to renew, a DEA registration to manufacture marihuana, and (2) fees charged for the sale of marihuana by DEA.

DEA believes that economic forces will not only drive the types, varieties and strains of marihuana materials that will be produced by growers, but that such forces will also drive the fees that DEA-registrants will be willing to pay for marihuana used for research purposes. Accordingly, DEA proposes to allow market forces to direct prices for marihuana grown by the manufacturer and purchased by DEA. As we have stated elsewhere in this proposal, DEA will establish limits on individual production based on bona fide supply agreements between the grower and the end user (a DEA registered manufacturer or a schedule I researcher). Accordingly, DEA will use these terms as the basis for purchasing marijuana from the grower and additionally, for the basis by which it will sell that same marihuana to an end user.

In addition to that negotiated fee, DEA is proposing to add a variable administrative cost (per kilogram (kg)) which it intends to add onto the sales price of the marihuana it sells to end users. The purpose of this administrative fee is to ensure the full recovery by DEA of the costs of administering the program as required by 21 U.S.C. 886a(1)(C). DEA will calculate this variable cost annually by taking the preceding fiscal year's cost to operate the program and dividing it by the quantity in kg of the manufacturing quota for marihuana issued during the current quota year. For example, based on the economic analysis provided below, DEA would calculate an administrative fee of $304 per kg for marihuana distributed to end users. The calculation below is illustrative:

Variable Administrative Fee = $607,644/2,000 kg = $304 per kg[17]

DEA proposes to establish this fee no less than annually and proposes to publish this rate on its website by December 15th of the year preceding the year in which the administrative fee will be collected.

[15] The proposed rule provides that, in determining the legitimate demand for marihuana and its derivatives in the United States, the Administrator shall consult with the Department of Health and Human Services, including its components.

[16] The United States Department of Agriculture has issued regulations and guidance to implement a program for the commercial production of industrial hemp in the United States under the framework of the AIA. *See Establishment of a Domestic Hemp Production Program,* 84 FR 58522 (Oct. 31, 2019).

[17] Rounded to nearest whole dollar. The cost of $607,644 is explained below.

Regulatory Analyses

Executive Orders 12866 (Regulatory Planning and Review), 13563 (Improving Regulation and Regulatory Review), and 13771 (Reducing Regulation and Controlling Regulatory Costs)

This proposed rule was developed in accordance with the principles of Executive Orders 12866, 13563, and 13771. Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, if regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health, and safety, and other advantages; distributive impacts; and equity). Executive Order 13563 is supplemental to and reaffirms the principles, structures, and definitions governing regulatory review established in Executive Order 12866. Section 3(f) of Executive Order 12866 classifies a ''significant regulatory action,'' requiring review by the Office of Management and Budget (OMB), as any regulatory action that is likely to result in a rule that may: (1) Have an annual effect on the economy of $100 million or more or adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, or tribal governments or communities; (2) create a serious inconsistency or otherwise interfere with an action taken or planned by another agency; (3) materially alter the budgetary impact of entitlements, grants, user fees, or loan programs or the rights and obligations of recipients thereof; or (4) raise novel legal or policy issues arising out of legal mandates, the President's priorities, or the principles set forth in the Executive order.

DEA has determined that, although this proposed rule is not economically significant, it is a significant regulatory action under section 3(f) of Executive Order 12866, thus subjecting it to review by OMB.

I. Need for the Rule

This rule is needed to ensure that DEA complies with the CSA and grants registrations that are consistent with relevant treaty provisions as DEA seeks to increase the number of registered growers of marihuana. Specifically, this proposed rule would amend the provisions of the regulations governing applications by persons seeking to become registered with DEA to grow marihuana as bulk manufacturers and add provisions related to the purchase and sale of this marihuana by DEA. These amendments will ensure that DEA carries out all five functions under Article 23 and Article 28 of the Single Convention pertaining to marihuana, thus facilitating the planning and coordinated management of marihuana production necessary as the number of registered marihuana manufacturers increases.

II. Alternative Approaches

This proposed rule would amend DEA regulations only to the extent necessary to comply with the CSA and to ensure DEA grants registrations that are consistent with the Single Convention as it pertains to marihuana. In areas where DEA has discretion, such as in setting a fee structure to recover the cost of this proposed rule, alternative approaches would be discussed. However, because DEA does not have sufficient information at this time to discuss alternatives for either the future registration fees or the fees for the sale of marihuana, the alternative approaches for such provisions are not included in this proposed rule. Consistent with past agency practice, any proposed changes to registration fees will be the subject of a separate rulemaking proceeding, including a discussion of alternative approaches.

III. Analysis of Benefits and Costs

There are two key benefits associated with this proposed rule. First, DEA believes it is possible that the approval of new growers may increase the variety (quality, potency, etc.) of bulk marihuana for research, leading to more effective research and potentially resulting in the development of FDA-approved drug products. Second, this rule would ensure that DEA's regulations comply with the requirements of the CSA by granting registrations that are consistent with the Single Convention relating to marihuana. DEA is unable to quantify these benefits at this time.

DEA analyzed the costs of this proposed rule and estimates an annual cost of $607,644. The details of the analysis are below.

This proposed rule would amend the provisions of the regulations governing applications by persons seeking to become registered with DEA to grow marihuana as bulk manufacturers and add provisions related to the purchase and sale of this marihuana by DEA. If this proposed rule is promulgated, the following key changes are anticipated: More persons will be authorized to grow marihuana, DEA will purchase and take title to the crops of marihuana, and DEA will, with respect to marihuana, have the exclusive right of importing, exporting, wholesale trading, and maintaining stocks. These changes would mean that authorized purchasers of bulk marihuana to be used for research, product development, and other purposes permitted by the CSA may only purchase from DEA, except that DEA's exclusive rights would not extend to medicinal cannabis or cannabis preparations. The changes described above would affect three primary groups of entities: Growers and prospective growers, the authorizing agencies,[18] and purchasers (generally medical and scientific researchers). To examine the impact of the proposed rule, DEA first reviewed the current system for growing and distributing bulk marihuana, then examined the impact on each of the three affected groups.

Current System

Under current regulations, DEA has authorized one grower, the National Center, to cultivate marihuana for research. NIDA contracts with the National Center to grow marihuana from seeds supplied initially by NIDA for use in research studies.[19] The National Center has designated a secure plot of land or indoor grow facility where marihuana crops are grown every few years, based on current and expected demand. The marihuana is grown, harvested, stored, and made available as bulk marihuana or other purified elements of marihuana to use for research.[20] NIDA obligated approximately $1.5 million in Fiscal Year 2015 under this contract.[21] This amount included costs unrelated to growing and cultivating marihuana, such as extracting chemical components and producing marihuana cigarettes and other marihuana-related material. However, based on recent discussion with NIDA,[22] DEA estimates NIDA's expenses under the contract with the National Center (and any related

[18] The ''authorizing agency'' refers to federal government agencies, including NIDA and DEA.

[19] Production, Analysis, and Distribution of Cannabis and Related Materials, Federal Business Opportunities (Apr. 12, 2015), *https://www.fbo.gov/spg/HHS/NIH/NIDA-01/N01DA-15-7793/listing.html*.

[20] NIDA's Role in Providing Marijuana for Research, National Institute on Drug Abuse, *https://www.drugabuse.gov/drugs-abuse/marijuana/nidas-role-in-providing-marijuana-research*.

[21] Information on Marijuana Farm Contract, National Institute on Drug Abuse, *https://www.drugabuse.gov/drugs-abuse/marijuana/nidas-role-in-providing-marijuana-research/information-marijuana-farm-contract*.

[22] Conference call between DEA Regulatory Drafting and Policy Support section and members of NIDA's Marijuana Drug Supply Program, July 30, 2019.

subcontracts) for the bulk marihuana for 2019 are approximately $2.9 million.[23] The $2.9 million includes compensation for the cultivating and the 2019 manufacturing quota (MQ) of 2,000 kgs for NIDA (National Center) as well as all other duties required in the contract.[24]

Researchers may obtain marihuana for use in research through NIDA's DSP. Bulk marihuana plant material produced under the NIDA DSP is currently available at no cost to research investigators supported by a NIH grant. Marihuana is also available to research investigators who are funded through non-federal sources. Although NIDA considered charging for marihuana on a ''cost-reimbursement basis,'' [25] the current policy is to provide the marihuana at no charge.[26]

Changes to Growers

If this proposed rule is implemented, DEA anticipates approving more than one person to cultivate and harvest bulk marihuana. As explained earlier in this document, the CSA imposes limitations on the number of registrations that DEA may issue to bulk manufacturers of a given schedule I or II controlled substance. In addition, in deciding whether to grant an application for any such registration, the CSA requires DEA to consider the other public interest factors of 21 U.S.C. 823(a), which must be evaluated on an applicant-by-applicant basis. Further, DEA cannot accurately predict in advance which particular applications will be granted, or how many. Accordingly, DEA is unable to accurately estimate the number of registered bulk marihuana growers. As a result, to allow for this analysis, DEA will estimate the economic impact of this proposed rule under two different hypothetical scenarios, the first in which the number of growers expands to three growers, and the second in which the number of growers expands to 15 growers. It should be understood that this range of potential registrants is not necessarily reflective of the actual number of applications that DEA will grant.

In 2016, DEA issued a policy statement regarding applications to become registered to manufacture marihuana to supply research.[27] Since the publication of the 2016 policy statement, DEA has received approximately 35 pending applications for registration as bulk manufacturer of marihuana for research. As indicated above, the CSA requires DEA to limit the total number of registered bulk manufacturers of a given schedule I or II controlled substance to that necessary to produce an adequate and uninterrupted supply under adequately competitive conditions. Therefore, DEA believes a range of 3 to 15 growers is a reasonable estimate for purposes of this economic analysis, with the understanding that the actual number could vary considerably.

The Aggregate Production Quota (APQ), which includes the MQ, represents the annual quantity of marihuana that is necessary for the estimated medical, scientific, research and industrial needs of the United States, for lawful export requirements, and for the establishment and maintenance of reserve stocks.[28] Therefore, given a constant MQ, if more growers are approved to produce bulk marihuana, the quantities of bulk marihuana produced and the cost of production (and the reimbursement of production cost through sales) is transferred from the single incumbent grower to new growers. This means that there is only a transfer of economic activity rather than any new cost. The estimated economic activity of $2.9 million is transferred from the existing single grower to multiple growers.[29]

Transitioning from one large grower to multiple growers may introduce inefficiencies, driving up production or facility costs. Some growers may introduce more costly growing techniques to produce certain traits. Alternatively, some growers may introduce more efficient growing methods, driving down costs. Additionally, having more growers may spur more demand in bulk marihuana for research, pushing up the MQ. In particular, one of the goals of this new rule is to enhance marijuana availability for product development, which may have the effect of increasing the MQ. However, DEA does not have a basis to estimate the impact of these possibilities. Therefore, for the purposes of this analysis, DEA estimates that an increase in the number of approved growers does not impact the MQ. In summary, there is no new cost to growers.

Changes to Authorizing Agencies—Cost to DEA

DEA anticipates that there will be a transfer of economic activity from NIDA to DEA as well as several new costs as a result of this rule. This analysis should in no way be construed as a proposal to modify agency funding or funding sources.

As discussed above, assuming a constant MQ for bulk marihuana of 2,000 kgs, DEA estimates the cost of all the activities the National Center performs under its contract with NIDA and the purchase of the entire aggregate crop, regardless of the number of growers, is $2.9 million. This $2.9 million is not a new cost; it is a transfer. Rather than NIDA paying the current single grower, DEA would pay the multiple new growers. In practice, DEA anticipates crops from multiple growers will be purchased at different times of the year, allowing funds from sales of earlier purchases to pay for subsequent purchases. Therefore, to purchase and distribute $2.9 million in bulk marihuana, a working capital of a lesser amount is likely needed. However, due to many unknowns and to be conservative, for the purposes of this analysis, the estimated transfer and working capital requirement is $2.9 million.

DEA anticipates incurring new costs associated with the following activities: Taking title to the crops and employing personnel to administer the program. The growers, purchasers, and DEA would already understand prior to growing and harvesting, the quantities of marihuana to be distributed and to whom the distribution would be made because the bona fide supply agreements presented during the registration application process would provide such information. In most instances, DEA is expected to purchase and take title to the crop, then sell and distribute the crop to the purchaser on the same day at the grower's registered location. For the purposes of this analysis, DEA assumes the following process:

1. After marihuana is harvested and prepared for delivery to DEA, the registered manufacturer will contact

[23] Anticipated spending for the marihuana DSP for 2019 is $3.3 million to $3.4 million, of which 10%–15% meet the definition of ''hemp'' under the provisions of the AIA. Using the midpoint of these ranges, the estimated spending is $2.9 million for marihuana, excluding hemp. The figures are based on a general discussion, and actual figures may differ.

[24] The 2019 Aggregate Production Quota for all marihuana is 2,450 kgs. 2,000 of the 2,450 kgs are for the NIDA (National Center) cultivating and manufacturing quota of bulk marihuana. *See* 83 FR 67348.

[25] Marijuana Plant Material Available from the NIDA Drug Supply Program, National Institute on Drug Abuse, *https://www.drugabuse.gov/research/research-data-measures-resources/nida-drug-supply-program/marijuana-plant-material-available-nida-drug-supply-program.*

[26] *See* note 22.

[27] Applications to Become Registered Under the Controlled Substances Act to Manufacture Marijuana to Supply Researchers in the United States, 81 FR 53846 (Aug. 12, 2016). This proposed rule, if adopted, would supersede the 2016 policy statement.

[28] 21 CFR 1303.11(a).

[29] The phrase ''multiple growers'' includes the possibility that the current grower is one of ''multiple growers.''

DEA to inform it that the marihuana is ready for collection.

2. Within a reasonable timeframe, but in no event later than four months after the harvest, DEA will purchase and take title to the marihuana. Two DEA Special Agents (or Deputized Task Force Officers) from the nearest local DEA field office will drive an estimated 100 miles (200 miles roundtrip) to the registered manufacturer to take title. Any marihuana that is not immediately distributed is stored in a designated secure storage mechanism at the grower's registered location for later distribution. The number of trips by the two DEA Special Agents equals the number of harvests.

3. For marihuana distributed from storage at the grower's registered location, the grower distributes marihuana on DEA's behalf. If DEA deems it necessary to be present at such distribution, the distribution is scheduled to coincide with DEA's visit to take title to the next crop, requiring no additional trips by DEA to the grower.

4. Each grower has three harvests, requiring DEA to collect three times per year per grower.

For each collection, DEA estimates $2,071 of labor cost [30] and $116 of vehicle cost [31] for a total of $2,187 per collection. DEA understands that some growers, employing certain growing methods, may have more harvests per year. However, DEA does not have a basis to estimate these growers' methods or the number of harvests per year. Therefore, DEA believes three harvests per year is a reasonable estimate. Assuming three collections per year per grower, there would be nine collections with three approved growers and 45 collections with 15 approved growers. Applying the estimated cost of $2,187 per collection, DEA estimates a transport cost of $19,683 and $98,415 for scenarios with three and 15 growers, respectively.

Additionally, DEA anticipates it would need additional personnel resources to operate this program. There are many unknowns and no decisions have been made on hiring. However, for the purposes of this analysis, DEA estimates three full-time-equivalent (FTE) professional staff in the Diversion Control Division would be needed, consisting of one FTE diversion investigator (DI), and two FTE professional/administrative (PA) resources.

Applying the fully loaded annual cost of $211,981 per DI and $168,307 per PA, the estimated total cost of the three FTE employees is $548,595. For the purposes of this analysis, this cost does not vary with the number of growers. Table 1 below summarizes the costs associated with increased staffing.

TABLE 1—COST OF PERSONNEL RESOURCES

Position	Job category	Modular cost/ unit cost ($)	Number of FTEs	Cost ($)
Staff Coordinator	DI	211,981	1	211,981
Program Analyst	PA	168,307	2	336,614
Total	N/A	N/A	3	548,595

In summary the estimated cost to DEA is:

- $19,683 or $98,415 per year to purchase and take title to the bulk marihuana for scenarios with 3 or 15 authorized growers, respectively;
- $548,595 per year for three DEA FTE employees;
- The estimated total annual cost is $568,278 with three growers and $647,010 with 15 growers and no offsetting cost savings at NIDA. Using the average of the two values, the estimated cost to DEA is $607,644. Table 2 summarizes the costs.

TABLE 2—DEA COST SUMMARY

	Low ($)	High ($)	Average ($)
Transport Cost	19,683	98,415	N/A
Personnel Cost	548,596	548,595	N/A
Total Cost	568,278	647,010	607,644

Changes Affecting Researchers

DEA anticipates minimal procedural change for authorized researchers who plan to acquire bulk marihuana for research. The only anticipated procedural change is that some researchers would acquire the bulk marihuana from DEA, rather than from NIDA. As discussed earlier, the only new cost associated with this proposed regulation is the cost to DEA of $607,644, an average of high and low scenarios, which would be recovered by adding an administrative fee of $304 per kg. As discussed earlier, the administrative fee would be adjusted annually.

While the purchaser would purchase marihuana from DEA, this rule does not in any way affect the purchaser's source of funds to purchase from DEA. If marihuana for research is funded by a third party, the researcher may not experience any cost increase. In particular, NIH has long served as a third-party funder for research through grants, including grants to researchers studying marihuana. Nothing in this rule prohibits NIH from continuing to fund such research by continuing to cover the cost of marihuana materials

[30] DEA's loaded hourly rate of a Special Agent is $103.54. Assuming 10 hours each (full work-day) for two agents, the total labor cost associated with collection from a registered manufacturer is $2,071. ''Loaded hourly rate'' includes wages, benefits, and ''loading'' of ''non-productive'' hours, *i.e.,* leave, training, travel, etc.

[31] $116 is based on IRS standard mileage rates for 2019 of $0.58 per mile multiplied by the estimated 200 miles driven, roundtrip.

used in research, via grants to researchers.

Cost Summary

DEA estimates the cost of producing the 2019 MQ for bulk marihuana of 2,000 kgs and operating NIDA's marihuana DSP is $2.9 million per year. Under the proposed rule, DEA anticipates more bulk marihuana producers would be approved. DEA estimates the $2.9 million in economic activity would be transferred across multiple growers, without introducing new costs.

DEA's purchase of bulk marihuana is not a new cost (to the economy); it is a transfer from NIDA to DEA. However, $568,278 to $647,010 in operating costs would be incurred by DEA. DEA will recover the costs of carrying out the proposed new aspects of the diversion control program relating to marihuana by selling the marihuana to the buyer at the negotiated sale price, between the grower and the buyer, plus the administrative fee assessed on a per kg basis.

The net present values (NPVs) of the low cost estimate of $568,278 per year over 10 years are $4.8 million and $4.0 million at a three percent discount rate and 7 percent discount rate, respectively. The NPVs of the high cost estimate of $647,010 over 10 years are $5.5 million and $4.5 million at a three percent discount rate and seven percent discount rate, respectively. The average of the estimated low and high costs is $607,644. The NPVs of the average of $607,644 over 10 years are $5.2 million and $4.3 million at three percent and seven percent discount rates, respectively. Table 3 summarizes the estimated annual effect and NPVs calculation for each of the transfers and the three scenarios.

TABLE 3—SUMMARY OF ANNUAL EFFECT AND NPVS

	Annual effect ($)	NPVs at 3% ($M)	NPVs at 7% ($M)
Cost (Low)	568,278	4.8	4.0
Cost (Average)	607,644	5.2	4.3
Cost (High)	647,010	5.5	4.5

Executive Order 13771 (Reducing Regulation and Controlling Regulatory Costs)

This proposed rule is expected to be a deregulatory action for the purposes of Executive Order 13771. The rule is an enabling rule which, coincidentally with other provisions, expands the number of authorized bulk marihuana growers.

Executive Order 12988 (Civil Justice Reform)

This proposed rule meets the applicable standards set forth in sections 3(a) and 3(b)(2) of Executive Order 12988, Civil Justice Reform, to eliminate ambiguity, minimize litigation, establish clear legal standards, and reduce burdens on regulated parties and the court system.

Executive Order 13132 (Federalism)

This proposed rule does not have federalism implications warranting the application of Executive Order 13132. The proposed rule does not have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government.

Executive Order 13175 (Consultation and Coordination With Indian Tribal Governments)

This proposed rule does not have tribal implications warranting the application of Executive Order 13175. It does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal Government and Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes.

Regulatory Flexibility Act

In accordance with the Regulatory Flexibility Act (RFA), DEA evaluated the impact of this rule on small entities. DEA's evaluation of economic impact by size category indicates that the proposed rule will not, if promulgated, have a significant economic impact on a substantial number of these small entities.

The RFA requires agencies to analyze options for regulatory relief of small entities unless the agency can certify that the rule will not have a significant impact on a substantial number of small entities. For purposes of the RFA, small entities include small businesses, nonprofit organizations, and small governmental jurisdictions. DEA evaluated the impact of this rule on small entities and a discussion of its findings is below.

As discussed in the section of this proposed rulemaking relating to Executive Orders 12866, 13565, and 13771, this proposed rule would amend the provisions of the regulations governing applications by persons seeking to become registered with DEA to grow marihuana as bulk manufacturers, and add provisions related to the purchase and sale of this marihuana by DEA. If this proposed rule is promulgated, the following key changes are anticipated: More persons will be authorized to grow marihuana; DEA will purchase and take physical possession of crops; and DEA will, with respect to marihuana, have the exclusive right of importing, exporting, wholesale trading, and maintaining stocks. These changes, as explained above, would mean that authorized purchasers of bulk marihuana may only purchase from DEA, except that DEA's exclusive right would not extend to medicinal cannabis or cannabis preparations as these terms are defined in paragraphs (b) and (c), respectively, of proposed § 1318.02 of this proposed rule.

The changes described above would affect three primary groups of entities: Growers and prospective growers, the authorizing agencies (including NIDA and DEA), and purchasers (generally researchers). Because any economic impact on federal agencies is outside the scope of the RFA, the transfer of economic activity between the agencies is excluded from this discussion. To examine the impact of the proposed rule, DEA first reviewed the current system for growing and distributing bulk marihuana, then examined the impact on each of the two affected non-federal groups: Growers (bulk manufacturers of marihuana) and researchers.

Current System

Under current regulations, DEA has authorized one grower, the National Center, to cultivate marihuana for research. NIDA contracts with the National Center to grow marihuana for

use in research studies.[32] The National Center designates a secure plot of land where marihuana crops are grown every few years, based on current and expected demand. The marihuana is grown, harvested, stored, and made available as bulk marihuana or other purified elements of marihuana to use for research.[33] As explained previously, DEA estimates NIDA's expenses under the contract with the National Center (and any related subcontracts) for the bulk marihuana for 2019 are approximately $2.9 million.[34] The $2.9 million includes compensation for the cultivating and the 2019 MQ of 2,000 kgs for NIDA as well as all other duties required in the contract.[35]

Researchers may obtain marihuana for use in research through NIDA's DSP. Bulk marihuana plant material produced under the NIDA DSP is available at no cost to research investigators who are supported by an NIH grant. Marihuana is also available to research investigators who are funded through non-federal sources. Although NIDA considered charging for marihuana on a ''cost-reimbursement basis,'' [36] the current policy is to provide the marihuana at no charge.[37]

Impact on Growers

If this proposed rule is implemented, DEA anticipates approving more than one person to cultivate and harvest bulk marihuana. In 2016, DEA issued a policy statement regarding applications to become registered to manufacture marihuana to supply research.[38] Since the publication of the 2016 policy statement, there are approximately 35 pending applications for registration as bulk manufacturer of marihuana for research. Additionally, some applicants may not meet the statutory and regulatory criteria for holding a registration as a bulk manufacture and will be denied. Therefore, for the purposes of this analysis, DEA will estimate the economic impact of this proposed rule at three and 15 growers with the understanding that the actual number could vary considerably.

The APQ, which includes the MQ, represents the annual quantity of marihuana that is necessary for the estimated medical, scientific, research and industrial needs of the United States, for lawful export requirements, and for the establishment and maintenance of reserve stocks.[39] Therefore, given a constant MQ, if more growers are approved to produce bulk marihuana, the quantities of bulk marihuana produced and the cost of production (and reimbursement of their production cost through sales) is transferred from the incumbent grower to new growers. This means that there is no new cost; instead, there is only a transfer of economic activity. The estimated economic activity of $2.9 million is transferred from the existing single grower to multiple growers.[40]

Transitioning from one large grower to multiple smaller growers may reduce production efficiency, driving up cost. Some growers may introduce more costly growing techniques in order to produce certain traits. Alternatively, some growers may introduce more efficient growing methods, driving down cost. Additionally, having more growers may spur more demand in bulk marihuana for research, pushing up the MQ. However, DEA does not have a basis to estimate the impact of these possibilities.

Impact on Researchers

DEA anticipates minimal procedural change for authorized researchers who plan to acquire bulk marihuana for research. The only anticipated procedural change is that the researcher would acquire the bulk marihuana from DEA, rather than from NIDA or the National Center. As discussed earlier, the only new cost associated with this proposed regulation is the cost to DEA of $607,644, which would be recovered by adding an administrative fee of $304 per kg. As discussed earlier, the administrative fee would be adjusted annually. While purchasers would purchase marihuana from DEA, this rule does not in any way affect the purchasers' source of funds to purchase from DEA. If marihuana for research is funded by a third party, the researcher may not experience any cost increase.

Affected Number of Small Entities

This proposed rule affects the current and prospective bulk manufacturers of marihuana for research and researchers. Based on the discussion above, DEA anticipates up to 15 bulk manufacturers are affected by this proposed rule. Additionally, based on a discussion with NIDA,[41] DEA estimates 40 researchers are affected by this proposed rule. The 40 researchers represent the approximate number of researchers that receive marihuana from NIDA's marihuana DSP.

Based on a review of representative North American Industry Classification System (NAICS) codes for bulk manufacturers and researchers, the following number of firms may be affected:[42]

- 421 firms related to 'Medicinal and Botanical Manufacturing' (325411)[43]
- 9,634 firms related to 'Research and Development in the Physical, Engineering, and Life Sciences (except Biotechnology)' (541712)[44]

The United States Small Business Administration (SBA) sets size standards that determine how large an entity can be and still qualify as a small business for federal government programs. For the most part, size standards are based on the average annual receipts or the average number of employees of a firm. The SBA size standard for both industries identified by the NAICS codes above is 1,000 employees.[45]

Comparing the SBA size standards to the U.S. Census Bureau, Statistics of U.S. Businesses (SUSB) detailed data on establishment size by NAICS code for each affected industry, DEA estimates

[32] Production, Analysis, and Distribution of Cannabis and Related Materials, Federal Business Opportunities (Apr. 12, 2015), *https://www.fbo.gov/spg/HHS/NIH/NIDA-01/N01DA-15-7793/listing.html*.

[33] NIDA's Role in Providing Marijuana for Research, National Institute on Drug Abuse, *https://www.drugabuse.gov/drugs-abuse/marijuana/nidas-role-in-providing-marijuana-research*.

[34] Anticipated spending for the marihuana DSP for 2019 is $3.3 million to $3.4 million, of which 10 percent to 15 percent meet the definition of ''hemp'' under the provisions of the AIA. Using the midpoint of these ranges, the estimated spending is $2.9 million. The figures are based on a general discussion, and actual figures may differ.

[35] The 2019 APQ for all manufacturers of marihuana is 2,450 kgs. 2,000 kgs are for cultivating and manufacturing of bulk marihuana. *See* 83 FR 67348.

[36] Marijuana Plant Material Available from the NIDA Drug Supply Program, National Institute on Drug Abuse, *https://www.drugabuse.gov/research/research-data-measures-resources/nida-drug-supply-program/marijuana-plant-material-available-nida-drug-supply-program*.

[37] *See* note 22.

[38] Applications to Become Registered under the Controlled Substances Act to Manufacture Marijuana to Supply Researchers in the United States, 81 FR 53846 (2016). This proposed rule, if adopted, would superseded the 2016 policy statement.

[39] 21 U.S.C. 826(a).

[40] The phrase ''multiple growers'' includes the possibility that the current grower is one of the ''multiple growers.''

[41] *See* note 22.

[42] For the purposes of this analysis, the term ''firms'' is synonymous with ''entities.''

[43] 2015 SUSB Annual Datasets by Establishment Industry, U.S. & States, NAICS, Detailed Employment Sizes (U.S., 6-digit and States, NAICS Sectors), United States Census Bureau, *https://www.census.gov/data/datasets/2015/econ/susb/2015-susb.html*.

[44] *Ibid.*

[45] Table of Small Business Size Standards Matched to North American Industry Classification System Codes, United States Small Business Association (Oct. 1, 2017). The NAICS code was updated for 'Research and Development in the Physical, Engineering, and Life Sciences (except Biotechnology)' from 541712 to 541715. The 2015 SUSB data uses 541712 and the 2017 SBA size standard uses 541715 for the same industry.

the following number of small entities and percent of firms that are small entities by industry:

- 392 (93.1 percent of total) firms in the area of 'Medicinal and Botanical Manufacturing' (325411)
- 9,090 (94.4 percent of total) firms in the area of 'Research and Development in the Physical, Engineering, and Life Sciences (except Biotechnology)' (541712)

Table 4 details the calculation for the number of small entities by industry.

TABLE 4—NUMBER OF SMALL ENTITIES BY INDUSTRY

NAICS description	Firm size by average employees	Firms	SBA size standard	Small entities	% Small entities
325411—Medicinal and Botanical Manufacturing	<500	384	1,000	384	100
	500–749	3		3	100
	750–999	5		5	100
	1,000–1,499	6			0
	1,500–1,999	2			0
	2,000–2,499	1			0
	2,500–4,999	7			0
	5,000+	13			0
Total		421		392	93.1
541712—Research and Development in the Physical, Engineering, and Life Sciences (except Biotechnology)	<500	8,972	1,000	8,972	100
	500–749	68		68	100
	750–999	50		50	100
	1,000–1,499	70			0
	1,500–1,999	40			0
	2,000–2,499	35			0
	2,500–4,999	132			0
	5,000+	267			0
Total		9,634		9,090	94.4

Applying the calculated respective percentage for small entities to the number of affected bulk manufacturers and researchers, DEA estimates 14 (15 × 93.1 percent) bulk manufacturers and 38 (40 × 94.4 percent) researchers, for a total of 52 small entities, will be affected by this proposed rule. The 14 affected small entity bulk manufacturers represent four percent of the estimated 392 small entities in the 'Medicinal and Botanical Manufacturing' (325412) industry, and the 38 affected small entity researchers represent 0.4 percent of the estimated 9,090 small entities in the 'Research and Development in the Physical, Engineering, and Life Sciences (except Biotechnology)' (541712) industry. Table 5 summarizes the calculations for the percentage of small entities that are affected by the proposed rule.

TABLE 5—PERCENT OF SMALL ENTITIES AFFECTED BY INDUSTRY

NAICS description	Number of firms	SBA size standard	Estimated number of small entities	Estimated number of affected small entities	Percentage of small entities affected
325411—Medicinal and Botanical Manufacturing	421	1,000	392	14	4
541712—Research and Development in the Physical, Engineering, and Life Sciences (except Biotechnology)	9,634	1,000	9,090	38	0.4
Total	10,055	N/A	9,482	52	N/A

DEA generally uses a threshold of 30 percent as a ''substantial'' number of affected small entities. Thus, the above analysis reveals that a non-substantial amount of small bulk manufacturer entities (4 percent) and of small researcher entities (0.4 percent) will be affected by this proposed rule.

DEA generally considers impacts that are greater than three percent of annual revenue to be a ''significant economic impact'' on an entity. As discussed earlier, DEA estimates that there will be a new cost to DEA of $568,278 to $647,010 per year, or the average of the high and low estimates of $607,644 per year. DEA will recover the costs of carrying out the proposed new aspects of the diversion control program relating to marihuana by selling the marihuana to the buyer at the negotiated sale price, between the grower and the buyer, plus the administrative fee assessed on a per kg basis. Based on the average of the high and low estimates of $607,644 and MQ of 2,000 kgs, the administrative fee is $304 per kg, adjusted annually.

Furthermore, NIH-funded or other third-party funded researchers are likely to request and receive enough funding

for the full price of marihuana, including the administrative fee. There would be no impact to these researchers. However, DEA does not have sufficient information to estimate the number of small entity researchers that would fall under this category. Although DEA is unable to quantify the economic impact for the estimated 14 small entity bulk manufacturers and 38 small entity researchers, the number of affected small entity manufacturers and researchers is not a substantial number of small entities in their respective industries.

Based on the analysis above, and because of these facts, DEA believes this proposed rule, if promulgated, will not have a significant economic impact on a substantial number of small entities.

Unfunded Mandates Reform Act of 1995

In accordance with the Unfunded Mandates Reform Act of 1995 (UMRA), 2 U.S.C. 1501 *et seq.,* DEA has determined that this action would not result in any Federal mandate that may result ''in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any 1 year.'' *See* 2 U.S.C. 1532(a). Therefore, neither a Small Government Agency Plan nor any other action is required under the UMRA.

Paperwork Reduction Act of 1995

Pursuant to the Paperwork Reduction Act of 1995 (PRA), 44 U.S.C. 3501 *et seq.,* DEA has identified the following collections of information related to this proposed rule. A person is not required to respond to a collection of information unless it displays a valid OMB control number. Copies of existing information collections approved by OMB may be obtained at *https://www.reginfo.gov/.*

A. Collections of Information Associated With the Proposed Rule

Title: Application for Registration (DEA Form 225); Renewal Application for Registration (DEA Form 225A); Affidavit for Chain Renewal (DEA Form 225B).

OMB control number: 1117–0012.

Form numbers: DEA–225, DEA–225A, DEA–225B.

Type of information collection: Revision of a currently approved collection.

Applicable component of the department sponsoring the collection: Department of Justice/Drug Enforcement Administration, Diversion Control Division.

Affected public who will be asked or required to respond: Business or other for-profit.

Abstract: The Controlled Substances Act requires all businesses and individuals who manufacture, distribute, import, export, or conduct research and laboratory analysis with controlled substances to register with DEA. 21 U.S.C. 822; 21 CFR 1301.11, 1301.13. Registration is a necessary control measure that helps to detect and prevent diversion by ensuring that the closed system of distribution of controlled substances can be monitored by DEA, and that the businesses and individuals handling controlled substances are accountable.

If adopted, this proposed rule would amend the regulations governing applications by persons seeking to become registered with DEA to grow marihuana as bulk manufacturers and add provisions related to the purchase and sale of this marihuana by DEA. Persons seeking to become registered with DEA to grow marihuana as bulk manufacturers would still apply for registration using the same DEA Form 225 as other bulk manufacturers, but DEA would use a new supplemental questionnaire unique to marihuana manufacturers in order to gather additional information about applicants. There would also be new questionnaires used for importer applicants and non-marihuana bulk manufacturer applicants. Forms 225, 225A, and 225B would all receive minor revisions to improve clarity and usability for registrants.

DEA estimates the following number of respondents and burden associated with this collection of information:

- *Number of respondents:* 15,919.
- *Frequency of response:* 1 per respondent per year.
- *Number of responses:* 15,919.
- *Burden per response:* 0.1304 hours.
- *Total annual burden in hours:* 2,076.

B. Request for Comments Regarding the Proposed Collections of Information

Written comments and suggestions from the public and affected entities concerning the proposed collections of information are encouraged. Under the PRA, DEA is required to provide a notice regarding the proposed collections of information in the **Federal Register** with the notice of proposed rulemaking and solicit public comment. Pursuant to section 3506(c)(2) of the PRA (44 U.S.C. 3506(c)(2)), DEA solicits comment on the following issues:

- Whether the proposed collection of information is necessary for the proper performance of the functions of DEA, including whether the information shall have practical utility.
- The accuracy of DEA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used.
- Recommendations to enhance the quality, utility, and clarity of the information to be collected.
- Recommendations to minimize the burden of the collection of information on those who are to respond, including through the use of automated collection techniques or other forms of information technology.

Please send written comments to the Office of Information and Regulatory Affairs, OMB, Attention: Desk Officer for DOJ, Washington, DC 20503. Please state that your comments refer to RIN 1117–AB54/Docket No. DEA–506. All comments must be submitted to OMB on or before May 22, 2020. The final rule will respond to any OMB or public comments on the information collection requirements contained in this proposed rule.

If you need a copy of the proposed information collection instrument(s) with instructions or additional information, please contact the Regulatory Drafting and Policy Support Section (DPW), Diversion Control Division, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152–2639; Telephone: (571) 362–3261.

List of Subjects

21 CFR Part 1301

Administrative practice and procedure, Drug traffic control, Security measures.

21 CFR Part 1318

Administrative practice and procedure, Drug traffic control.

For the reasons stated in the preamble, DEA proposes to amend 21 CFR chapter II as follows:

PART 1301—REGISTRATION OF MANUFACTURERS, DISTRIBUTORS, AND DISPENSERS OF CONTROLLED SUBSTANCES

■ 1. The authority citation for part 1301 continues to read as follows:

Authority: 21 U.S.C. 821, 822, 823, 824, 831, 871(b), 875, 877, 886a, 951, 952, 956, 957, 958, 965 unless otherwise noted.

■ 2. In § 1301.33, revise paragraph (c) and add paragraph (d) to read as follows:

§ 1301.33 Application for bulk manufacture of Schedule I and II substances.

* * * * *

(c) Except as provided in paragraph (d) of this section, this section shall not apply to the manufacture of basic classes of controlled substances listed in Schedule I or II as an incident to research or chemical analysis as authorized in § 1301.13(e)(1).

(d) An application for registration to manufacture marihuana that involves the planting, cultivating, growing, or harvesting of marihuana shall be subject to the requirements of this section and the additional requirements set forth in part 1318 of this chapter.

■ 3. Add part 1318 to read as follows:

PART 1318—CONTROLS TO SATISFY THE REQUIREMENTS OF THE ACT APPLICABLE TO THE MANUFACTURING OF MARIHUANA

Sec.

Authority: 21 U.S.C. 801(7), 821, 822(a)(1), (b), 823(a), 871(b), 886a.

§ 1318.01 Scope of this part.

Procedures governing the registration of manufacturers seeking to plant, grow, cultivate, or harvest marihuana are set forth by this part.

§ 1318.02 Definitions.

(a) Except as provided in paragraph (e) of this section, the term *cannabis* means any plant of the genus Cannabis.

(b) Except as provided in paragraph (e) of this section, the term *medicinal cannabis* means a drug product made from the cannabis plant, or derivatives thereof, that can be legally marketed under the Federal Food, Drug, and Cosmetic Act.

(c) Except as provided in paragraph (e) of this section, the term *cannabis preparation* means cannabis that was delivered to the Administration and subsequently converted by a registered manufacturer into a mixture (solid or liquid) containing cannabis, cannabis resin, or extracts of cannabis.

(d) Except as provided in paragraph (e) of this section, the term *cannabis resin* means the separated resin, whether crude or purified, obtained from the cannabis plant.

(e) As used in this part, the terms *cannabis, medicinal cannabis,* and *cannabis preparation* do not include any material, compound, mixture, or preparation that falls outside the definition of marihuana in section 102(16) of the Controlled Substances Act (the Act) (21 U.S.C. 802(16)).

(f) The term *Single Convention* means the Single Convention on Narcotic Drugs, 1961 (18 U.S.T. 1407).

(g) The term *bona fide supply agreement* means a letter of intent, purchase order or contract between an applicant and a researcher or manufacturer registered under the Act.

(h) The term *registered researcher or manufacturer* means a person registered under the Act to perform research or manufacture of marihuana in Schedule I.

§ 1318.03 Implementation of statutory requirements.

(a) As provided in section 303(a) of the Act (21 U.S.C. 823(a)), the Administrator may grant an application for a registration to manufacture marihuana, including the cultivation of cannabis, only if he determines that such registration is consistent with the public interest and with United States obligations under the Single Convention.

(b) In accordance with section 303(a) of the Act and § 1301.44(a) of this chapter, the burden shall be on the applicant to demonstrate that the requirements for such registration have been satisfied.

§ 1318.04 Specific control measures applicable to the bulk manufacture of marihuana.

For a registration to manufacture marihuana that involves the cultivation of cannabis, the following provisions must be satisfied:

(a) All registered manufacturers who cultivate cannabis shall deliver their total crops of cannabis to the Administration. The Administration shall purchase and take physical possession of such crops as soon as possible, but not later than four months after the end of the harvest. The Administration may accept delivery and maintain possession of such crops at the registered location of the registered manufacturer authorized to cultivate cannabis consistent with the maintenance of effective controls against diversion. In such cases, the Administration shall designate a secure storage mechanism at the registered location in which the Administration may maintain possession of the cannabis, and the Administration will control access to the stored cannabis. If the Administration determines that no suitable location exists at the registered location of the registered manufacturer authorized to cultivate cannabis, then the Administration shall designate a location for the authorized grower to deliver the crop as soon as possible, but not later than four months after the end of the harvest. However, in all cases the registrant must comply with the security requirements specified in part 1301 of this chapter.

(b) The Administration shall, with respect to cannabis, have the exclusive right of importing, exporting, wholesale trading, and maintaining stocks other than those held by registered manufacturers and distributors of medicinal cannabis or cannabis preparations. Such exclusive right shall not extend to medicinal cannabis or cannabis preparations. The Administration may exercise its exclusive right by authorizing the performance of such activities by appropriately registered persons. The Administration shall require prior written notice of each proposed importation, exportation, or distribution of cannabis that specifies the quantity of cannabis to be imported, exported, or distributed and the name, address, and registration number of the registered manufacturer or researcher to receive the cannabis before authorizing the importation, exportation, or distribution. All importation and exportation shall be performed in compliance with part 1312 of this chapter, as applicable. Under no circumstance shall a registered manufacturer authorized to grow cannabis import, export, or distribute cannabis without the express written authorization of the Administration.

(c) A registered manufacturer authorized to grow cannabis shall notify in writing the Administration of its proposed date of harvest at least 15 days before the commencement of the harvest.

§ 1318.05 Application of the public interest factors.

(a) In accordance with section 303(a) of the Act (21 U.S.C. 823(a)), the Administrator shall consider the public interest factors set forth in paragraphs (a)(1) through (6) of this section:

(1) Maintenance of effective controls against diversion of particular controlled substances and any controlled substance in schedule I or II compounded therefrom into other than legitimate medical, scientific, research, or industrial channels, by limiting the importation and bulk manufacture of such controlled substances to a number of establishments which can produce an adequate and uninterrupted supply of these substances under adequately

competitive conditions for legitimate medical, scientific, research, and industrial purposes;

(2) Compliance with applicable State and local law;

(3) Promotion of technical advances in the art of manufacturing these substances and the development of new substances;

(4) Prior conviction record of applicant under Federal and State laws relating to the manufacture, distribution, or dispensing of such substances;

(5) Past experience in the manufacture of controlled substances, and the existence in the establishment of effective control against diversion; and

(6) Such other factors as may be relevant to and consistent with the public health and safety.

(b) The Administrator's determination of which applicants to select will be consistent with the public interest factors set forth in section 303(a), with particular emphasis on the following criteria:

(1) Whether the applicant has demonstrated prior compliance with the Act and this chapter;

(2) The applicant's ability to consistently produce and supply cannabis of a high quality and defined chemical composition; and

(3)(i) In determining under section 303(a)(1) of the Act (21 U.S.C. 823(a)(1)) the number of qualified applicants necessary to produce an adequate and uninterrupted supply of cannabis under adequately competitive conditions, the Administrator shall place particular emphasis on the extent to which any applicant is able to supply cannabis or its derivatives in quantities and varieties that will satisfy the anticipated demand of researchers and other registrants in the United States who wish to obtain cannabis to conduct activities permissible under the Act, as demonstrated through a bona fide supply agreement with a registered researcher or manufacturer as defined in this subpart.

(ii) If an applicant seeks registration to grow cannabis for its own research or product development, the applicant must possess registration as a schedule I researcher with respect to marihuana under § 1301.32 of this chapter. As specified in § 1301.13 of this chapter, chemical analysis and preclinical research (including quality control analysis) are not coincident activities of a manufacturing registration for schedule I substances, including cannabis. In determining under section 303(a)(1) of the Act (21 U.S.C. 823(a)(1)) the number of qualified applicants necessary to produce an adequate and uninterrupted supply of cannabis under adequately competitive conditions, the Administrator shall consider the holding of an approved marihuana research protocol by a registered schedule I researcher seeking to grow cannabis for its own research or product development as evidence of the necessity of the applicant's registration under this factor.

(c) Applications accepted for filing after [EFFECTIVE DATE OF FINAL RULE] will not be considered pending for purposes of paragraph (a) of this section until all applications accepted for filing on or before [EFFECTIVE DATE OF FINAL RULE] have been granted or denied by the Administrator. Where an application is subject to section 303(i) of the Act (21 U.S.C. 823(i)), that section shall apply in lieu of this paragraph (c).

(d) In determining the legitimate demand for cannabis and its derivatives in the United States, the Administrator shall consult with the U.S. Department of Health and Human Services, including its components.

§ 1318.06 Factors affecting prices for the purchase and sale by the Administration of cannabis.

(a) In accordance with section 111(b)(3) of Public Law 102–395 (21 U.S.C. 886a(1)(C)), seeking to recover the full costs of operating the aspects of the diversion control program that are related to issuing registrations that comply with the Controlled Substances Act (CSA), the Administration shall assess an administrative fee. To set the administrative fee, the Administration shall annually determine the preceding fiscal year's cost of operating the program to cultivate cannabis and shall divide the prior fiscal year's cost by the number of kgs of cannabis authorized to be manufactured in the current year's quota to arrive at the administrative fee per kg. The administrative fee per kg shall be added to the sale price of cannabis purchased from the Administration. The administrative fee shall be paid to the Diversion Control Fee Account.

(b) As set forth in § 1318.04, the Administration shall have the exclusive right of, among other things, wholesale trading in cannabis that it purchases from registered manufacturers. The Administration will, therefore, buy from such manufacturer, sell cannabis to registered researchers and manufacturers, and establish prices for such purchase and sale. The Administration will set such prices in the following manner:

(1) Bulk growers of cannabis shall negotiate directly with registered researchers and manufacturers authorized to handle cannabis to determine a sale price for their cannabis. Upon entering into a contract for the provision of bulk cannabis and prior to the exchange of cannabis, the parties shall pay to the Administration an administrative fee assessed based on the number of kgs to be supplied. The administrative fee shall not be recoverable in the event that delivery is rejected by the buyer.

(2) The Administration shall sell the cannabis to the buyer at the negotiated sale price plus the administrative fee assessed on a per kg basis. Prior to the purchase of the cannabis by the Administration, the buyer shall pay the negotiated purchase price and administrative fee to the Administration. The Administration shall hold funds equal to the purchase price in escrow until the delivery of the cannabis by the grower to the Administration. The administrative fee shall not be recoverable in the event that delivery is rejected by the buyer.

(3) After receiving the purchase price and administrative fee from the buyer, the Administration shall purchase the cannabis from the grower, on behalf of the buyer, at the negotiated sale price. The Administration shall retain the administrative fee. In the event the buyer fails to pay the purchase price and the administrative fee, the Administration shall have no obligation to purchase the crop and may order the grower to destroy the crop if the grower cannot find an alternative buyer within four months of harvest.

(4) In instances where the grower of the cannabis is the same entity as the buyer of the cannabis, or a related or subsidiary entity, the entity may establish a nominal price for the purchase of the cannabis. The Administration shall then purchase the entity's cannabis at that price and sell the cannabis back to the entity, or a related or subsidiary entity, at the same price with the addition of the administrative fee.

(c) Administrative fees set in accordance with this part will be made available, on an updated basis, on the Administration's website, no later than December 15th of the year preceding the year in which the administrative fee will be collected.

(d) Nothing in this section shall prohibit the U.S. Department of Health and Human Services from continuing to fund the acquisition of cannabis for use in research by paying, directly or indirectly, the purchase cost and administrative fee to the Administration.

§ 1318.07 Non-liability of Drug Enforcement Administration.

The Administration shall have no liability with respect to the performance of any contractual terms agreed to by a grower and buyer of bulk cannabis, including but not limited to the quality of any cannabis delivered to a buyer. In the event that a buyer deems the delivered cannabis to be defective, the buyer's sole remedy for damages shall be against the grower and not the Administration.

Dated: March 16, 2020.

Uttam Dhillon,

Acting Administrator.

[FR Doc. 2020–05796 Filed 3–20–20; 8:45 am]

BILLING CODE 4410–09–P

DEPARTMENT OF DEFENSE

Department of the Army, Corps of Engineers

33 CFR Part 209

[COE–2016–0016]

RIN 0710–AA72

Use of U.S. Army Corps of Engineers Reservoir Projects for Domestic, Municipal & Industrial Water Supply; Withdrawal

AGENCY: Army Corps of Engineers, DoD.

ACTION: Proposed rule; withdrawal.

SUMMARY: As a result of a policy determination by the Assistant Secretary of the Army (Civil Works), the U.S. Army Corps of Engineers (Corps) is withdrawing the proposed rule titled ''Use of U.S. Army Corps of Engineers Reservoir Projects for Domestic, Municipal & Industrial Water Supply,'' which was published on December 16, 2016.

DATES: The Corps is withdrawing the proposed rule published December 16, 2016 (81 FR 91556) as of March 23, 2020.

ADDRESSES: U.S. Army Corps of Engineers, 441 G Street NW, Washington, DC 20314.

FOR FURTHER INFORMATION CONTACT: Amy K. Frantz, Planning and Policy (CECW–P); telephone number: (202) 761–0106; email address: *WSRULE2016@usace.army.mil*; or Daniel Inkelas, Chief Counsel's Office (CECC–L); phone number (202) 761–0345; email address: *WSRULE2016@usace.army.mil*.

SUPPLEMENTARY INFORMATION: None.

Dated: March 16, 2020.

R.D. James,

Assistant Secretary of the Army, (Civil Works).

[FR Doc. 2020–05919 Filed 3–20–20; 8:45 am]

BILLING CODE 3720–58–P

DEPARTMENT OF EDUCATION

34 CFR Chapter III

[Docket No. ED–2020–OPE–0044]

Proposed Waiver and Extension of the Project Period for the Predominantly Black Institutions Competitive Grant Program

AGENCY: Office of Postsecondary Education (OPE), Department of Education.

ACTION: Proposed waiver and extension of project period.

SUMMARY: The Secretary proposes to waive the requirements in the Education Department General Administrative Regulations that generally prohibit project periods exceeding five years and project period extensions involving the obligation of additional Federal funds. The proposed waiver and extension would enable 23 projects under CFDA number 84.382A to receive funding for an additional period, not to exceed September 30, 2021.

DATES: We must receive your comments on or before April 22, 2020.

ADDRESSES: Submit your comments through the Federal eRulemaking Portal or via postal mail, commercial delivery, or hand delivery. We will not accept comments submitted by fax or by email or those submitted after the comment period. To ensure that we do not receive duplicate copies, please submit your comments only once. In addition, please include the Docket ID at the top of your comments.

If you are submitting comments electronically, we strongly encourage you to submit any comments or attachments in Microsoft Word format. If you must submit a comment in Adobe Portable Document Format (PDF), we strongly encourage you to convert the PDF to print-to-PDF format or to use some other commonly used searchable text format. Please do not submit the PDF in a scanned format. Using a print-to-PDF format allows the Department to electronically search and copy certain portions of your submissions.

- *Federal eRulemaking Portal:* Go to *www.regulations.gov* to submit your comments electronically. Information on using *Regulations.gov,* including instructions for accessing agency documents, submitting comments, and viewing the docket, is available on the site under ''Help.''
- *Postal Mail, Commercial Delivery, or Hand Delivery:* The Department strongly encourages commenters to submit their comments electronically. However, if you mail or deliver your comments about the proposed waiver and extension, address them to: The Predominantly Black Institutions Competitive Grant Program, CFDA number 84.382A, Attention: Bernadette Miles, U.S. Department of Education, 400 Maryland Avenue SW, Room 250–22, Washington, DC 20202.

Privacy Note: The Department's policy is to make all comments received from members of the public available for public viewing in their entirety on the Federal eRulemaking Portal at *www.regulations.gov.* Therefore, commenters should be careful to include in their comments only information that they wish to make publicly available.

FOR FURTHER INFORMATION CONTACT: Bernadette Miles, U.S. Department of Education, 400 Maryland Avenue SW, Room 250–22, Washington, DC 20202. Telephone: 202–453–7892. Email: *Bernadette.Miles@ed.gov.*

If you use a telecommunications device for the deaf (TDD) or a text telephone (TTY), call the Federal Relay Service (FRS), toll free, at 1–800–877–8339.

SUPPLEMENTARY INFORMATION:

Invitation to Comment: We invite you to submit comments regarding this proposed waiver and extension.

We invite you to assist us in complying with the specific requirements of Executive Orders 12866, 13563, and 13771 and their overall requirement of reducing regulatory burden that might result from this proposed waiver and extension. Please let us know of any further ways we could reduce potential costs or increase potential benefits while preserving the effective and efficient administration of the program.

During and after the comment period, you may inspect all public comments about this proposed waiver and extension of the project period in Room 5059, 550 12th Street SW, Washington, DC, between the hours of 8:30 a.m. and 4:00 p.m., Eastern time, Monday through Friday of each week, except Federal holidays.

Assistance to Individuals with Disabilities in Reviewing the Rulemaking Record: On request, we will provide an appropriate accommodation or auxiliary aid to an individual with a disability who needs assistance to review the comments or other

from South Dakota (Mr. McGOVERN), the Senator from Utah (Mr. Moss), the Senator from Maryland (Mr. TYDINGS), and the Senator from Texas (Mr. YARBOROUGH), would each vote "yea."

Mr. SCOTT. I announce that the Senators from Vermont (Mr. AIKEN and Mr. PROUTY), the Senator from Oklahoma (Mr. BELLMON), the Senator from Utah (Mr. BENNETT), the Senator from Kentucky (Mr. COOK), the Senator from Michigan (Mr. GRIFFIN), the Senator from Idaho (Mr. JORDAN), the Senator from Kansas (Mr. PEARSON), and the Senator from Illinois (Mr. SMITH) are necessarily absent.

The Senator from Florida (Mr. GURNEY), the Senator from New York (Mr. JAVITS), the Senator from Maryland (Mr. MATHIAS), the Senator from Oregon (Mr. PACKWOOD), and the Senator from Illinois (Mr. PERCY) are absent on official business.

The Senator from South Dakota (Mr. MUNDT) is absent because of illness.

If present and voting, the Senator from Vermont (Mr. AIKEN), the Senator from Oklahoma (Mr. BELLMON), the Senator from Utah (Mr. BENNETT), the Senator from Kentucky (Mr. COOK), the Senator from Michigan (Mr. GRIFFIN), the Senator from Florida (Mr. GURNEY), the Senator from Idaho (Mr. JORDAN), the Senator from Maryland (Mr. MATHIAS), the Senator from South Dakota (Mr. MUNDT), the Senator from Kansas (Mr. PEARSON), and the Senators from Illinois (Mr. PERCY and Mr. SMITH) would each vote "yea."

The result was announced—yeas 73, nays 1, as follows:

[No. 10 Leg.]

YEAS—73

Allen	Fulbright	Nelson
Allott	Goldwater	Pastore
Anderson	Goodell	Pell
Baker	Gore	Proxmire
Bible	Hansen	Randolph
Boggs	Hart	Ribicoff
Brooke	Hartke	Russell
Burdick	Hatfield	Saxbe
Byrd, Va.	Holland	Schweiker
Byrd, W. Va.	Hruska	Scott
Cannon	Hughes	Smith, Maine
Case	Jackson	Sparkman
Cooper	Jordan, N.C.	Spong
Cotton	Kennedy	Stennis
Cranston	Long	Stevens
Curtis	Magnuson	Symington
Dodd	Mansfield	Talmadge
Dole	McClellan	Thurmond
Dominick	McGee	Tower
Eagleton	McIntyre	Williams, N.J.
Eastland	Miller	Williams, Del.
Ellender	Mondale	Young, N. Dak.
Ervin	Montoya	Young, Ohio
Fannin	Murphy	
Fong	Muskie	

NAYS—1

Metcalf

NOT VOTING—26

Aiken	Harris	Mundt
Bayh	Hollings	Packwood
Bellmon	Inouye	Pearson
Bennett	Javits	Percy
Church	Jordan, Idaho	Prouty
Cook	Mathias	Smith, Ill.
Gravel	McCarthy	Tydings
Griffin	McGovern	Yarborough
Gurney	Moss	

So the bill (S. 30) was passed.

Mr. MANSFIELD. Mr. President, I move to reconsider the vote by which the bill was passed.

Mr. McCLELLAN. I move to lay that motion on the table.

The motion to lay on the table was agreed to.

Mr. MANSFIELD. Mr. President, may I be the first to take my hat off to the senior Senator from Arkansas (Mr. McCLELLAN) for the outstanding service he has performed to this body and to the Nation as a whole. His leadership on this bill, S. 30, the Organized Crime Control Act of 1970 was absolutely outstanding.

This measure is designed to augment the fight against crime. I am not an expert in crime control. I am not even a lawyer, but I understand that this proposal complements very well the Omnibus Crime Control and Safe Streets Act of 1968. In this regard, it is designed to cut down on the activities of those engaged in organized crime. It gives our enforcement officials some vital assistance. It certainly is my hope and the hope of every Member of this body, that it will meet with the greatest success.

I would urge the other body to act expeditiously in considering this matter. I believe it represents a constructive effort and a cooperative effort. Certainly there was the cooperation by Members on both sides of the aisle. Cooperation certainly existed between Congress and the administration.

The important factor is that the crime problem is being faced. It is a problem of great concern. In the past year alone crime has risen dramatically in many of the cities of this country. In the weeks and months ahead it will be our task to attempt in every way possible to stem and reverse this trend.

The measure just adopted by the Senate will aid immensely in this effort. Senator McCLELLAN deserves the gratitude of this entire body for his outstanding leadership. The Senate is grateful as well for the efforts of the senior Senator from Massachusetts (Mr. KENNEDY) who offered his own strong and sincere views on this measure. Senator KENNEDY along with the senior Senator from Michigan (Mr. HART) and the Senator from New York (Mr. GOODELL) are to be commended for their contributions to the discussion.

I think the entire Senate may be proud of this effort, of this great achievement. It was obtained expeditiously and with full regard for the views of every Member.

ORDER FOR ADJOURNMENT TO 10. A.M. TOMORROW

Mr. MANSFIELD. Mr. President, I ask unanimous consent that when the Senate completes its business today, it stand in adjournment until 10 o'clock tomorrow morning.

The PRESIDING OFFICER. Without objection, it is so ordered.

CONTROLLED DANGEROUS SUBSTANCES ACT OF 1969

Mr. MANSFIELD. Mr. President, I ask unanimous consent that the Senate proceed to the consideration of Calendar No. 609, S. 3246.

The PRESIDING OFFICER. The bill will be stated by title.

The BILL CLERK. A bill (S. 3246) to protect the public health and safety by amending the narcotic, depressant, stimulant, and hallucinogenic drug laws, and for other purposes.

The PRESIDING OFFICER. Is there objection to the present consideration of the bill?

There being no objection, the Senate proceeded to consider the bill.

Mr. DODD obtained the floor.

Mr. MANSFIELD. Mr. President, may I suggest the absence of a quorum, without the Senator from Connecticut losing his right to the floor?

The PRESIDING OFFICER. The clerk will call the roll.

The bill clerk proceeded to call the roll.

Mr. MANSFIELD. Mr. President, I ask unanimous consent that the order for the quorum call be rescinded.

The PRESIDING OFFICER. Without objection, it is so ordered.

Mr. ALLOTT. Mr. President, will the Senator from Connecticut yield, so that I may ask a question of the Senator from Montana?

Mr. DODD. I yield.

Mr. ALLOTT. Did the Senator make a request for the Senate to convene at 10 o'clock tomorrow morning?

Mr. MANSFIELD. Yes.

Mr. ALLOTT. Will the pending bill be the legislation tomorrow morning?

Mr. MANSFIELD. Yes; the Controlled Dangerous Substances Act of 1969.

Mr. ALLOTT. I appreciate the courtesy of the distinguished Senator from Connecticut and I thank the Senator from Montana.

Mr. HUGHES. Mr. President, will the Senator from Connecticut yield?

Mr. DODD. I am happy to yield to the Senator from Iowa.

Mr. HUGHES. Mr. President, it had been by intention to ask for a referral of the bill now before the Senate to the Committee on Labor and Public Welfare.

In discussing this with the Senator from Connecticut, who chaired the subcommittee that conducted the hearings on this bill, I believe that we have arrived at a conclusion that, though not entirely satisfactory to either of us, will help us mount a total approach to the problem of narcotics addiction and drug abuse in the country.

I appreciate and share the determination of the administration and of my colleagues of both parties to expedite legislation to meet one of America's most terrifying problem areas.

I would have you know, Mr. President, that I would not have considered the motion I intended to make if I did not believe with all of my heart that this is a matter of life or death to our shared objective of taking decisive action to meet the drug problem in the United States.

Let me explain the reasons I feel this way.

This bill, S. 3246, was introduced by the Senator from Connecticut (Mr. DODD), for himself and the Senator from Nebraska (Mr. HRUSKA) on December 16, 1969. On that same day it was read twice, referred to the Judiciary Committee, and reported by the Senator from Connecticut without amendment.

The bill is in fact an outgrowth of Senator DODD's earlier bill, S. 1895, and the administration bill originally introduced by the late Senator from Illinois (Mr. Dirksen) and the Senator from Nebraska (Mr. HRUSKA) as S. 2637.

Both of these earlier bills had been referred to the Committee on the Judiciary. Hearings were held before its Subcommittee To Investigate Juvenile Delinquency beginning on September 15 and concluding on October 20, 1969.

The reference of these measures to the Committee on the Judiciary was apparently on the basis of its jurisdiction over "revision and codification of the statutes of the United States" under rule XXV of the Standing Rules of the Senate. In fact, these bills, and the original bill reported by the committee, are not a "revision and codification" as those terms are normally understood. The bills make extensive changes in the present laws relating to narcotics, marihuana, and drugs now subject to the Drug Abuse Control Amendments of 1965 to the Food, Drug, and Cosmetic Act.

The report of the Committee on the Judiciary on S. 3246—Report No. 91–613—begins with the assertion, quite accurately, that it has had "under consideration legislation to protect the public health and safety by amending the narcotic, depressant, stimulant, and hallucinogenic drug laws," and the bill itself is denominated "a bill to protect the public health."

I believed, therefore, that before action is taken by the Senate on this legislation, it should be referred to its Committee on Labor and Public Welfare, pursuant to that committee's jurisdiction over legislation relating to the public health. Such referral would have been entirely consistent with the traditional procedures of the committee system in the Senate when dual jurisdiction occurs.

In the executive branch, the responsibility for drafting this legislation was given to the Department of Justice. It was felt necessary to collect in a single statute the laws relating to narcotics, marihuana, and other so-called dangerous drugs as a further step in the 1968 reorganization plan which transferred to a new bureau in the Department of Justice the drug law enforcement functions formerly assigned to the Bureau of Narcotics in the Treasury Department and the Bureau of Drug Abuse Control of the Food and Drug Administration.

I do not question that the collection in one place of these scattered laws—passed over a period of many years and not wholly consistent in their provisions—is probably desirable. Neither do I question that the sweeping revisions of criminal penalties, procedures for the issuance of search warrants, and authorizations for search without either warrants of notice, should not be undertaken without the Senate having had the benefit of the recommendations of its Committee on the Judiciary.

However, there are extensive provisions in this bill which relate not to law enforcement but to matters of public health; and it seemed to me that these are areas on which the Senate should not act without the benefit of the recommendations of its Committee on Labor and Public Welfare.

Let us consider the extent to which this bill involves matters of medical science. It authorizes the Attorney General to subject drugs to the special controls under the bill, or to change the regulatory status of a particular drug under the bill, and specifically directs that, in order to do so intelligently, he must consider scientific evidence of its pharmacological effect, the state of current scientific knowledge regarding it—its psychic or physiological dependence, liability, and generally, the risk to the public health from the drug's abuse—section 201(a), page 12. The committee's report recognizes that this is a highly controversial delegation of authority. The report, on page 5, states:

> There has been a point of controversy evident among the professions involved in drug control and drug research on whether or not the Justice Department has the expertise to schedule or reschedule drugs since such decisions require special medical knowledge and training.
>
> This difficulty is resolved by the provision contained in this title which requires the Attorney General to seek advice from the Secretary of Health, Education, and Welfare and from the Scientific Advisory Committee on whether or not a substance should be added, deleted or rescheduled with respect to the provisions of the bill.

I must admit, in all frankness, that this is one practical way to resolve the issue. But it is not the only way. And I am deeply convinced that it is the wrong way, if we are really determined to get at the roots of the drug problem in America.

The bill establishes four separate schedules of drugs, based on their relative medical usefulness and the extent of their potential for abuse. Neither the standards used for the assignment of drugs to particular schedules nor the makeup of the schedules themselves correspond to those under existing law.

However, and this is even more significant, neither do they correspond to the recommendations of the World Health Organization's Expert Committee on Drug Dependence nor of the United Nations Commission on Narcotic Drugs, which is meeting today in Geneva to complete work on an international treaty called the International Protocol on Psychotropic Substances. The treaty will classify the nonnarcotic drugs covered by this bill and specify the measures which signatories of the treaty should undertake with respect to their control.

The bill authorizes the Attorney General to license the manufacture and distribution of any drug subject to its provisions and forbids their manufacture or distribution except pursuant to his license. With respect to drugs on two of the schedules, it authorizes the Attorney General to establish production quotas for each drug after determining the amount of the drug which will be required for medical, scientific, and industrial purposes in the United States—section 306, page 35.

The bill directs the Attorney General to carry out education and research relating to the effects of dangerous drugs and relating to the identification and description of their abuse potential—matters wholly scientific and, more particularly, medical in nature. It authorizes him to enter into contracts for educational and research activities without limitation as to their nature or cost, and without requiring any consultation as to possible duplication of existing programs of other agencies.

The bill gives to the Attorney General a virtual veto over scientific and medical research with these substances.

Finally, the bill establishes a committee on marihuana to conduct studies and research into its pharmacology and medical and social effects—section 801, page 87.

The foregoing only illustrates the extent to which this bill involves directly questions of public health and the extent to which it involves the Department of Justice in the making of essentially scientific decisions, in the control and direction of scientific research, and in the direction of public educational campaigns.

While extensive hearings were held before the Subcommittee To Investigate Juvenile Delinquency, under the chairmanship of the Senator from Connecticut (Mr. DODD), and witnesses from the scientific agencies of the Government were heard, a cursory study of this legislation and of the record of the hearings indicates that not a single significant change was made in the legislation originally recommended by the Department of Justice. Furthermore, I can find no criticism or recommendation originating with any witness, other than those of the Department of Justice, that was incorporated in this bill.

This measure—in concept, in spirit, and in detail—is a law-enforcement measure. It only approaches one side of the problem of drug abuse. It seeks to cure, by criminal penalty, ills that also need scientific research and medical treatment. And to the extent that it recognizes the necessity for such research and such treatment, it commits the responsibility for those functions to a law-enforcement agency rather than to a medical or scientific one.

So I appeal to my colleagues to also let medicine be heard. Let science also be heard. Let medical science be heard before a committee whose responsibility is medical science and whose primary concern is the medical and scientific aspects of the problem in this country.

That consideration will result in recommendations for legislation in the future. I ask nothing more than the opportunity for the Committee on Labor and Public Welfare to bring its proposals before the Senate and to have them considered equally. I think this is vitally important.

Hearings on similar legislation have not yet been held in the other body. In this connection, it is interesting to note that the administration proposals are being considered in the House by its Committee on Interstate and Foreign Commerce—whose jurisdiction over health matters parallels that of your Committee on Labor and Public Welfare—and also by its Committee on Ways

and Means, because of its jurisdiction over the Narcotic and Marihuana Tax Acts which this bill would repeal.

The problem of drug abuse has already been subject to extensive hearings before the Subcommittee on Alcoholism and Narcotics of the Committee on Labor and Public Welfare. It can therefore consider the detailed provisions of legislation against an extensive background of knowledge of the scientific and social aspects of the problem of drug abuse—a necessary corollary to the law enforcement aspects which understandably preoccupied the Committee on the Judiciary.

It is contemplated that we are here enacting permanent legislation, long-term provisions to arrest and reverse the worsening pattern of drug abuse. Let us then be equally concerned for the ways in which medicine, science, and education can best contribute to our common goal.

Mr. President, the questions of jurisdiction and of content of this bill bring the drug problem U.S.A. into sharp focus for the first time.

What we have before us is a law enforcement bill which is directed at a problem area of public health, and certainly also one of law enforcement in relation to the distribution of products.

I do not question the need for improved enforcement.

I do not question the need for revision of the various statutes providing penalties for drug and narcotics possession and traffic.

I do not question the need for beefing up our enforcement capabilities in these areas.

But when we have done all of these things, Mr. President, we still have not come to grips with the central problem—the health problem of drug abuse and narcotics addiction.

Addiction is a disease first; we have made it a crime by statute.

What are we going to do about curing the disease?

The bill before us, S. 3246, changes nothing basic.

We already have tough laws and strict enforcement; this bill toughens some of the laws, moderates others. Grant that it is an improvement.

We still have not come within a country mile of solving one of the Nation's most grievous problems.

We are simply doing more of what we have already been doing.

And the record is clear—this course has not been successful by itself.

The Senate Labor and Public Welfare Subcommittee on Alcoholism and Narcotics has held hearings on drug abuse and narcotics addiction in Washington, Los Angeles, Denver, and New York City.

We have heard scores of qualified witnesses—doctors, psychiatrists, hospital superintendents, addicts from all walks of life, penologists, lawyers, and judges.

The thrust of all of this testimony is that the big hiatus in our approach to the drug problem is that we have failed to provide adequate programs of treatment, rehabilitation, education, and prevention to enable sick people to kick this dread disease or avoid it in the beginning.

We can assemble a narcotics squad as big as the Russian Army.

We can fill our prisons to the overflowing, and we can build more costly security facilities.

We can revise our laws.

But we are already going this route.

And we have seen that neither severity of the law nor diligence of enforcement—in the absence of attention to the fundamental health problem involved—will cure, prevent, or even effectively deter people from obtaining and abusing drugs and narcotics.

I submit, Mr. President, that coupled with the commendable enforcement provisions of this bill we need action on the health front to solve the basic problem in this country. I submit such action should be under the jurisdiction of qualified doctors and scientists and professional health administrators. Let the Justice Department handle enforcement problems and let qualified professional ment in Health, Education, and Welfare handle problems in their assigned areas.

In his message of July 14, 1969, to the Congress on "The Drug Problem," President Nixon outlined how, in the last decade, "the abuse of drugs has grown from essentially a local police problem into a serious national threat to the health and safety of millions of Americans." The President cited the need for additional programs of research, education, and rehabilitation, rightly stating, "It has been a common oversimplification to consider narcotics addiction, or drug abuse, to be a law enforcement problem alone."

With full respect for the distinguished and dedicated Members of this body who have worked on this legislation long and ably in a job well done, I would tell them bluntly that, if we put this legislation into effect without other adequate legislation for getting at the roots of the drug problem, we will have failed in our stated aim. We will have done only part of the job, and we will have locked ourselves on a course that has already failed dramatically to arrest the terrible growth of drug abuse and narcotics addiction in America. The well-being and perhaps the very survival of oncoming generations is at stake.

Mr. President, I no longer intend to make a motion to refer this legislation to the Committee on Labor and Public Welfare. I have discussed with the distinguished Senator from Connecticut the serious problems in this field that are matters of jurisdiction of the Committee on Labor and Public Welfare of the Senate.

I have serious concern in connection with the delegation of certain authority to the Attorney General. I would welcome the opportunity to discuss with the distinguished Senator from Connecticut and the distinguished Senator from Nebraska, or any other Senator, some of the points I have raised in this presentation.

Mr. DODD. Mr. President, I commend the Senator from Iowa for his statement. I am pleased that he is not going to ask that the matter be referred to another committee, even for a short period of time.

I think the Senator will find that I and the Senator from Nebraska are in great sympathy with the views expressed by the Senator from Iowa. The Senator from Nebraska is here. I know he has to catch a plane and that he would like to be heard on this subject. I yield to him at this time.

Mr. HRUSKA. I thank the Senator from Connecticut. He is his usual courteous self.

Mr. KENNEDY. Mr. President, a parliamentary inquiry.

The PRESIDING OFFICER. The Senator will state it.

Mr. KENNEDY. Mr. President, does the Senator from Iowa still have the floor?

Mr. HUGHES. The Senator from Connecticut yielded to me for a statement. I hope we will have an opportunity later to develop some of these points. The Senator from Nebraska, I understand, asked, as a point of convenience, to be heard.

Mr. KENNEDY. Fine.

Mr. HRUSKA. Mr. President, we have here a very grave problem. Everyone in the Senate and in the Congress is well aware of this fact. It is a problem that has an impact which is great and vast in scope, geographically, and through all segments of the population, as all of us know.

In most legislative proposals that are as big as this one there is normally an area in which we find room for the argument that there is an overlapping of committee jurisdiction. That is particularly true in this situation, as has been outlined by the Senator from Iowa so well.

Originally the bill proposed by the Senator from Connecticut was encyclopedic in extent, very ambitious, and it considered the entire gamut of the problems which arise from the abuse of drugs and dangerous substances. This was justifiably from the standpoint of trying to get something into one piece of legislation so we can tie into this subject and deal with it intelligently and effectively. As time went on, however, it was realized that was not the practical way to do it. Certainly, in the judgment of the Department of Justice that was true when they had analyzed the situation from a number of aspects, to which I shall refer soon.

When there were further discussions with the Senator from Connecticut, this Senator, and other Senators, it was realized there are two separate and distinct problems and fields of endeavor that should be treated separately. That does not mean they are exclusive of each other. There will be overlapping and duplication of points. But there will be these two general classifications. One, there is the thrust of law enforcement upon the problem at hand. That would be the immediate problem. The long-range consideration would consist of those activities which would take longer to develop and even longer to manifest themselves in some sort of result that will bring an amelioration of the terrifically bad situation that exists among the population of America on abuse of drugs and dangerous substances. That would include rehabilitation, education, and research; and it would include the scientific effort to learn more about all these things; and, at that time, legislation in

both of these categories in light of the findings of the scientists, and so forth.

Insofar as the enforcement of the drug laws of America are concerned, as they exist now, we know that basically the sanctions and penalties for the illegal acts are pretty much based on a law that is almost 60 years old, the Harrison Narcotic Act.

In the tenure of both the Senator from Connecticut and this Senator we have witnessed various amendments that have been made to that basic law, particularly in the field of penalties and penology, as well as some new substances. These were very unsatisfactory. It must be brought up to date, and it has to be modernized to include many new substances and substances considered dangerous and not yet in use, which will develop as time goes on. Then, there must be some scheme or system of penalties for those who do not obey regulations and the requirements of the statute and other things covered in the bill.

Other features in the bill would include distribution, dispensing, importation, exportation, as well as administrative provisions and enforcement provisions. We have to have most of these things, virtually all of them, in order to write an immediate and effective law enforcement statute.

However, I would be the first to concur wholeheartedly with the Senator from Iowa on the proposition that to look at this situation alone is inadequate and it would be disastrous. I would be the first to subscribe to the proposition that I will lend any support I can to any supplemental effort, and even an effort that will dovetail with the bill before us, S. 3246, which will evolve from the Committee on Labor and Public Welfare or from any other source, because it is generally recognized that there is this second aspect of the longer range requirements that is so necessary in this field of rehabilitation, education, and research, trying to turn around the public attitude toward this entire problem for a real impact upon it.

Some of the provisions in the bill, for example, relate to the Attorney General's classifying drugs one way or another, which might fall within the purview of a measure coming from the Committee on Labor and Public Welfare, as a result of scientific efforts. No matter where it goes, there has to be an interplay between that Department and the Department of Justice. There just has to be. We recognize that in the bill because it is provided, on page 12, starting on line 12, that—

> Before doing so, the Attorney General shall request the advice in writing from the Secretary of Health, Education, and Welfare and from the Scientific Advisory Committee—

and so forth, whether this substance should be added, deleted, or transferred. That is a recognition of the proposition that there are many facets to this problem.

If that duty of rescheduling or adding or deleting should be vested in the Secretary of Health, Education, and Welfare, there would have to be a similar provision that, before he did that, he would have to consult with the Attorney General to see whether that reclassification would be practicable from the standpoint of law enforcement and from the standpoint of visiting penalties or sanctions, as the case may be.

Mr. HUGHES. Mr. President, will the Senator yield?

Mr. HRUSKA. I am happy to yield to the distinguished Senator from Iowa.

Mr. HUGHES. I appreciate the statements of the distinguished Senator from Nebraska and I agree in general with what he has said. My concern is in the area he is presently talking about, research and scientific information and consulting with the Secretary of Health, Education, and Welfare. I agree that the legislation provides for that. My concern is that if there is going to be research and scientific investigation in the Department of Health, Education, and Welfare, under the supervision of its Secretary, it would seem logical that he should do all of the research and investigation, and perhaps the Attorney General should seek from him advice and consultation on what drugs or narcotics they thought, from their best knowledge, should be reviewed.

That was the real question I was raising about the research provisions. In emphasizing this point, the Senator is performing a good service. That was one of my points of contention.

Mr. HRUSKA. I am in complete sympathy with that, but whether it is done in the way provided in the bill or another way, there would still be the necessity to go back and forth to reconcile differences to carry out the missions of the two departments.

Mr. HUGHES. Then the Senator agrees that this provision does not preclude the Secretary of Health, Education, and Welfare from scientific research and development.

Mr. HRUSKA. Absolutely. The functioning of the committee would not preclude that. In fact, I think it would encourage it. In my judgment, the way I have observed the way this matter works—certainly with the Department of Health, Education, and Welfare and other departments—there would be a conscious effort to avoid repetition and duplication.

Mr. HUGHES. Then the legislative intent would not be to give to the Attorney General total authority in this field?

Mr. HRUSKA. By all means. That is indicated on page 67 of S. 3246, subsection (1):

> The Advisory Committee shall be composed of persons selected by the Attorney General after consultation with the Secretary of Health, Education, and Welfare from a list drawn by the National Academy of Sciences.

First of all, the list will be furnished by the National Academy of Sciences. From that consultation between the Attorney General and the Secretary of Health, Education, and Welfare, they will work out a list suitable for the purposes at hand.

That is one of the brain children of the Senator from Connecticut, in common with many other provisions which he seeks to provide.

Mr. HUGHES. Would the Senators have any objection to allowing the Secretary of Health, Education, and Welfare to make some of those appointments, rather than simply consult about them?

Mr. HRUSKA. That is a possibility. I do not know that this is an arm's-length proposition. We used to talk a lot about a troika, but even a troika has only one driver. You can have three horses if you want to, but there is only one driver. For the purpose of administrative convenience, this is the formula that is used not only in situations like this, but elsewhere where there should be a focus of responsibility. That is the way it is.

I am confident, with the comity that exists between Cabinet members, there will be no difficulty. It will not be the case of one irresistible force against another object which would be immovable in character. There will be amicable settlements of any differences. If one feels greatly aggrieved, there is always the resident in the White House to contend with. Normally, he exerts a paternal and effective benefit toward differences and in working them out.

Mr. HUGHES. If the Senator will excuse a personal reference, I found, as chief executive of the great State of Iowa, that frequently men I appointed to different departments seemed to forget the man in the State house.

Mr. HRUSKA. I am sure that if such disagreements had manifested themselves sufficiently, the man in the State house would have called them by telephone and said, "Boys, come in here and let us reason together."

Mr. HUGHES. I think the points the Senator has made have clarified the situation. Perhaps, as I consult with the Senator from Connecticut, I may want to offer amendments in this area to reassure myself and to let the Senate work its will. Generally, this colloquy has been useful for clarifying the legislative intent. I think it has been very helpful.

I thank the distinguished Senator from Nebraska for yielding.

Mr. HRUSKA. I know we are all aware that, as the President referred to yesterday in his message, there have been some 13 proposals in the field of criminal law that were transmitted last year, and not one has reached a decision. This Chamber has done itself proud. I imagine half of those have been processed in this body, and with this one perhaps more than half of them; and we will let them go to another body that happens to be a part of this Congress. So we have done well.

Without assessing that situation one way or another, the point is we ought to get along with the law enforcement part of this task. There are others to follow, but the situation is grave, and I fear that if there should be a reference of this bill to another committee, even for the purpose of suggestions and guidance, delay would be involved. From that standpoint, I think it would be desirable—and I hope it is a part of the thinking of the Senator from Iowa—that there be dispatch and quick action.

Again, I want to thank the Senator from Connecticut for yielding to me as he has. I am sorry I cannot remain to hear what he is about to discuss, but we will catch up with him when he gets into the merits of the bill itself.

Mr. HUGHES. Mr. President, will the Senator from Connecticut yield to me?

Mr. DODD. In a moment. Let me say, because the Senator from Nebraska must leave, that I and all the members of the committee appreciate the great work that the Senator put into the bill. This was truly a nonpartisan measure in our committee. Everybody pitched in and produced the best possible piece of legislation, and the Senator from Nebraska deserves great credit for his contribution.

Mr. HRUSKA. I thank the Senator.

Mr. DODD. I yield now to the Senator from Iowa.

Mr. HUGHES. Mr. President, I would like to quote from the testimony of Attorney General Mitchell before the subcommittee on September 15, 1969, at page 213, to further support the considerations that we have been developing in this colloquy:

> In this legislation, however, we have not sought to incorporate all of the Government's research and educational efforts, but only those which relate to the functions of the Department of Justice. Crucial areas, such as the provision for treatment and rehabilitation of addicts and abusers, have not been included. It is believed that these are subjects which should be handled as separate and distinct legislative efforts.
>
> The Department of Health, Education and Welfare has the primary functions of providing for research, education and treatment in the field of drug abuse. To have placed all of these programs inone package would have been unwieldly and in our opinion very confusing.

According to my reference here, that is on page 213 of the committee's report.

Mr. DODD. Yes, I have it.

Mr. HUGHES. Is that what the Senator finds there? Have I quoted accurately from the Attorney General's testimony?

Mr. DODD. Yes, that is accurate. That is in the RECORD.

Mr. HUGHES. The Attorney General himself was not seeking sole jurisdiction in the fields of scientific research, education, and development of programs of public education in the country, but has recognized the separation of authority and the authority of the Department of Health, Education, and Welfare in these matters; is that correct?

Mr. DODD. That is absolutely correct. I am glad that the distinguished Senator has quoted the language of the Attorney General from the RECORD, because I think he establishes the position that we have taken here, and that is that we recognize that, the Department of Health, Education, and Welfare has the primary function of providing for research, education, and training in the field of drug abuse. That was and is our intent. It never has been our intention to do anything else with respect to research, education, and treatment in the field of drug abuse.

Mr. HUGHES. Mr. President, if the Senator will yield further, I should like to say that the distinguished Senator from Connecticut and I have met on numerous occasions over the last 6 months to discuss his particular approach on these pieces of legislation—his own bill, which was later let lie, and this bill taken up as the replacement for it and including, I believe, the majority of his original proposals in the field of law.

Mr. DODD. Yes.

Mr. HUGHES. And we thought we could reconcile the different approaches that we were taking to the drug abuse and narcotics addiction problems in the United States. It was with some reluctance that I arrived at a conclusion to seek jurisdiction over this particular piece of legislation, because I felt that there is a genuine jurisdictional question involved. But, as a result of the fact that both the distinguished Senator from Connecticut and the distinguished Senator from Nebraska (Mr. HRUSKA), had said that they supported the approaches we were taking in the subcommittee that I chair, and in the hope and belief that we can reconcile our other differences, I have not made such a request today.

Mr. DODD. Yes. I respond to the Senator from Iowa by saying, first of all, that he states the facts accurately and correctly, as he always does. I remember many meetings with the Senator from Iowa about this legislation, and I always found myself in agreement with him. I am in agreement with him today. I have no conflict with his view at all. I think that what he says about research, rehabilitation, and education is exactly right. The Department of Justice is not the executive agency responsible for these activities. It is within the province of the Secretary of Health, Education, and Welfare, as the Attorney General pointed out in his testimony.

This aspect of this drug problem is just as important—perhaps I should say that it is more important in the long run—than the law enforcement aspect of the problem. My recognition of the position of the Senator from Iowa goes that far. And I say, in no fulsome way, here in the Senate at this hour, that the Senator from Iowa is one of the most knowledgeable men in the field of narcotics addiction and the problems related to it. He knows a great deal about it, and his contribution to the solution of the problem has already been magnificent, in my opinion. I want to see him go ahead with his own legislation, after we have concluded our work on this law enforcement portion of the problem. I hope he will introduce his own bill, which will cover the aspects of rehabilitation, education, research, and information. I want to assure him that I will cooperate with him 1,000 percent.

That is my position on this problem. The legislation before us is a law enforcement bill. I did try to work into the original draft of the bill which I introduced last April rehabilitation and treatment features. I think they were good features, but, as the Senator from Nebraska pointed out after we had all mulled it over—and I see the distinguished assistant majority leader is present; he knows about this also—we concluded it would be better to keep this particular piece of legislation a law enforcement measure.

Let us get at those people who import and distribute these hard drugs, the smugglers, the peddlers and the pushers. That is the first thing we have got to do, and that is the reason we approached it this way.

As for myself, I want to say for the RECORD that I will lend my support to every effort on the part of the Senator from Iowa to adequately deal with the treatment, education, and information aspects of the problem.

Mr. HUGHES. If the distinguished Senator from Connecticut will yield further, I want to express my appreciation to the Senator for his own dedication to this particular problem, the great amount of work that he has given to it, and certainly the great value of his contribution to the people of this country. I appreciate his support. It has great value because of his vast experience in the fields in which he is presenting legislation today, which is certainly an area that must logically be covered.

There are certain areas of this bill, naturally, with which I differ. Generally, I support the thrust of it, and over the course of the next few days, we will independently develop our differences and our agreements. But I appreciate this opportunity for colloquy today, and I hope and expect that in the future my own subcommittee in the next few months will develop and bring forth massive legislation in the fields we have been talking about. That legislation, I hope, will be before the Senate sometime in April; and with that, then, we can complete a program which will be a total approach to this gigantic problem.

Mr. DODD. This is certainly good news, I am sure, to the entire Senate and to the Nation as well.

The Senator knows my respect and my affection for him. I am sure he understands that we will cooperate in every possible way to help him.

I yield to the Senator from Massachusetts.

Mr. KENNEDY. Mr. President, I want to commend the distinguished Senator from Iowa for his statement to the Senate on what I think is really one of the most important questions and problems that face us as a Nation and a society. I think that the Senate is the stronger for the kind of comments that have been made by the Senator from Iowa this afternoon, and is made a great deal stronger by the action that he has taken in his service as chairman of a subcommittee of the Committee on Labor and Public Welfare, that is concerning itself with alcoholism and with drugs.

Mr. President, I have the good fortune to serve as a member of the Committee on the Judiciary, and also on the Committee on Labor and Public Welfare. So, Mr. President, I have had the opportunity, on the one hand, to serve under the distinguished Senator from Connecticut (Mr. DODD), who has worked so hard and with such interest and such capacity in the development of this legislation, and also to serve on the subcommittee of the distinguished Senator from Iowa (Mr. HUGHES), and see his great ability brought to bear on this most searching question.

I, too, share the sentiments which have been expressed by the distinguished Senator from Iowa that, if we are really serious about meeting this problem in

terms of drugs and drug addiction, we cannot restrict the efforts of this body and of Congress as a whole solely to the field of law enforcement.

As the distinguished Senator from Iowa has stated, and as others have suggested who would have liked to see the proposed legislation move to the Committee on Labor and Public Welfare for a short period of time, we agree as to the importance of the alterations and changes in many parts of this bill—not all, but many parts of the bill. But as the Senator from Iowa has pointed out, in the fields of education, rehabilitation, and research, we have been reminded by those who are most closely concerned with this problem of the great importance and signifiance of addressing ourselves to these other questions as well.

Therefore, I would have supported the Senator from Iowa if he had exercised his parliamentary rights here to try to get this matter transferred for a short period of time. I thought his request was reasonable. But unfortunately, indications were given that there would be objection to any request for unanimous-consent agreement or other motion for referral. Therefore, he has taken this other road, and I respect his judgment in doing so.

Mr. President, I would certainly hope—and I think I speak for many Members of this body—that, having heard the distinguished Senator from Nebraska and the distinguished Senator from Connecticut voice their opinions about how important education, rehabilitation, and research are, we could move ahead in these areas, either on this bill or on other legislation in the near future, based on the extensive experience of the distinguished Senator from Iowa and on the experience of the committee he so ably chairs. I certainly would support the Senator from Iowa if he chooses to offer amendments to this bill.

I think that action on education and research and rehabilitation would be something which the administration should support. I am reminded that President Nixon made a similar comment to the distinguished Senator from Connecticut and the distinguished Senator from Iowa at the recent Governors' Conference on Narcotics at the White House. The President said:

When they—

Referring to the briefing meetings—

first started, I thought the answer was more penalties. I thought that the answer was simply enforce the law and that will stop people from using drugs. But it is not that. . . . The answer is information. The answer is understanding. . . . [A] campaign of education and information, in my opinion, is probably more important than criminal penalties.

As we begin this debate and the elaboration of the provisions of this bill, I, for one, certainly hope that during it we will benefit from the judgment, compassion, and knowledge that have been so amply demonstrated by the Senator from Iowa, whose interest and understanding in this issue are, I feel, above that of all others in this body; and I hope that in this session we will really come to grips with this problem and that we will meet our responsibilities to the American people in a more effective way.

When we pass the Controlled Dangerous Substances Act of 1969, we do not want to have some euphoria come over the American people that will cause them to say, "Now that we have passed a drug abuse act, nothing remains to be done." As has been brought out so ably by the Senator from Iowa, the Senator from Connecticut, the Senator from Nebraska, and the President of the United States, that really is only a part of a vastly complex, complicated, and weighty problem.

I salute the Senator from Iowa for the comments he has made here this afternoon. I express applause to the Senator from Connecticut for his views on this question and his sympathy, understanding, and appreciation for the approach to this problem that has been exercised by the Senator from Iowa; and, hopefully, we will see these sentiments reflected in legislation enacted by this Congress on this tremendously important subject.

Mr. HUGHES. Mr. President, will the Senator yield?

Mr. DODD. I yield.

Mr. HUGHES. I would like to respond to the distinguished Senator from Massachusetts by saying that I am grateful for the very kind and learned comments he has just made. But, as I look further down this legislative path on which we are proceeding, when the bill goes to the House and the conference resulting, because of the procedures in this body, no members of the Committee on Labor and Public Welfare will be on the conference committee. They all will be from the Judiciary Committee, as the result of the assignment of the bill to that committee, unless the bill were referred to the Committee on Labor and Public Welfare.

Mr. DODD. Mr. President, will the Senator yield?

Mr. HUGHES. I yield.

Mr. DODD. When we get to that point, I think it would be proper to suggest that, when conferees are appointed, the Senator from Iowa and perhaps others from the Labor and Public Welfare Committee be made conferees.

Mr. HUGHES. That is a very generous gesture by the distinguished Senator from Connecticut, and it would be very helpful, indeed, if appropriate amendments were attached and adopted.

This has been one of my concerns as we look ahead down the legislative course this measure has to travel.

I apologize for taking so much of the time of the distinguished Senator from Connecticut. I appreciate his generosity in waiting to make his statement so that I could clarify my position in general support for the approaches that have been taken in the bill.

Mr. DODD. The Senator need not apologize. He has helped very substantially.

Mr. President, my remarks will be brief this afternoon. With the agreement of the assistant majority leader, I assume we could thereafter go over until tomorrow morning. I should like to make a few remarks about the matter we have been discussing.

Since I became chairman of this subcommittee in 1961 we have conducted 32 days of public hearings on narcotics, dangerous drugs, marihuana, peyote and LSD. We have taken testimony from 144 witnesses ranging from addicts and convicts, through doctors, lawyers, attorneys general and Governors. We have heard from experts at every step along the way.

As a direct result of that effort on July 8, 1965 the Congress adopted the Drug Abuse Control Amendments of 1965, which by the way did not cover marihuana, which established the Bureau of Drug Abuse Control under the Department of Health, Education, and Welfare.

That Bureau was recently merged with the Federal Bureau of Narcotics of the Treasury Department and by an Executive order of President Johnson was moved to the Justice Department as the Bureau of Narcotics and Dangerous Drugs. That means one-half of the Federal law enforcement personnel in existence today are a result of the 1965 bill.

In 1966 I introduced S. 2152, the Narcotics Rehabilitation Act which was signed into law on November 8, 1966.

The subcommittee has been investigating the current drug problem in addition to reevaluating the Federal laws relating to narcotics since early 1968. Hearings were held in March of 1968 and they resulted in the introduction, on April 18, 1969, of my bill, the Omnibus Narcotic and Dangerous Drug Control and Addict Rehabilitation Act of 1969, which is part of the legislation we are discussing today.

In addition to my bill, the Dirksen-Hruska bill was referred to the subcommittee and we quickly held hearings. We sat for 10 days and heard 30 witnesses.

I review this involvement of the subcommittee to investigate juvenile delinquency with narcotics addiction to indicate our decade of concern with what Senator HUGHES referred to as one of America's most terrifying problems.

Mr. President, in response to another comment of the Senator from Iowa, I must say that the bill before the Senate has no conceivable connection with welfare programs or labor problems or other areas which are the normal concern of the Labor and Welfare Committee.

The proposed legislation contains no provisions whatever for medical or psychiatric treatment or other rehabilitative services for those caught in the web of drug abuse.

S. 3246 is strictly and entirely a law enforcement measure. It is intended to deal with the control of the illicit drug traffic, the diversion of legal drugs into illegal and nonmedical channels, and the enforcement of the drug laws by the Justice Department, through its Bureau of Narcotics and Dangerous Drugs.

Provision is made for technical assistance to be provided by the Department of Health, Education, and Welfare, through the Food and Drug Administration and a Scientific Advisory Committee with regard to drug classification for enforcement purposes.

The bill represents a recodification of the Federal drug laws and places the necessary controls within one Federal statute.

It also revises the penalty structure for violations of the Federal drug laws,

consistent with the expert testimony given before the Juvenile Delinquency Subcommittee's exhaustive and lengthy hearings. The penalties provided are alined with the degree of abuse potential of each of the enumerated drugs.

S. 3246 has been subjected to extensive study and review. The subcommittee held 10 days of hearings on the bill, during which 30 expert witnesses were heard—lawyers in and out of Government; physicians; pharmacists; psychiatrists; social scientists.

The full Judiciary Committee only reported the proposed legislation out after a thorough and protracted study of all of its provisions.

The proposed legislation provides a regulatory schedule for the lawful manufacture, distribution, and dispensing of controlled drugs to furnish us with better law enforcement tools so that the rampant drug abuse problem can finally be curbed effectively.

It provides for international control mechanisms consistent with our international treaty obligations and commmitments.

To increase our knowledge of the drug syndrome in general, and reduce our scientific uncertainties about marihuana specifically, the bill provides for an in-depth study of marihuana for 2 years. The findings of this study will go a long way to remove present uncertainties which are reflected in today's wide range of penalty structures regarding this drug.

There is of course another side to the drug problem; beyond the necessity to control and prevent the drug abuse that is so rampant in our Nation.

There is a great need for detached, unemotional research; for education and rehabilitation of those who have become dependent on drug abuse of one kind or another, whether it is hard narcotics, amphetamines, barbiturates, or marihuana.

All these and particularly the problem of rehabilitation, will need further legislative proposals on the Federal level.

I am now planning to introduce legislation for the treatment of addicts and other drug abusers. It is a subject that should fall squarely within the purview of the Committee on Labor and Public Welfare to which it should be referred.

But it cannot be overemphasized that the bill before the Senate today is entirely concerned with enforcement.

It contains no medical or rehabilitative provisions.

It is designed to crack down hard on the narcotics pusher and the illegal diverters of pep pills and goof balls. And that is what it will do, but it has to be passed first.

The bill has the backing of the administration. Last fall, in a meeting with the President, it was given substantial bipartisan support by the Senate and House leadership.

S. 3246 should be acted upon now because the hour is late.

I am pleased that Senator HUGHES agrees that we should not delay this measure by having the long, hard work of the Judiciary Committee reviewed by yet another committee.

Mr. President, I now refer to Senator HUGHES' concern over the question of section 602 of S. 3246. It should be pointed out that the education and research function of the Attorney General is clearly limited.

In terms of the language of the bill itself that function is limited to "programs necessary for the effective enforcement of this act."

The effective enforcement of this act requires knowledge on the effects of drugs as they apply to the operation of enforcement.

The effective enforcement of this act requires education and training of enforcement officers.

It also involves education of the public regarding the law enforcement process in the drug field.

These are research and educational activities that have been recognized as essential for the operation of any law enforcement agency in the country.

They do not in any way infringe on the basic research, education, and treatment responsibilities of the Department of Health, Education, and Welfare.

They are staff functions that are a recognized and necessary part of any administrative organization.

It is in the nature of assessing and improving the execution of the act.

Finally, let me point out that the other parts of section 602, parts (b), (c), and (d) do not enhance the Attorney Generals role in drug education and research, but rather enable him to assist other agencies and other departments in carrying out these functions.

Mr. President, I would also like to comment on Senator HUGHES' references to the idea of putting all narcotic enforcement activities under the Justice Department.

Let me remind Senators in this Chamber that as far back as 1963 President Kennedy's Advisory Commission on Narcotic and Drug Abuse recognized the need to centralize drug control in the Department of Justice.

The Commission set forth the finding that "the present activity of the Federal Government regarding drug abuse is fragmented. The divisions, agencies, and bureaus of five Cabinet departments are involved."

It then made the following two major recommendations:

The Commission recommends that the functions of the Bureau of Narcotics relating to the investigation of the illicit manufacture, sale or other distribution, or possession of narcotic drugs and marihuana be transferred from the Department of the Treasury to the Department of Justice.

The Commission recommends that the responsibility for the investigation of the illicit traffic in dangerous drugs be transferred from the Department of Health, Education, and Welfare to the Department of Justice.

Although the Commission did recommend that limited drug control functions remain in the Department of Health, Education, and Welfare this proposal was negated by President Johnson's reorganization plan issued in 1968 which removed the Drug Abuse Control Bureau from the Department of Health, Education, and Welfare and placed all drug control in the Department of Justice.

President Johnson said:

Today, Federal investigation and enforcement of our narcotics laws are fragmented. One major element—the Bureau of Narcotics—is in the Treasury Department and responsible for the control of marihuana and narcotics such as heroin. Another—the Bureau of Drug Abuse Control—is in the Department of Health, Education, and Welfare, and is responsible for the control of dangerous drugs including depressants, stimulants, and hallucinogens such as LSD.

Neither is located in the agency which is primarily concerned with Federal law enforcement—the Department of Justice.

The Reorganization Plan No. 1 of 1968 was based on the finding that a separation of responsibilities "has complicated and hindered our response to a national menace."

To correct this problem the plan gave the Attorney General "full authority and responsibility for enforcing the Federal laws relating to narcotics and dangerous drugs."

I point to this to make it clear that S. 3246 is truly a bipartisan response to a grave problem.

I also want to repeat that this bill recognizes the legitimate responsibility of the Department of Health, Education, and Welfare in the area of drugs. This involves research, testing of drugs and treatment of drug users.

This responsibility is confirmed by the provisions of S. 3246 which require the "advice and consent," as it were, of the Secretary of Health, Education, and Welfare for establishing research plans and programs and for scheduling and rescheduling of drugs under S. 3246.

But, let me stress again that the control of the traffic in drugs involves law enforcement activity which is properly a function of the Department of Justice.

Efforts to separate drug law enforcement is based on the fallacy that it is possible to separate the controls over the criminal traffic in drugs on the one hand and the legitimate traffic on the other.

We have found in extensive hearings going back to 1965, that through the process of diversion, at some point the legitimate traffic in drugs or the legitimate flow of drugs becomes illegitimate.

This has been a serious problem through the years which requires enforcement activity that is and should be the jurisdiction of the Department of Justice.

This is the Department that deals with crime.

This is the Department that contains the investigators and law enforcement officers trained to cope with the narcotics and dangerous drug traffic.

And this is where narcotic law enforcement should remain.

Any effort to change the bill before us to the contrary will be a step backward rather than ahead in our effort to meet the drug challenge.

Mr. President, I would make one final comment on Senator HUGHES' statement that the bill before us does not reflect the concern of the Nation's health officials. I point out to him that scores of scientists and doctors were consulted prior to and during the preparation of this bill. That is why they did not object to it. In fact, that is why they have endorsed it.

Many of the top health officials in the United States testified before our subcommittee on the bill and endorsed it, including Dr. Roger O. Egeberg, Assistant Secretary for Health and Scientific Affairs of the Department of Health, Education, and Welfare; Dr. Stanley F. Yolles, Director of the National Institute of Mental Health; Dr. Sidney Cohen, Director of the Division of Narcotic Addiction and Drug Abuse, National Institute of Mental Health; and Dr. Henry Brill from the American Medical Association.

Finally, for the record, let me say to the Senator from Iowa that this is the best possible bill that we could produce. But if he has an amendment that will improve it, we will be happy to make it a part of this legislation. That may very well happen. I certainly have no hard or fast attitude about it at all.

I am certain that in the course of the debate tomorrow and next week, we can produce a measure that we can all agree is best for the country.

Let me say to the distinguished Senator from Massachusetts that I thank him for his great help along the line. He is a member of the Juvenile Delinquency Subcommittee and a very valuable one. He has rendered a great deal of service in his work on the bill, both in the subcommittee and in the full Judiciary Committee. I know of his great interest in this matter, and that he is aware we must work still harder to get a good piece of legislation out of this body.

Mr. KENNEDY. Mr. President, there was a time when drug abuse was something that happened in the shadows of the ghetto or in the unknown worlds across our borders to the south, or in strange foreign countries with unpronounceable names.

But now we know better. Drug abuse is a modern American blight, tragically fixed to the inner city, the affluent suburb, and the rural back county. It is here, it is now, and it is an unwelcome fact of life for millions of Americans.

The Senate should waste no more time in its efforts to combat drug abuse. Senator DODD has done a commendable job in developing the Controlled Dangerous Substances Act of 1969.

The bill is a proper step in the direction of more comprehensive control of drugs and other dangerous substances. It is a correct statement of the difficulties involved in curbing illegal narcotics traffic; and it outlines meaningful procedures for resolving those difficulties.

But the bill is an incomplete solution to the total drug abuse problem. Control of substances and methods of enforcement make up one dimension of the drug abuse phenomenon. But the bill does not address itself to the education of a drug-oriented society: It does not address itself to the rehabilitation and restoration of broken bodies and minds; it does not address itself to the training of professionals to deal effectively with the drug abuse crisis at the community level.

The Judiciary Committee, of which I am a member, has made a good start. But I believe it is proper at this time to talk briefly about the provisions left out of this bill. The House of Representatives recently passed a Drug Abuse Education Act by a 300-plus margin; at the present time, several drug abuse education bills are awaiting final action in the Labor and Public Welfare Committee. These acts of legislative commitment suggest that we should consider very carefully the role to be played by drug abuse education in attacking the total problem.

Many important programs of drug abuse education are already underway under the auspices of the National Institute of Mental Health, the Bureau of Narcotics and Dangerous Drugs, and the Department of Defense. Then, too, there are several worthwhile programs created and administered by private, volunteer organizations. With varying degree in these programs, emphasis is placed on several key factors:

Identification of major drug abuse problems—including the scope, nature of abuse, characteristics of the abusers, sociological framework for abuse and so forth.

Evaluation of existing drug abuse education material, and creation and dissemination of new materials designed to meet the specific needs of problem areas and problem situations.

Training for professions to cope with drug abuse where it happens, as it happens, but particularly before it happens.

Technical assistance to local communities to aid them in planning and carrying out education and information programs.

Creating and disseminating resource materials for use by community professionals, educators, lay leaders, and by abusers themselves.

If congressional action on drug abuse is to be complete, it must take these needs into account. Various provisions contained in the House-passed drug education bill, and in the Senate bills awaiting committee action, should be strongly endorsed and enacted quickly into law. I would like to call these provisions to the attention of the Senate, and to suggest that in acting on the Controlled Dangerous Substances Act, we commit ourselves to action as soon as possible on the education, research, and training provisions contained in the other legislation.

First, we need to launch a major effort to improve and expand our programs of drug abuse education. A generation of Americans is growing up confused, but very curious, about drugs and their use. Through school programs, media campaigns, community meetings, lectures, personal reading and listening, peer-group associations, "street savvy" and the rest, people are finding out about drugs. Congress should equip the professionals and nonprofessionals alike with the best resources available to help them come up with answers when young people ask the hard, compelling questions.

Drug abuse education could best be served by applying a five-step formula along the general lines suggested by the House-passed Drug Abuse Education Act, and developed by provisions in pending Senate bills. The steps are: First, develop new and imaginative curriculums on drug abuse for use in the schools; second, test these new materials and techniques in model programs, and follow up on the tests with evaluations of the effectiveness of the curriculums; third, disseminate those materials found to be workable, productive and effective; fourth, train teachers, law enforcement personnel, counselors, social workers, doctors and other professionals in the dimensions of drug abuse and the techniques for grappling with it; and, fifth, assemble total community education programs for use by local planners and parents, opinion leaders, businessmen and others at the local level who could do more about drug abuse if they knew more about drug abuse.

Throughout this educational process, we need to learn from past mistakes, and to avoid the fallacy of single cause. Drug abuse is not only a law enforcement problem, or only a medical problem; it is a legal, moral, medical, psychological, educational, social and cultural phenomenon. In our education planning and programing, we need to draw on all the disciplines if the final skills and mix of resources are to be varied enough, and rich enough, to do the job.

Second, in addition to education, a major emphasis on research and investigation is needed. Present research into drug effects and consequences is vital, of course, and should be continued. But research must be expanded to consider the other factors—beyond just drug chemistry—which are related to drugs. Specifically, we need to extend our research horizons to include causes of abuse, applicability of rehabilitation techniques, diagnostic methods, approaches to prevention, and administration of ongoing and intended drug abuse programs.

Research is a component part of control. Without clearer understanding of the forces which cause dependence, we will be forced to make assumptions—about body chemistry, human behavior, and the interaction of the two. These assumptions may, in time, prove correct, but the risks involved in that long wait are too great.

Third, we need to go immediately to work on improving our systems of treatment and rehabilitation for drug abusers. Formal, medically oriented rehabilitation programs are practically nonexistent. Fort Worth and Lexington are the two U.S. Government facilities for narcotics addicts. In addition, there are limited numbers of federally supported methadone centers around the country.

Our total action on drug abuse ought to include a major commitment to establishing and maintaining treatment and rehabilitation centers. In the absence of Federal help in this field, local communities have generated their own network of treatment centers. These programs, running on shoestring budgets and often staffed by volunteers, are the frontline against the cycle of drug abuse. They are the visible signs of a concerned society. But there are not enough, and the time is at hand to supplement such programs with help from the Federal Government.

Evidence is all around us that without this comprehensive, multifaceted attack on drug abuse, we will be walking the treadmill of continued frustration. Senator DODD acknowledged the complexity

of the drug abuse challenge when he introduced his bill in April of last year. He said:

We should see the whole problem, see the problem in all of its ramifications.

Dr. Sidney Cohen, Director of the Division of Narcotic Addiction and Drug Abuse, National Institute of Mental Health, wrote recently:

The mere passage of laws . . . as a device to eliminate noxious behavior is an ineffective technique . . . What is needed in addition to sagacious laws is public education and public cooperation with those laws.

The bill now before the Senate is a beginning. It opens the discussion in the Senate on drugs—the threat of their misuse in modern society, and the steps that must be taken to meet the threat. I suggest that while we consider this measure, we develop a strategy for adoption of the education, research, and rehabilitation provisions contained in the various other drug bills. To do less would be to abandon the addict, ignore the anguished community, and give up the search for a base of information. If we commit ourselves to full action on drug abuse, we must, by definition, commit ourselves to meeting these other aspects of the problem.

Drug abuse and the social upheaval it brings do not fall into neat patterns. They are jumbled by the complexities of society, and they feed on the tensions, anxieties, and frustrations of America. To end the despair, we need the tools of education and information. Congress would be derelict in its responsibility if it did not provide these tools.

ADJOURNMENT UNTIL 10 A.M. TOMORROW

Mr. KENNEDY. Mr. President, if there is no further business to come before the Senate, I move, pursuant to the order previously entered, that the Senate stand in adjournment until 10 o'clock tomorrow morning.

The motion was agreed to; and (at 5 o'clock and 7 minutes p.m.) the Senate adjourned until tomorrow, Saturday, January 24, 1970, at 10 o'clock a.m.

NOMINATIONS

Executive nominations received by the Senate, January 23, 1970:

Ambassador Extraordinary and Plenipotentiary

Jerome H. Holland, of Virginia, to be Ambassador Extraordinary and Plenipotentiary of the United States of America to Sweden.

Robert Strausz-Hupé of Pennsylvania, to be Ambassador Extraordinary and Plenipotentiary of the United States of America to Ceylon, and to serve concurrently and without additional compensation as Ambassador Extraordinary and Plenipotentiary of the United States of America to the Republic of Maldives.

The following-named persons, who were appointed during the last recess of the Senate, to the offices indicated:

Whitney North Seymour, Jr., of New York, to be U.S. Attorney for the southern district of New York for a term of 4 years, vice Robert M. Morgenthau.

A. Roby Hadden, of Texas, to be U.S. attorney for the eastern district of Texas for a term of 4 years, vice Richard B. Hardee.

Marshall F. Rousseau, of Texas, to be U.S. marshal for the southern district of Texas for a term of 4 years, vice Marion M. Hale.

Sam H. Roberts, of Texas, to be U.S. marshal for the western district of Texas for a term of 4 years, vice Jesse L. Dobbs.

U.S. Circuit Judge

Wilbur F. Pell, Jr., of Indiana, to be a U.S. circuit judge, seventh circuit, vice John S. Hastings, retired.

U.S. District Judge

G. Thomas Eisele, of Arkansas, to be U.S. district judge for the eastern district of Arkansas, vice Gordon E. Young, died.

U.S. Attorney

William C. Lee, of Indiana, to be U.S. attorney for the northern district of Indiana for the term of 4 years, vice Alfred W. Moellering.

U.S. Marshal

John L. Buck, of Pennsylvania, to be U.S. marshal for the middle district of Pennsylvania for the term of 4 years, vice Frank W. Cotner, term expired.

Laurence C. Beard, of Oklahoma, to be U.S. marshal for the eastern district of Oklahoma for the term of 4 years, vice Jackie V. Robertson.

Anthony T. Greski, of New Jersey, to be U.S. marshal for the district of New Jersey for the term of 4 years, vice Leo A. Mault.

Kenneth M. Link, Sr., of Missouri, to be U.S. marshal for the eastern district of Missouri for the term of 4 years, vice Olin N. Bell, Sr.

John T. Pierpont, Jr., of Missouri, to be U.S. marshal for the western district of Missouri for the term of 4 years, vice Francis M. Wilson, term expired.

Arthur F. Van Court, of California, to be U.S. marshal for the eastern district of California for the term of 4 years, vice John C. Begovich.

Donald W. Wyatt, of Rhode Island, to be U.S. marshal for the district of Rhode Island for the term of 4 years, vice Peter J. Foley.

California Debris Commission

I nominate Brig. Gen. Frank A. Camm, Corps of Engineers, U.S. Army, to be a member of the California Debris Commission, under the provision of section 1 of the act of Congress approved March 1, 1893 (27 Stat. 507) (33 U.S.C. 661), vice Brig. Gen. William M. Glasgow, Jr., who retired in December 1969.

Missouri River Commission

I nominate Brig. Gen. Harold R. Parfitt, U.S. Army, to be a member of the Mississippi River Commission, under the provisions of section 2 of an act of Congress approved June 28, 1879 (21 Stat. 37) (33 U.S.C. 642), vice Brig. Gen. C. Craig Cannon, who retired on November 30, 1969.

U.S. Air Force

I nominate the following officer to be placed on the retired list in the grade of lieutenant general under the provisions of section 8962, title 10 of the United States Code.

Lt. Gen. William B. Kieffer, [redacted] FR (major general, Regular Air Force) U.S. Air Force.

I nominate the following-named officers to be assigned to positions of importance and responsibility designated by the President in the grade indicated, under the provisions of section 8066, title 10, United States Code:

In the grade of lieutenant general

Maj. Gen. James C. Sherrill, [redacted] FR, Regular Air Force.

Maj. Gen. Otto J. Glasser [redacted] FR, Regular Air Force.

Maj. Gen. Jay T. Robbins, [redacted] FR, Regular Air Force.

Maj. Gen. Russell E. Dougherty, [redacted] FR, Regular Air Force.

I nominate the following-named officers for temporary appointment in the U.S. Air Force under the provisions of chapter 839, title 10 of the United States Code:

To be brigadier general

Col. Carlton L. Lee, [redacted] FR, Regular Air Force.

Col. Walter R. Tkach, [redacted] FR, Regular Air Force, Medical.

Col. Charles E. Williams, Jr., [redacted] FR, Regular Air Force.

Col. John J. Gorman, [redacted] FR, Regular Air Force.

Col. Darrell S. Cramer [redacted] FR, Regular Air Force.

Col. Geoffrey P. Wiedeman, [redacted] FR, Regular Air Force, Medical.

Col. Hamilton B. Webb [redacted] FR, Regular Air Force, Medical.

Col. Bryan M. Shotts, [redacted] FR, Regular Air Force.

Col. Morton J. Gold, [redacted] FR, Regular Air Force.

Col. John H. Germeraad [redacted] FR, Regular Air Force.

Col. Robert R. Scott, [redacted] FR, Regular Air Force.

Col. Leroy J. Manor, [redacted] FR, Regular Air Force.

Col. Eugene Q. Steffes, Jr., [redacted] FR, Regular Air Force.

Col. Roy M. Terry, [redacted] FR, Regular Air Force Chaplain.

Col. William H. Best, Jr. [redacted] FR, Regular Air Force.

Col. Frank L. Gailer, Jr. [redacted] FR, Regular Air Force.

Col. Joseph E. Krysakowski, [redacted] FR, Regular Air Force.

Col. Robert E. Brofft, [redacted] FR, Regular Air Force.

Col. Thomas B. Hoxie, [redacted] FR, Regular Air Force.

Col. Winston P. Anderson, [redacted] FR, Regular Air Force.

Col. Roger Hombs, [redacted] FR, Regular Air Force, Dental.

Col. Harold F. Knowles, [redacted] FR, Regular Air Force.

Col. Lawrence W. Steinkraus, [redacted] FR, Regular Air Force.

Col. William C. McGlothlin, Jr., [redacted] FR, Regular Air Force.

Col. Herbert A. Lyon, [redacted] FR, Regular Air Force.

Col. Eugene L. Hudson [redacted] FR, (Lieutenant Colonel Regular Air Force) U.S. Air Force.

Col. Edwin J. White, Jr. [redacted] FR, Regular Air Force.

Col. Edward O. Martin, [redacted] FR, Regular Air Force.

Col. Louis O. Alder, [redacted] FR, Regular Air Force.

Col. Robert H. Gaughan [redacted] FR, Regular Air Force.

Col. Walter T. Galligan [redacted] FR, Regular Air Force.

Col. Edward Ratkovich, [redacted] FR, Regular Air Force.

Col. Frank W. Elliott, Jr. [redacted] FR, Regular Air Force.

Col. John R. Hinton, Jr. [redacted] FR, Regular Air Force.

Col. Wesley L. Pendergraft, [redacted] FR, Regular Air Force.

Col. William R. Hayes [redacted] FR (lieutenant colonel Regular Air Force), U.S. Air Force.

Col. William M. Schoning, [redacted] FR (major Regular Air Force), U.S. Air Force.

Col. John F. Albert, [redacted] FR, Regular Air Force, Chaplain.

Col. Daniel James, Jr [redacted] FR, Regular Air Force.

Col. Harry N. Cordes [redacted] FR, Regular Air Force.

Col. John F. Gonge, [redacted] FR, Regular Air Force.

able early warning reporting system on the abuse of controlled and non-controlled drugs.

5. Development of an accurate statistical reporting system on abuse data associated with crime and criminal activity, including an improved addict reporting system.

6. Studes to show the relationship between crime and drug dependent persons, studies to identify predisposing factors to illicit drug activity and development of tests to be used by enforcement personnel to better perform their functions.

7. Detection of abuse substances by remote sensing devices.

8. Studies to evaluate the nature and sources of the supply and flow patterns of legal and illegal drugs throughout the country.

9. Studies to compare and evaluate the deterrent effects of various strategies on drug use and abuse.

10. Studies to evaluate the direct and indirect costs of drug abuse to society.

11. Development of eradication techniques for the destruction of plant species from which controlled drugs may be derived.

To effect the foregoing and to implement the intents of this memorandum, it is agreed that within 10 working days following the signing of the document, a joint committee be established as a working subcommittee of the now existing Departmental Liaison Committee. The subcommittee will be composed of two representatives (one alternate) from each of the signatory agencies. The functions of this committee will be to effectuate the goals of this memorandum and to discuss and resolve problems and issues of concern to signatory agencies which arise in the course of carrying out their repective functions.

JOHN E. INGERSOLL,
Director, Bureau of Narcotics and Dangerous Drugs.

JAMES D. ISBISTER,
Acting Director, National Institue of Mental Health.

Mr. DODD. Mr. President, I am delighted with the tremendous change in direction this bill signifies for the Congress and the nation.

The government has finally eliminated mandatory minimum sentences for drug violations and further, has reduced first offender possession violations to misdemeanors, punishable by up to one year's imprisonment.

The bill gives judges much greater latitude in handling the increasing numbers of drug abusers, thousands of whom are not youths with delinquent or criminal records.

However, penalties for drug pushers remain strong, as a necessary deterrent to this practice.

The bill authorizes additional enforcement personnel for the Bureau of Narcotics and Dangerous Drugs and provides the Attorney General and the Bureau with new and necessary enforcement tools including the right to obtain and execute no-knock search warrants in certain, specified instances.

Title III of the bill regulates the import and export of controlled drugs and provides for limits on the amount of crude opium that may be imported into the United States. The controls embodied in this title should be sufficient to stem the diversion of drugs from legitimate channels into the illicit markets, a practice which has been ongoing utilizing the method of export and re-entry as a means of diversion.

On balance this is a good bill.

While the Senate did not prevail on all issues, I believe that the Conference Report should be accepted.

I urge Senators to do so.

Mr. HUGHES. Mr. President, will the Senator yield?

Mr. McCLELLAN. I yield.

Mr. HUGHES. Mr. President, I think that the members of the committees in both Houses, who have labored for many hours over this particular piece of legislation are to be congratulated. As we all know, their work was difficult, there were many complex problems to be resolved, and there were many jurisdictional overlaps which, with a good deal of cooperation, had to be worked out. There was much give and take on the part of all interested parties, and the final legislation, I am convinced, was the better for it.

To my mind, this legislation constitutes an extremely important step forward in dealing with the drug epidemic in this country—in the fields of prevention and rehabilitation as well as in the field of law enforcement. It is beyond contention that in dealing with the illicit distribution of narcotics and dangerous drugs, stern laws and strict enforcement are essential. It is just as true, however, that the most efficient possible system of enforcement and punishment cannot do the job alone. This bill makes major advances in both of these areas.

The present bill constitutes a great improvement over the original legislation in this area which was first considered by the Senate. At the time that legislation was being considered by the Senate, I offered amendments which would have: limited the Attorney General's authority for conducting educational and research programs to those directly related to enforcement of the control provisions of the legislation; given greater authority to the Secretary of Health, Education, and Welfare in the classification of controlled substances; and provided for the confidentiality of information about patients or research subjects who have been promised anonymity by a Government agency in exchange for highly personal information.

At the time those amendments were originally proposed, they were not successful. I am pleased to be able to say today that the amendments or the concepts behind them are a part of the legislation which we have before us today. I am also pleased that the conference committee saw fit to retain my amendment making those persons who are guilty of distributing marihuana for no remuneration subject to the same penalties as those persons who are charged with possession, rather than subject to the severe penalties for trafficking and distribution.

These were dramatic steps toward giving the legislation the proper balance between law enforcement and prevention, rehabilitation, and research.

If there are many reasons to be pleased about the legislation, there are also several reasons to be concerned. I feel that the no-knock provisions, which give law enforcement officers the authority to break and enter without announcing their identity or purpose constitute an unnecessary intrusion into the private lives and rights of our citizens. I am not convinced that we have yet given our law enforcement officers the kinds of determined and complete backing they need to obtain and use legitimate tools of unquestioned constitutionality at the present time. Until that has been done, I do not believe that we can be justified in moving into this questionable area.

One other brief point along this line. H.R. 18583 fails to distinguish between the relative harmfulness of the various drugs for purposes of criminal sanctions. For example, in the distribution area, the same penalty attaches for distribution of LSD as for the distribution of marihuana; in the possession area the same penalty attaches for possession of all drugs, whether heroin, LSD, amphetamines, or marihuana.

This difficulty is caused by the type of classification structure which is used in the proposed legislation. Classification in the bill depends primarily upon whether there is an accepted medical use for the drug. Because heroin and marihuana have no recognized medical use, they are classified in the same category. Such a classification is valid for purposes of manufacturing controls and reporting requirements. If there is no valid use for a drug, there is a sound reason to impose the strictest manufacturing and record-keeping controls. But criminal sanctions for illegal distribution and use should be based upon the danger to society and the individual, not upon whether there is any valid medical use.

I am hopeful that this situation will be remedied and compensated for somewhat by the Departments of Health, Education, and Welfare and Justice, working together to develop a classification of substances based upon the harm of controlled substances to the individual and to society. Such information could be used to provide relevant information to the judiciary for their discretionary consideration and use in determining appropriate sanctions in cases involving violations of sections 401 and 404 of title II of the act—that is, the possession and distribution sections.

If this is not done administratively certainly it will then have to be done later legislatively, so that our courts can have available to them the scientific, medical, and law enforcement data upon which they can base an intelligent and compassionate decision with respect to sanctions.

Finally, I would like to comment on title I of the bill. That title deals with prevention and rehabilitation programs. The substitute amendment to this title which I proposed, which was cosponsored by all of the members of the Labor and Public Welfare Committee, and which passed the Senate 44 to 23, would have established a National Institute for the Prevention, and Treatment of Drug Abuse and Drug Dependence with responsibilities which were spelled out in the law; would give greater emphasis to grants for programs which were developed at the State and local community levels; would have established prevention and rehabilitation programs for Federal employees; and would have increased authorizations reasonably for the prevention and rehabilitation area. The House was unwilling to accept these changes in emphasis for Federal programs at this late date, but indicated their willingness to hold hearings on the policy questions involved in the near future.

Several important changes were made in the legislation because of the amend-

(3) require that the General Services Administration take custody of the property and remove it to an appropriate location for disposition in accordance with law.

(d) All provisions of law relating to the seizure, summary, and judicial forfeiture, and condemnation of property for violation of the customs laws; the disposition of such property or the proceeds from the sale thereof; the remission or mitigation of such forfeitures; and the compromise of claims and the award of compensation to informers in respect of such forfeitures shall apply to seizures and forfeitures incurred, or alleged to have been incurred, under the provisions of this Act, insofar as applicable and not inconsistent with the provisions hereof: *Provided*, That such duties as are imposed upon the customs officer or any other person with respect to the seizure and forfeiture of property under the customs laws shall be performed with respect to seizures and forfeitures of property under this Act by such officers, agents, or other persons as may be authorized or designated for that purpose by the Attorney General, except to the extent that such duties arise from seizures and forfeitures effected by any customs officer.

(e) Whenever property is forfeited under this Act the Attorney General may—

(1) retain the property for official use;

(2) sell any forfeited property which is not required to be destroyed by law and which is not harmful to the public, provided that the proceeds be disposed of for payment of all proper expenses of the proceedings for forfeiture and sale including expenses of seizure, maintenance of custody, advertising and court costs;

(3) require that the General Services Administration take custody of the property and remove it for disposition in accordance with law; or

(4) forward it to the Bureau of Narcotics and Dangerous Drugs for disposition. Such disposition may include delivery for medical or scientific use to any Federal or State agency under regulations of the Attorney General.

(f) All substances listed in schedule I that are possessed, transferred, sold or offered for sale in violation of the provisions of this Act shall be deemed contraband and seized and summarily forfeited to the United States. Similarly, all substances listed in schedule I, which are seized or come into the possession of the Government, the owners of which are unknown, shall be deemed contraband and summarily forfeited to the United States.

(g) (1) All species of plants from which controlled substances in schedules I and II may be derived which have

been planted or cultivated in violation of this Act, or of which the owners or cultivators are unknown, or which are wild growths, may be seized and summarily forfeited to the United States.

(2) The failure, upon demand by the Attorney General, or his duly authorized agent, of the person in occupancy or in control of land or premises upon which such species of plants are growing or being stored, to produce an appropriate registration, or proof that he is the holder thereof, shall constitute authority for the seizure and forfeiture.

(3) The Attorney General, or his duly authorized agent, shall have authority to enter upon any lands, or into any dwelling pursuant to a search warrant, to cut, harvest, carry off, or destroy such plants.

INJUNCTIONS

SEC. 705. (a) The district courts of the United States and all courts exercising general jurisdiction in the territories and possessions of the United States shall have jurisdiction in proceedings in accordance with the Federal Rules of Civil Procedure to enjoin violations of this Act.

(b) In case of an alleged violation of an injunction or restraining order issued under this section, trial shall, upon demand of the accused, be by a jury in accordance with the Federal Rules of Civil Procedure.

ENFORCEMENT PROCEEDINGS

SEC. 706. Before any violation of this Act is reported by the Director of the Bureau of Narcotics and Dangerous Drugs to any United States attorney for institution of a criminal proceeding, the Director may require that the person against whom such proceeding is contemplated be given appropriate notice and an opportunity to present his views, either orally or in writing, with regard to such contemplated proceeding.

IMMUNITY AND PRIVILEGE

SEC. 707. Whenever in the judgment of the United States attorney the testimony of any witness, or the production of books, papers, or other evidence by any witness, in any case or proceeding before any grand jury or court of the United States with respect to violation of any provision of this Act, is necessary to the public interest, he, upon the approval of the Attorney General, shall make application to the court that the witness shall be instructed to testify or produce evidence subject to the provisions of this section, and upon order of the court such witness shall not be excused from testifying or from producing books, papers, or other evidence on the grounds that the testimony or evidence required of him may tend to incriminate him or subject him to a penalty or forfeiture. But no such witness shall be

prosecuted or subjected to any penalty or forfeiture for or on account of any transaction, matter, or thing concerning which he is compelled, after having claimed his privilege against self-incrimination to testify or produce evidence, nor shall testimony so compelled be used as evidence in any criminal proceeding, except prosecution described in the next sentence, against him in any court. No witness shall be exempt under this section from prosecution for perjury or contempt committed while giving testimony or producing evidence under compulsion as provided in this section.

BURDEN OF PROOF; LIABILITIES

SEC. 708. (a) It shall not be necessary for the United States to negative any exemption or exception set forth in this Act in any complaint, information, indictment, or other pleading or in any trial, hearing, or other proceeding under this Act, and the burden of proof of any such exemption or exception shall be upon the person claiming its benefit.

(b) In the absence of proof that a person is the duly authorized holder of an appropriate registration or order form issued under this Act, he shall be presumed not to be the holder of such registration or form, and the burden of proof shall be upon him to rebut such presumption.

(c) The burden of establishing that a vehicle, vessel, or aircraft used in connection with the substances listed in schedule I of this Act was used in accordance with the

provisions of this Act shall be on the persons engaged in such use.

(d) No liability shall be imposed by virtue of this Act upon any duly authorized Federal officer engaged in the enforcement of this Act, or upon any duly authorized officer of any State, territory, political subdivision thereof, the District of Columbia, or any possession of the United States, who shall be engaged in the enforcement of any law or municipal ordinance relating to controlled dangerous substances.

PAYMENTS AND ADVANCES

SEC. 709. (a) The Attorney General is authorized to pay any person, from funds appropriated for the Bureau of Narcotics and Dangerous Drugs, for information concerning a violation of this Act, such sum or sums of money as he may deem appropriate, without reference to any moieties or rewards to which such person may otherwise be entitled by law.

(b) Moneys expended from appropriations of the Bureau of Narcotics and Dangerous Drugs for purchase of controlled dangerous substances and subsequently recovered shall be reimbursed to the current appropriation for the Bureau.

(c) The Attorney General is authorized to direct the

advance of funds by the Treasury Department in connection with the enforcement of this Act.

TITLE VIII—MISCELLANEOUS

REPEALERS

SEC. 801. The laws specified in the following schedule are repealed except with respect to rights and duties which matured, penalties which were incurred, and proceedings which were begun before the effective date of this Act:

STATUTES AT LARGE

(a) Act of February 23, 1887 (ch. 210, secs. 1, 2, 24 Stat. 409), as amended (title 21, secs. 191–193).

(b) Act of February 9, 1909 (ch. 100, 35 Stat. 614), as amended (title 21, secs. 171, 173, 174–184, 185).

(c) Section 1 of the Act of March 28, 1928 (ch. 266, 45 Stat. 374), as amended (title 31, sec. 529a).

(d) Act of June 14, 1930 (ch. 488, sec. 6, 46 Stat. 587; title 21, sec. 173a).

(e) Act of June 14, 1930 (ch. 488, secs. 7, 8), as amended (title 21, secs. 197, 198).

(f) Act of July 3, 1930 (ch. 829, 46 Stat. 850; title 21, sec. 199).

(g) Section 6 of the Act of August 7, 1939 (ch. 566, 53 Stat. 1263; title 31, sec. 529g).

(h) Act of December 11, 1942 (ch. 720, 56 Stat. 1045), as amended (title 21, secs. 188–188n).

(i) Act of August 11, 1955 (ch. 800, secs. 1–3, 69 Stat. 684; title 21, secs. 198a–c).

(j) Section 15 of the Act of August 1, 1956 (ch. 852, 70 Stat. 910; title 48, sec. 1421m).

(k) Section 1 of the Act of July 18, 1956 (ch. 629, title I), as amended (title 21, sec. 184a).

(l) Act of April 22, 1960 (74 Stat. 55; title 21, secs. 501–517).

UNITED STATES CODE

(a) Title 18, sections 1401–1407.

(b) Title 18, section 3616.

(c) Title 26, sections 4701–4776.

(d) Title 26, sections 7237–7238.

(e) Title 26, section 7491.

CONFORMING AMENDMENTS

SEC. 802. (a) Section 1114 of title 18, United States Code, is amended by striking out "the Bureau of Narcotics" and inserting "the Bureau of Narcotics and Dangerous Drugs".

(b) Section 1952 of title 18 of the United States Code is amended by—

(1) inserting in subsection (b) (1) the words "other controlled dangerous substances," immediately following the word "narcotics".

(2) striking subsection (c) and substituting the following new section:

"(c) Investigation of violations under this section involving liquor shall be conducted under the supervision of the Secretary of the Treasury.

(c) Section 4251(a) of title 18 of the United States Code is amended by striking out the words "section 4731 of the Internal Revenue Code of 1954, as amended," and substituting "the Controlled Narcotic Drug Act of 1969".

(d) Section 584 of the Act of June 17, 1930 (ch. 497, title IV, 46 Stat. 748), as amended by section 10 of the Act of July 1, 1944 (ch. 377, 58 Stat. 722), and section 9 of the Act of March 8, 1946 (ch. 81, 60 Stat. 39; title 19, sec. 1584), is amended by striking out the last sentence of the second paragraph and substituting the following new sentence: "The words 'opiate' and 'marihuana' as used in this paragraph shall have the same meaning as defined in the Controlled Narcotic Drug Act of 1969."

(e) Section 801(a) of the Federal Food, Drug, and Cosmetic Act (title 21, sec. 381(a)), as amended, is amended in the last sentence thereof by striking out "This paragraph" and substituting therefor "Clause (2) of the third sentence of this paragraph," and by striking out the words "section 2 of the Act of May 26, 1922, as amended

(U.S.C. 1934 edition, title 21, sec. 173)" and substituting "the Controlled Narcotic Drug Act of 1969".

(f) Section 4901(a) of title 26 of the United States Code is amended by deleting the words "4721 (narcotic drugs), or 4751 (marihuana)" and by inserting the word "or" before the number "4461".

(g) Section 4905(b) of title 26 of the United States Code is amended by deleting the words "narcotics, marihuana," and "4722, 4753".

(h) Section 6808 of title 26 of the United States Code is amended by striking out subsection (8) and renumbering subsections (9), (10), (11), (12), and (13), as (8), (9), (10), (11), and (12).

(i) Section 7012 of title 26 of the United States Code is amended by striking out subsections (a) and (b) and renumbering (c), (d), (e), (f), (g), (h), (i), and (j) as (a), (b), (c), (d), (e), (f), (g), and (h).

(j) Section 7103 of title 26 of the United States Code is amended by striking out subsection (d) (3) (D) and renumbering (E) and (F) as (D) and (E).

(k) Section 7326 of title 26 of the United States Code is amended by striking out subsection (b) and relettering (c) as (b).

(l) Section 7607 of title 26 of the United States Code

is amended by deleting all words prior to the word "officers" and by capitalizing the word "officer"; and by deleting in subsection (2) the words "section 4731" and "section 4761" and inserting in subsection (2) in lieu thereof the words "Controlled Narcotic Drug Act of 1969".

(m) Section 7651 of title 26 of the United States Code is amended by deleting the words "sections 4705(b), 4735, and 4762 (relating to taxes on narcotic drugs and marihuana)".

(n) Section 7655 of the United States Code is amended by deleting subsections (3) and (4).

(o) Section 7609 of the United States Code is amended by striking out subsections (a)(3) and (a)(4) and renumbering (5) and (6) as (3) and (4).

(p) Section 7641 of the United States Code is amended by striking out the words "opium suitable for smoking purposes,".

(q) Section 2901(a) of title 28 of the United States Code is amended by striking out the words "section 4731 of the Internal Revenue Code of 1954, as amended," and substituting "the Controlled Narcotic Drug Act of 1969".

(r) Section 3 of the Act of August 7, 1939 (ch. 566, 53 Stat. 1263; title 31, sec. 529d), is amended by striking out the words "or the Commissioner of Narcotics, as the case may be,".

(s) Section 4 of the Act of August 7, 1939 (ch. 566, 53 Stat. 1263; title 31, sec. 529e), is amended by striking out the words "or narcotics" and "or narcotic".

(t) Section 5 of the Act of August 7, 1939 (ch. 566, 53 Stat. 1263; title 31, sec. 529f) is amended by striking out the words "or narcotics".

(u) Section 308(c)(2) of the Act of August 27, 1935 (ch. 740), as amended (49 Stat. 880; title 40, sec. 304(m)), is amended by striking out the words "Narcotic Drugs Import and Export Act" and substituting "Controlled Narcotic Drug Act of 1969".

(v) Section 302(a) of the Act of July 1, 1944 (ch. 373; title III), as amended (58 Stat. 692; title 42, sec. 242(a)) is amended by striking out the words "Narcotic Drugs Import and Export Act" and substituting "Controlled Narcotic Drug Act of 1969".

(w) Section 301(a) of the Act of November 8, 1966 (ch. 175, title III), as amended (80 Stat. 1444; title 42, sec. 3411) is amended by striking out the words "section 4731 of the Internal Revenue Code of 1954 and substituting "the Controlled Narcotic Drug Act of 1969".

(x) Section 1(a) of the Act of July 15, 1954 (ch. 512), as amended (68 Stat. 484; title 46, sec. 239a) is amended by striking out the words "paragraph (a) of the first section of the Narcotic Drugs Import and Export Act, as

amended (21 U.S.C. 171(a))" and substituting "the Controlled Narcotic Drug Act of 1969"; and by striking out the words "section 3238(b) of the Internal Revenue Code" and substituting "the Controlled Narcotic Drug Act of 1969".

(y) Section 7(d) of the Act of August 9, 1939 (ch. 618), as amended (53 Stat. 1292; title 49, sec. 787) is amended by striking out the words "Narcotic Drugs Import and Export Act, the internal revenue laws or any amendments thereof, or the regulations issued thereunder" and substituting "Controlled Narcotic Drug Act of 1969"; and striking out the words "Marihuana Tax Act of 1937 or the regulations issued thereunder" and substituting "Controlled Narcotic Drug Act of 1969".

PENDING PROCEEDINGS

SEC. 803. (a) Prosecutions for any violation of law occurring prior to the effective date of this Act shall not be affected by these repealers or amendments, or abated by reason thereof.

(b) Civil seizures or forfeitures and injunctive proceedings commenced prior to the effective date of this Act shall not be affected by the repealers or amendments, or abated by reason thereof.

(c) All administrative proceedings pending before the

Bureau of Narcotics and Dangerous Drugs on the effective date of this enactment shall be continued and brought to final determination in accord with laws and regulations in effect prior to the date of this enactment. Such drugs placed under control prior to enactment of this Act which are not listed within schedules I through IV shall automatically be controlled by the Attorney General and listed in the appropriate schedule.

(d) The provisions of this Act shall be applicable to violations of law, seizures and forfeiture, injunctive proceedings, administrative proceedings and investigations which occur following its effective dates.

CONTINUATION OF REGULATIONS

SEC. 804. Any orders, rules, and regulations which have been promulgated under any law affected by this Act and which are in effect on the day preceding enactment of this title shall continue in effect until modified, superseded, or repealed by the Attorney General.

SEVERABILITY

SEC. 805. If a provision of this Act is held invalid, all valid provisions that are severable shall remain in effect. If a provision of this Act is held invalid in one or more of its applications, the provision shall remain in effect in all its valid applications that are severable.

AUTHORIZATION OF APPROPRIATIONS

SEC. 806. There are hereby authorized to be appropriated such sums as may be necessary to carry out the purposes of this Act.

SAVING PROVISION

SEC. 807. Nothing in this Act, except this title and, to the extent of any inconsistency, section 309 of this Act, shall be construed as in any way affecting, modifying, repealing, or superseding the provisions of the Federal Food, Drug, and Cosmetic Act.

EFFECTIVE DATE

SEC. 808. This Act shall take effect on the one hundred and eightieth day following the date of its enactment.

The CHAIRMAN. There is a Presidential message on this subject which will also be included in the record at this point.

(The President's message referred to follows:)

[H. Doc. No. 91–138, 91st Cong., first sess.]

COMBATING DRUG ABUSE

To the Congress of the United States:

Within the last decade, the abuse of drugs has grown from essentially a local police problem into a serious national threat to the personal health and safety of millions of Americans.

A national awareness of the gravity of the situation is needed; a new urgency and concerted national policy are needed at the Federal level to begin to cope with this growing menace to the general welfare of the United States.

Between the years 1960 and 1967, juvenile arrests involving the use of drugs rose by almost 800 percent; half of those now being arrested for the illicit use of narcotics are under 21 years of age. New York City alone has records of some 40,000 heroin addicts, and the number rises between 7000 and 9000 a year. These official statistics are only the tip of an iceberg whose dimensions we can only surmise.

The number of narcotics addicts across the United States is now estimated to be in the hundreds of thousands. Another estimate is that several million American college students have at least experimented with marihuana, hashish, LSD, amphetamines, or barbiturates. It is doubtful that an American parent can send a son or daughter to college today without exposing the young man or woman to drug abuse. Parents must also be concerned about the availability and use of such drugs in our high schools and junior high schools.

The habit of the narcotics addict is not only a danger to himself, but a threat to the community where he lives. Narcotics have been cited as a primary cause of the enormous increase in street crimes over the last decade.

As the addict's tolerance for drugs increases, his demand for drugs rises, and the cost of his habit grows. It can easily reach hundreds of dollars a day. Since an underworld "fence" will give him only a fraction of the value of goods he steals, an addict can be forced to commit two or three burglaries a day to maintain his habit. Street robberies, prostitution, even the enticing of others into addiction to drugs—an addict will reduce himself to any offense, any degradation in order to acquire the drugs he craves.

However far the addict himself may fall, his offenses against himself and society do not compare with the inhumanity of these who make a living exploiting the weakness and desperation of their fellow men. Society has few judgments too severe, few penalties too harsh for the men who make their livelihood in the narcotics traffic.

It has been a common oversimplification to consider narcotics addiction, or drug abuse, to be a law enforcement problem alone. Effective control of illicit drugs requires the cooperation of many agencies of the Federal and local and State governments; it is beyond the province of any one of them alone. At the Federal level, the burden of the national effort must be carried by the Departments of Justice, Health, Education, and Welfare, and the Treasury. I am proposing ten specific steps as this Administration's initial counter-moves against this growing national problem.

I. FEDERAL LEGISLATION

To more effectively meet the narcotic and dangerous drug problems at the Federal level, the Attorney General is forwarding to the Congress a comprehensive legislative proposal to control these drugs. This measure will place in a single statute, a revised and modern plan for control. Current laws in this field are inadequate and outdated.

I consider the legislative proposal a fair, rational and necessary approach to the total drug problem. It will tighten the regulatory controls and protect the public against illicit diversion of many of these drugs from legitimate channels. It will insure greater accountability and better recordkeeping channels. It will give law enforcement stronger and better tools that are sorely needed so that those charged with enforcing these laws can do so more effectively. Further, this proposal creates a more flexible mechanism which will allow quicker con-

trol of new dangerous drugs before their misuse and abuse reach epidemic proportions. I urge the Congress to take favorable action on this bill.

In mid-May the Supreme Court struck down segments of the marihuana laws and called into question some of the basic foundations for the other existing drug statutes. I have also asked the Attorney General to submit an interim measure to correct the constitutional deficiencies of the Marihuana Tax Act as pointed out in the Supreme Court's recent decision. I urge Congress to act swiftly and favorably on the proposal to close the gap now existing in the Federal law and thereby give the Congress time to carefully examine the comprehensive drug control proposal.

II. STATE LEGISLATION

The Department of Justice is developing a model State Narcotics and Dangerous Drugs Act. This model law will be made available to the fifty State governments. This legislation is designed to improve State laws in dealing with this serious problem and to complement the comprehensive drug legislation being proposed to Congress at the national level. Together these proposals will provide an interlocking trellis of laws which will enable government at all levels to more effectively control the problem.

III. INTERNATIONAL COOPERATION

Most of the illicit narcotics and high-potency marihuana consumed in the United States is produced abroad and clandestinely imported. I have directed the Secretary of State and the Attorney General to explore new avenues of cooperation with foreign governments to stop the projection of this contraband at its source. The United States will cooperate with foreign governments working to eradicate the production of illicit drugs within their own frontiers. I have further authorized these Cabinet officers to formulate plans that will lead to meetings at the law enforcement level between the United States and foreign countries now involved in the drug traffic either as originators or avenues of transit.

IV. SUPPRESSION OF ILLEGAL IMPORTATION

Our efforts to eliminate these drugs at their point of origin will be coupled with new efforts to intercept them at their point of illegal entry into the United States. The Department of the Treasury, through the Bureau of Customs, is charged with enforcing the nation's smuggling laws. I have directed the Secretary of the Treasury to initiate a major new effort to guard the nation's borders and ports against the growing volume of narcotics from abroad. There is a recognized need for more men and facilities in the Bureau of Customs to carry out this directive. At my request, the Secretary of the Treasury has submitted a substantial program for increased manpower and facilities in the Bureau of Customs for this purpose which is under intensive review.

In the early days of this Administration, I requested that the Attorney General form an inter-departmental Task Force to conduct a comprehensive study of the problem of unlawful trafficking in narcotics and dangerous drugs. One purpose of the Task Force has been to examine the existing programs of law enforcement agencies concerned with the problem in an effort to improve their coordination and efficiency. I now want to report that this Task Force has completed its study and has a recommended plan of action, for immediate and long-term implementation, designed to substantially reduce the illicit trafficking in narcotics, marihuana and dangerous drugs across United States borders. To implement the recommended plan, I have directed the Attorney General to organize and place into immediate operation an "action task force" to undertake a frontal attack on the problem. There are high profits in the illicit market for those who smuggle narcotics and drugs into the United States; we intend to raise the risks and cost of engaging in this wretched traffic.

V. SUPPRESSION OF NATIONAL TRAFFICKING

Successful prosecution of an increased national effort against illicit drug trafficking will require not only new resources and men, but also a redeployment of existing personnel within the Department of Justice.

I have directed the Attorney General to create, within the Bureau of Narcotics and Dangerous Drugs, a number of special investigative units. These special forces will have the capacity to move quickly into any area in which intelligence indicates major criminal enterprises are engaged in the narcotics traffic. To carry out this directive, there will be a need for additional manpower

within the Bureau of Narcotics and Dangerous Drugs. The budgetary request for FY 1970 now pending before the Congress will initiate this program. Additional funds will be requested in FY 1971 to fully deploy the necessary special investigative units.

VI. EDUCATION

Proper evaluation and solution of the drug problem in this country has been severely handicapped by a dearth of scientific information on the subject—and the prevalence of ignorance and misinformation. Different "experts" deliver solemn judgments which are poles apart. As a result of these conflicting judgments, Americans seem to have divided themselves on the issue, along generational lines.

There are reasons for this lack of knowledge. First, widespread drug use is a comparatively recent phenomenon in the United States. Second, it frequently involves chemical formulations which are novel, or age-old drugs little used in this country until very recently. The volume of definitive medical data remains small—and what exists has not been broadly disseminated. This vacuum of knowledge—as was predictable—has been filled by rumors and rash judgments, often formed with a minimal experience with a particular drug, sometimes formed with no experience or knowledge at all.

The possible danger to the health or well-being of even a casual user of drugs is too serious to allow ignorance to prevail or for this information gap to remain open. The American people need to know what dangers and what risks are inherent in the use of the various kinds of drugs readily available in illegal markets today. I have therefore directed the Secretary of Health, Education, and Welfare, assisted by the Attorney General through the Bureau of Narcotics and Dangerous Drugs, to gather all authoritative information on the subject and to compile a balanced and objective educational program to bring the facts to every American—especially our young people.

With this information in hand, the overwhelming majority of students and young people can be trusted to make a prudent judgment as to their personal course of conduct.

VII. RESEARCH

In addition to gathering existing data, it is essential that we acquire new knowledge in the field. We must know more about both the short and long-range effects of the use of drugs being taken in such quantities by so many of our people. We need more study as well to find the key to releasing men from the bonds of dependency forged by any continued drug abuse.

The National Institute of Mental Health has primary responsibility in this area, and I am further directing the Secretary of Health, Education, and Welfare to expand existing efforts to acquire new knowledge and a broader understanding in this entire area.

VIII. REHABILITATAION

Considering the risks involved, including those of arrest and prosecution, the casual experimenter with drugs of any kind, must be considered at the very least, rash and foolish. But the psychologically dependent regular users and the physically addicted are genuinely sick people. While this sickness cannot excuse the crimes they commit, it does help to explain them. Society has an obligation both to itself and to these people to help them break the chains of their dependency.

Currently, a number of federal, state and private programs of rehabilitation are being operated. These programs utilize separately and together, psychiatry, psychology and "substitute drug" therapy. At this time, however, we are without adequate data to evaluate their full benefit. We need more experience with them and more knowledge. Therefore, I am directing the Secretary of Health, Education, and Welfare to provide every assistance to those pioneering in the field, and to sponsor and conduct research on the Federal level. This Department will act as a clearinghouse for the collection and dissemination of drug abuse data and experience in the area of rehabilitation.

I have further instructed the Attorney General to insure that all Federal prisoners, who have been identified as dependent upon drugs, be afforded the most up-to-date treatment available.

IX. TRAINING PROGRAM

The enforcement of narcotics laws require considerable expertise, and hence considerable training. The Bureau of Narcotics and Dangerous Drugs provides the bulk of this training in the Federal government. Its programs are extended to include not only its own personnel, but State and local police officers, forensic chemists, foreign nationals, college deans, campus security officers, and members of industry engaged in the legal distribution of drugs.

Last year special training in the field of narcotics and dangersous drug enforcement was provided for 2700 State and local law enforcement officials. In fiscal year 1969 we expanded the program an estimated 300 percent in order to train some 11,000 persons. During the current fiscal year we plan to redouble again that effort—to provide training to 22,000 State and local officers. The training of these experts must keep pace with the rise in the abuse of drugs, if we are ever to control it.

X. LOCAL LAW ENFORCEMENT CONFERENCES

The Attorney General intends to begin a series of conferences with law enforcement executives from the various States and concerned Federal officials. The purposes of these conferences will be several first, to obtain firsthand information, more accurate data, on the scope of the drug problem at that level; second, to discuss the specific areas where Federal assistance and aid can best be most useful; third, to exchange ideas and evaluate mutual policies. The end result we hope will be a more coordinated effort that will bring us visible progress for the first time in an alarming decade.

These then are the first ten steps in the national effort against narcotic marihuana and other dangerous drug abuse. Many steps are already underway. Many will depend upon the support of the Congress. I am asking, with this message, that you act swiftly and favorably on the legislative proposals that will soon be forthcoming, along with the budgetary requests required if our efforts are to be successful. I am confident that Congress shares with me the grave concern over this critical problem, and that Congress will do all that is necessary to mount and continue a new and effective Federal program aimed at eradicating this rising sickness in our land.

RICHARD NIXON.

THE WHITE HOUSE, *July 14, 1969.*

The CHAIRMAN. We will hear first today from the Honorable John N. Mitchell, the Attorney General, who will be followed this afternoon by the Secretary of the Treasury, the Honorable David M. Kennedy.

Tomorrow we will hear from Dr. Roger O. Egeberg, Assistant Secretary of HEW, and Dr. Bertram S. Brown, Director, National Institute of Mental Health.

Following the testimony of these administration officials, we will then receive testimony from the interested public.

Mr. Attorney General, we welcome you. We understand you have with you Messrs. John E. Ingersoll, Director, and Michael R. Sonnenreich, Deputy Chief Counsel, Bureau of Narcotics and Dangerous Drugs.

This is your first public appearance before the Ways and Means Committee. We are delighted to have you with us and we will be pleased to hear from you.

STATEMENT OF HON. JOHN N. MITCHELL, ATTORNEY GENERAL, U.S. DEPARTMENT OF JUSTICE; ACCOMPANIED BY JOHN E. INGERSOLL, DIRECTOR, AND MICHAEL R. SONNENREICH, DEPUTY CHIEF COUNSEL, BUREAU OF NARCOTICS AND DANGEROUS DRUGS

Attorney General MITCHELL. Thank you, Mr. Chairman.

Mr. Chairman and members of the committee, I deeply appreciate your invitation to appear before you today to discuss legislation dealing with control of dangerous drugs. I assure you that the need for more effective control is a matter of the deepest concern to the President and to the Department of Justice and to me, just as I know it is to the Congress and the members of this committee.

In a few weeks the young people of our Nation will be returning to school—an event which American parents once looked upon with a smile and a sigh of relief. Today, it is a sad fact that parents view the opening of school with trepidation and concern since the drug traffic in narcotics and pills has penetrated the schoolrooms and schoolyards of America at virtually every level.

It is no exaggeration to say that the drug danger threatens the moral and physical health of an entire generation.

I am accompanied today by Mr. John E. Ingersoll, Director of the Bureau of Narcotics and Dangerous Drugs, and by Mr. Michael R. Sonnenreich, Deputy Chief Counsel of the Bureau. I would like to address my testimony to the major features of the legislation recommended by the administration and I have asked Mr. Ingersoll to discuss the more technical aspects of the bill.

On July 14, 1969, the President sent a message to the Congress relating exclusively to the narcotics and dangerous drug problem in the United States. At that time, he expressed the administration's concern with the serious problem caused by drug abuse and misuse in the United States and outlined 10 specific steps the administration would take as initial countermoves against this growing national problem.

Mr. Chairman, the President's 10-point program is directed at the many facets of the drug abuse problem. The program calls for new Federal and State laws, new cooperation with foreign governments and increased effort at our borders to halt the flow of drugs into the United States from outside sources; it calls for improved and increased training and resources for law enforcement; and finally, it recognizes that new laws and increased enforcement alone will not solve the drug abuse problem—rather we must also have effective programs of research, public education, and addict rehabilitation.

For the convenience of the committee, I have attached a copy of the President's message to my statement and would like to request that it be included in the record following my statement. (See p. 195.)

All of these areas discussed in the President's message are vital in our Federal effort to deal with the problem. Today, however, I shall focus my comments principally on the law enforcement aspects of the problem, since this is the area of major concern to the Department of Justice.

Education, research, and rehabilitation are the long-term answers to the drug abuse problem in the United States. But while we plan, pre-

pare and explore in detail each of these areas, it is important that we regulate the manufacture, importation and distribution of narcotics and dangerous drugs through a logical and enforceable control scheme.

On July 15, 1969, the administration sent to Congress the proposed "Controlled Dangerous Substances Act." This is the proposal the President promised in his message. This legislation, amended during consideration in the Senate, passed that body as S. 3246 on January 28, 1970 by a unanimous vote—82–0.

In the House of Representatives, there has been a jurisdictional problem of which you are well aware, and the original bill was divided between this committee and the Interstate and Foreign Commerce Committee. The Subcommittee on Public Health and Welfare of the Interstate and Foreign Commerce Committee commenced hearings on February 3, 1970, and is about to conclude its work on the legislation. This committee has several drug proposals before it; however, H.R. 17463, introduced by Chairman Mills and Mr. Byrnes, embodies the provisions recommended by the administration, H.R. 17463 is very similar to S. 3246, which the administration also endorses.

Since the introduction of H.R. 1763, representatives of the administration have had extensive and extended discussions with the Public Health and Welfare Subcommittee. As a result of these discussions, the administration has endorsed several changes in the provisions of our proposed bill which we believe improve the legislation and resolve the problems that many witnesses raised during the hearings before the Public Health and Welfare Subcommittee.

Accordingly, Mr. Chairman, we would like to submit to the committee later this week a number of recommended changes for H.R. 17463. I have asked Mr. Ingersoll in his testimony to highlight the major areas where we have sought to resolve apparent problems in the administration's legislation.

Mr. Chairman, if we are to have truly effective drug enforcement, we must have a new Federal law. It is very important that both your committee and the Interstate and Foreign Commerce Committee reach agreement with regard to the proposed revisions in the drug laws. Without such agreement, we are likely to have divergent acts emerge from the House of Representatives when our purpose is to unify and clarify the laws into a new code. We stand ready to assist this committee in any way we can to facilitate your consideration of this legislation and coordination of the work of your committee and the Interstate and Foreign Commerce Committee.

I would now like to briefly mention some of the problems that exist under our present system of narcotics and dangerous drug laws and the design of our proposed legislation to deal with these problems.

First, we presently have a hodgepodge of laws with differing regulatory features for controlling drugs. The disunity of the existing law is the result of piecemeal, ad hoc attempts over the last 50 years to deal with the problem of controlling dangerous drugs. Beginning with the Harrison Narcotic Act of 1914, nine major pieces of legislation have been enacted in the narcotic and dangerous drug field. An examination of these measures, from the Harrison Act through the Marihuana Tax Act of 1937, through the Narcotic Control Act of 1956, through the Drug Abuse Control Amendments of 1965, provides

both a chronology of our sporadic efforts to deal with a growing problem and an insight into our failure to do so effectively.

In passing these laws, use was made of the power to tax and, more recently, the power to regulate interstate commerce. They represent limited responses to what was deemed to be the given needs of the times. There was no conception of the problem growing to the dimensions it has reached today. Drug abuse has outstripped the growth of our technology and population, while our laws have remained static.

Today we have one Federal agency responsible for the enforcement of these laws, and it must approach its enforcement and regulatory responsibilities with divergent schemes of authority. For example, we have subpena power as to the narcotic drugs but not as to the other dangerous drugs. We have order forms and quota requirements as to the narcotic drugs and marihuana but not as to LSD and the other hallucinogens. We have registration requirements for the narcotics and Marihuana that are different from those of the other dangerous drugs. We have forfeiture powers as to the narcotics and marihuana but a completely different type of forfeiture for the dangerous drugs such as the hallucinogens and amphetamines.

Efficient law enforcement requires both an effective organizational structure and a sound, coherent legal basis. The administration's proposed legislation—as embodied in H.R. 17463—would create such a structure and basis by providing a single, integrated body of law and derivative regulations based solely on the power to regulate interstate commerce. Controls and other enforcement tools would be interrelated and consistent.

Second, as the result of a series of cases that have arisen recently—namely, the *Leary*, *Covington*, *Buie* and *Turner* cases—we no longer have an effective possession law for the narcotic drugs—except heroin, and marihuana. As I am sure you are all aware, the presumption of illegal importation as to marihuana, cocaine, and the other narcotics no longer exists. While possession offenses are not the major thrust of Federal law enforcement, they are a necessary concomitant to drug conspiracy cases against large-scale traffickers. We need a law that clearly defines possession as possession, and H.R. 17463 does this.

Third, there is ample evidence, both in the news media and in scholarly journals, that there is a real credibility gap among the population—both young and old—as to the existing penalties for marihuana, the dangerous drugs, and the narcotics. It is often pointed out that existing penalties are out of phase internally among themselves and externally with the rest of the Federal Criminal Code. This lack of credibility has not only a serious effect on the prosecution and sentencing of defendants but, undoubtedly, has also had the more insidious effect of undermining respect for the entire criminal justice system. There is a need for more careful delineation of the entire narcotic and dangerous drug area, both as to substantive offenses and penalties. We believe that the penalties of H.R. 17463 are realistic and an effective deterrent.

The bill makes simple possession of any drug as a first offense punishable as a misdemeanor. In addition, the first offender may receive the benefit of a special provision whereby he may fulfill probationary terms set by the court and earn dismissal of his case and elimination of a conviction record.

H.R. 17463 also eliminates most mandatory minimums, to which Federal judges are almost unanimously opposed. Individuals established as professional criminals, however, do face mandatory minimums, and a maximum of life imprisonment and substantial forfeitures.

Mr. Ingersoll will go into more detail on the penalty structure, if you so desire, but I can assure you of my satisfaction that these new penalties are both realistic and flexible enough to fit the offense and offender.

Fourth, the diversion of legitimately produced drugs from their normal channels of distribution into illicit sources must be halted. There has been a tremendous upsurge in this kind of diversion in the last 5 years, and we must tighten the regulatory controls now so that we are not faced with utter chaos in the future.

We need a better system of identification of those persons engaged in dealing with dangerous drugs, as well as better methods for inspection and the keeping of records. These are fundamentally law enforcement functions. There are many who say that the dimensions of the drug abuse problem in America today indicate that we are 10 years too late in effectively meeting it. Be that at it may, I feel that we must move more effectively into this area of regulation of the legitimate industry now, so that the same is not said of us in 1980. I should like to point out that H.R. 17463, as did S. 3246, borrows heavily from the existing narcotic regulatory controls that were shaped by this very committee. We feel they are necessary and will not hinder the legitimate manufacturers, distributors, and dispensers of these drugs.

Fifth, key inventory requirements under the drug abuse control amendments of 1965 have expired for most of those drugs, which means that these inventory requirements no longer must be maintained in accordance with law. This glaring loophole must be plugged to facilitate accountability audits to be conducted by Federal agents. H.R. 17463 closes this loophole by requiring inventories which must be conducted every 2 years.

Sixth, there is a need for a more flexible import-export control system to trace all legitimately produced controlled dangerous drugs. The Department of Justice must be able to follow the flow of drugs, not just within the United States, but also those drugs leaving the country and coming into it. This new system, which again borrows heavily from the existing narcotic laws, comports with the needs of protecting the public as well as the consumer. It will allow for a system of authorization by and notification of the Department of Justice on all shipments of drugs in and out of the United States, depending on their schedule classification.

Seventh, H.R. 17463 provides new and important law enforcement tools for the investigation of narcotic and dangerous drug cases. It provides for no knock. Some 31 States already have this authority.

Mr. Chairman, I would like to take a minute of the committee's time, while I am on this subject of no knock, to try to give a better perspective to this type of legislation.

The impression seemingly held by a wide audience is that if no knock is enacted into law, which I strongly hope will be the case, a policeman may, on his own decision, enter any private home at any time of the day or night. Nothing could be further from the truth.

Under the no knock provision, an agent may enter a person's premises without announcing his authority and purpose only if he has obtained a search warrant from a judge and the judge has been persuaded there is probable cause to believe that evidence will be quickly and easily destroyed or that there is a danger to life and limb of the agent.

I would remind you that we are dealing with clever and ruthless drug peddlers, who have no hesitation about taking the life of an agent. And the moment of entry is the moment of greatest peril. Without no knock an agent not only risks his life, but gives the drug peddler the opportunity to destroy the evidence at the same time.

The American people—and the news media which inform them—are fond of catchwords or phrases that neatly sum up what is often a complicated or intricate solution to a pressing problem. Unfortunately, these shortcuts may often lead to erroneous conclusions or opinions on behalf of our citizens—and, I might add, by many newsmen. Such is the case, I think, with the term "no knock" and its application in our uphill battle against drug traffickers.

If I were to try to supply a phrase to describe this type of operation, I would call it quick entry because that is what we seek to do. I might point out that during the most successful Operation Eagle, conducted by the Bureau of Narcotics and Dangerous Drugs last month, quick entry would have proven a valuable tool in four instances, three of which involved the destruction of evidence and one of which involved the safety of two agents.

H.R. 17463 also provides for an administrative inspection warrant procedure that comports with the Supreme Court rulings in the *Camara*, *See* and *Colonnade Catering* cases. Since administrative inspections are a prime means of uncovering drug diversion from legitimate channels, such an administrative inspection warrant procedure is vital to effective law enforcement.

The administrative procedures set out in H.R. 17463 have been streamlined, somewhat along the lines of the existing narcotics laws, to insure due process but not to cause undue delay in bringing drugs under control. Where a drug has a potential for abuse, there must be a quick procedure for bringing that drug under control, while allowing for an administrative hearing and judicial review.

Lastly, H.R. 17463 allows the Attorney General to deny, revoke, and suspend registrations to insure the integrity of the registration system, and to deny those persons who should not be allowed to deal in these drugs the ability to do so. I might point out that under present narcotic and dangerous drug laws, such authority does not exist, and it is sorely needed.

CONCLUSION

As you know, Mr. Chairman, drug abuse has reached the epidemic stage among our young people. It is a critical national problem that needs all the attention we can focus on it.

Virtually no area of the country has escaped this menace. It has invaded the country estates of our most wealthy families with the same ease that it has involved the most desperately poor. The pusher is just as comfortable and as readily available in the halls of our suburban high schools as he is in the halls of our ghetto apartment buildings.

As I said earlier, schools all across the country are about to reopen for the fall semester. Millions of young people will begin leaving for classes early in the morning, not to return until many hours later. Concerned parents will ask themselves. Is this the day that our son or daughter will swallow a pill or smoke a marihuana cigarette?

Mr. Chairman, this committee and the Congress can offer an exciting "back-to-school present" to the families of America by moving swiftly on this legislation and letting them know that more effective tools for drug control are on the way. And when these tools become available, I give you my personal assurance that the Department of Justice will use them to the full extent of the law.

And now I would like to have Mr. Ingersoll discuss the bill in more detail. We will be happy to answer any questions that the committee may have at the conclusion of this presentation.

The CHAIRMAN. Thank you, Mr. Attorney General. We appreciate having you with us, Mr. Ingersoll, and you are recognized.

STATEMENT OF JOHN E. INGERSOLL, DIRECTOR, BUREAU OF NARCOTICS AND DANGEROUS DRUGS

Mr. INGERSOLL. Thank you, Mr. Chairman.

It is also a pleasure for me to appear before you here today to discuss H.R. 17463, which has a most profound effect on my area of responsibility within the Department of Justice.

When I was appointed Director of the newly formed Bureau of Narcotics and Dangerous Drugs in 1968, my task was to unify Federal enforcement and regulatory functions in narcotics and dangerous drugs and develop other means to bring the drug abuse problem under control. We have accomplished the administrative organizing and structuring tasks.

I might add that the Congress has been understanding of the problems by providing additional resources for the Bureau of Narcotics and Dangerous Drugs to carry on its work. It was readily apparent, however, that administrative restructuring would not be enough.

New legislative tools were also necessary to carry out the Bureau's mission. The administration's proposed Controlled Dangerous Substances Act, which is basically embodied in H.R. 17463, is a legislative tool that the Bureau needs to add much to its activities in protecting the public against illicit drug diversion and trafficking.

With your permission, Mr. Chairman, I would like to submit a comprehensive comparative analysis between H.R. 17463 and the existing law, so that each member of the committee can see the differences that this legislation will bring about.

The CHAIRMAN. Mr. Ingersoll, I think also that would properly be a part of our hearing record and without objection we will include it at the conclusion of your statement.

Mr. INGERSOLL. Thank you, Mr. Chairman.

I hope that this will be more useful to the committee than a detailed oral discussion of the legislation on a section-by-section basis now.

At this time, however, I will give you an overview of the legislation so that the arguments, pro and con, can be placed in better perspective. I should emphasize also that although the bill contains a number of

innovations it also seeks to preserve much of the time-tested value of existing drug legislation where possible and consistent with current needs.

THE CONTROLLED DANGEROUS SUBSTANCES ACT

Title I of the Controlled Dangerous Substances Act sets out the constitutional basis on which this legislation is to be grounded, namely, the authority of Congress to control interstate and foreign commerce and to levy reasonable fees to create a system of control to protect the public interest. In addition, title I contains the many definitions necessary for the successful implementation of the bill, as well as repealers and conforming amendments.

Title II of the bill continues the present authority of the Attorney General to control those drugs enumerated as controlled dangerous substances. He may add, delete, or reschedule a drug within any one of the four schedules listed. This may be done either upon his own motion or that of any interested party.

However, before undertaking to bring a drug under control or remove a drug from control, the Attorney General must first consider the advice of the Secretary of Health, Education, and Welfare, and that of the Scientific Advisory Committee established under title VI of the bill. As well as providing for the necessary scientific and medical input into the Attorney General's determination to control a drug, nine criteria are set forth which he must consider before bringing any substance under control.

Drugs subject to control under the Controlled Dangerous Substances Act are listed in one of the four schedules. Each schedule has its own set of additional criteria which must also be met before a drug can be included within the particular schedule. Drugs are to be scheduled according to their relative hazard, potential for abuse, and therapeutic utility and safety.

Title III sets forth the provisions which govern the legitimate manufacture, distribution, and dispensing of controlled dangerous substances. All persons, except those few specifically exempted, who manufacture, distribute, or dispense controlled dangerous substances, must register with the Attorney General. There are also provisions for denial, suspension, or revocation of a registration by the Attorney General. This is an area of responsibility presently under the Attorney General's authority.

Title IV sets out the provisions relating to the importation and exportation of those substances under control. New and stiffer restrictions are imposed upon international trade involving the United States of any controlled dangerous substance. Such restrictions are aimed at decreasing the flow of illicit drugs at this country's borders, especially in the situation which exists now where drugs are legitimately exported from this country only to be brought back in and distributed into illicit channels.

A case in point is the instance where a drug company in Chicago shipped several hundred thousand amphetamines to an address in Tijuana, Mexico, which later turned out to be the eleventh hole of a golf course. Had these export provisions then been in effect, we would have had notice in advance of the export shipment, giving us the opportunity to verify whether or not the drugs were being shipped to a legitimate establishment.

Title V sets out the penalties imposed for violations of the various provisions of the act. In addition to the Attorney General's comments, it might be noted that in section 502, which deals with commercial violations, only civil fines are imposed if the violation is committed without knowledge. However, for willful violations, criminal sanctions will be imposed.

Title VI sets out the administrative provisions necessary for the successful implementation of the bill. Of key importance are the sections authorizing the Attorney General to conduct educational and research programs and establish cooperative arrangements between Federal, State, and local law enforcement agencies as is provided for in present law. Other provisions provide for the establishment of the Scientific Advisory Committee to advise the Attorney General as to the merits of bringing a particular drug under control; administrative hearings; the issuance of subpenas; and judicial review.

Title VII contains the enforcement provisions of the bill including authorization for Federal officers under certain circumstances to execute a search warrant which the issuing magistrate has endorsed for execution without the usual prior announcement of authority and purpose. This is the so-called no-knock warrant. The Attorney General has described sufficiently and adequately the reasons for that provision. This title also contains provisions for administrative inspections and warrants and for the forfeiture of the vehicles used by the drug traffickers.

Title VIII calls for the establishment of a Committee on Marihuana to carry out a study on all phases of marihuana use. This committee is to be composed of experts with diversified professional backgrounds. Also provided for is a Committee on Nongovernmental Drug Abuse Prevention and Control, which will disseminate information to private groups on what they can do to help stop drug abuse in this country.

Title IX, the last title of the bill, sets out the various technical provisions such as sections continuing pending proceedings and regulations, a section for authorization of appropriations, a section authorizing the republication of the schedules, and a severability clause.

CONTROVERSIAL ISSUES

Now, Mr. Chairman, I would like to focus on the major issues that have been discussed and debated about this legislation, both in hearings before the Subcommittee on Juvenile Delinquency of the Senate Judiciary Committee and in the testimony before the Subcommittee on Public Health and Welfare of the House Committee on Interstate and Foreign Commerce. The major portion of the legislation appears to be uncontroversial to those who have studied it. But, here are some parts that have generated controversy:

(*1*) *The Issue of Who Should Control a Drug Under This Bill*

A great deal of debate has occurred over who should make the final determination to bring a drug under control. Section 201 of H.R. 17463 would vest such authority in the Attorney General after he receives the advice in writing of the Secretary of Health, Education, and Welfare, and the independent Scientific Advisory Committee established in section 604 of the act. The advice of the Secretary of Health,

Education, and Welfare is not required under existing law nor has the Secretary ever had control decision authority over narcotic drugs.

The proposal, however, includes the narcotics and requires advice in writing from the Secretary and from the Scientific Advisory Committee so that it is public information. We feel this is an important step forward in that it makes the scientific information received from these two bodies public information, and allows those adversely affected to have in writing all of the reasons and analyses which led to the control decision.

Some people believe that the Secretary of Health, Education, and Welfare, as opposed to the Attorney General, should have the final control decision. Reorganization Plan No. 1 of 1968 vested that authority in the Attorney General. The Attorney General has exercised this power for 2 years, and none of those in opposition to the Attorney General's retention of this authority have made a case showing the Attorney General's abuse of this authority, or a lack of sensitivity on his part to scientific information or any of the other alleged problems that are supposed to occur by the Attorney General's exercising this authority.

The truth of the matter is that the reorganization plan has worked well, and the Attorney General's exercise of this control determination has worked equally well. In discussions with the Subcommittee on Public Health and Welfare we have been working to clearly distinguish the input of the Secretary of Health, Education, and Welfare from that of the Attorney General. We recognize that the Secretary must make the necessary medical and scientific determinations which shall be determinative on the Attorney General in terms of keeping a drug from being brought under control when such evidence demonstrates that a given drug should not be controlled.

However, the converse is not true. An affirmative decision to control involves more than medical and scientific determinations. It has important policy, legal and enforcement implications, as well. It is the responsibility of the Attorney General to determine whether or not all the facts and data support a conclusion that a given drug should be brought under control.

It is with this in mind that we are working out a solution to this problem and will suggest language later this week that we hope will resolve this controversy for all concerned. This language will retain in the Attorney General the final decision for bringing drugs under control under the foregoing conceptual formula.

(2) *Research in Schedule I Substances*

Some witnesses have expressed concern with the language in S. 3246, the Senate-passed version, dealing with research in Schedule I substances which are those having no approved medical use in the United States today. What use there is made of them is for research purposes only.

Since the intent of the legislation has always been not to unduly hamper research but to leave in the Department of Health, Education, and Welfare the responsibility for determining legitimate research protocols and the competency of scientic investigators, we have discussed a change with the Subcommittee on Public Health and Welfare which we feel adequately resolves the problem. The language change clearly vests in the Secretary of Health, Education, and Welfare and

not the Attorney General the authority to review the qualifications and competency of every practitioner requesting registration, as well as the limits of the research protocol.

The Attorney General would deny registration to a researcher approved by the Secretary only if the researcher had materially falsified his application, if he had committed a felony, or if he had had his state license rescinded. The Secretary is required to consult with the Attorney General prior to recommending approval of a researcher for registration to insure that there are adequate safeguards against potential diversion.

(3) Registration of Researchers

Many persons testified both in the Senate and in the House against the need to register researchers at all. The administration feels quite strongly that researchers should be registered so that we know who is dealing in these dangerous substances at all points in the chains of distribution.

The intent of the registration provisions of H.R. 17463 is to create a closed system similar in concept to the system that has been effective with regard to the narcotic laws. By requiring every person who manufactures, distributes, or dispenses these substances to register and have a corresponding registration number, we will be able to determine points of diversion from the legitimate channels into the illicit network more effectively. It is important that we have a closed registration system.

Diversion of legitimately produced drugs is a significant problem in the United States, and will tend to grow under the present system. The closed system will serve a valuable preventive purpose. We feel that such a system shows the public that the Government can move to prevent problems as well as just react to fait accomplis. We believe that the provisions dealing with registration will impose no hardship on the legitimate researcher or any other person required to register.

Opponents of this provision rest their claim on the allegation that research will be stifled. This, in our opinion, is hypothetical and speculative. In fact, research in marihuana now requires comparable registration and it has blossomed in the last several years.

For example, in 1966 there were 15 registered marihuana researchers; in 1967, 21; in 1968 (the first year of Reorganization Plan No. 1) there were 64 and in 1969, there were 87 registered. Our intent is to encourage research, but at the same time to insure that such research does not result in the diversion of dangerous substances.

(4) Education and Research Role of the Department of Justice

The Bureau of Narcotics and Dangerous Drugs in its relatively short life has contributed significantly to national research and educational activities in the area of narcotics and dangerous drugs. We feel research is a necessary concomitant to effective law enforcement. I think this is the feeling of most enlightened law enforcement administrators in this day. It is in the public interest that we continue these efforts and also continue our efforts in drug abuse prevention. We must have research and educational capabilities so that we can adequately disseminate information to the public, train state and local police, as well as other persons such as college deans and forensic

chemists, and improve our own enforcement investigative and regulatory work.

The Department of Justice feels that it should not be involved in basic research such as that primarily carried out by the National Institute of Mental Health. We feel that the two Departments' roles are clearly defined and will not come into conflict.

PROPOSED LANGUAGE CHANGE

Mr. Chairman, although we firmly support H.R. 17463, we recognize that it is an extremely complex piece of legislation and have constantly sought to improve the language to better reflect the administration's position and the feelings of those who are directly involved with its operation, should it become law.

In addition to trying to work out the foregoing controversial issues, we have prepared some alternate language to several other sections of the bill which we believe should improve the language and clarify its purpose.

For the past several weeks the administration has been working with the Subcommittee on Public Health and Welfare on these matters. With the chairman's permission, I would like to discuss some of these changes and recommend this committee's favorable consideration of them.

(*a*) *The registration of pharmacies versus pharmacists*

The use of the term practitioner in the registration sections apparently has not adequately stated the impact of registration in the case of pharmacies and pharmacists. The administration has repeatedly stated that it is the intent of the legislation to register pharmacies rather than pharmacists except in cases where the pharmacist is engaged in research or in testing. Then, of course, it would be the pharmacist who would be required to register.

However, to clarify this beyond a doubt, we feel that language should be inserted in subsection 303(f) of H.R. 17463 which will carry out this intent. It is easier to require records to be kept at a place as opposed to being tied to a person who can change employment from day to day.

Also, since the pharmacy is many times not owned by the pharmacist behind the counter, it seems more equitable to require the owner to have the burden of insuring that records and inventory requirements are maintained. It should be noted that it is the pharmacy, not the pharmacist, that is required to maintain record under the Federal Food, Drug and Cosmetic Act.

(*b*) *The dispensing practitioner—medical doctor*

Under existing law, physicians dispensing depressant, stimulant, and hallucinogenic drugs are not required to keep records unless they are "dispensing practitioners" which is defined by existing laws to include those who regularly engage in dispensing these drugs to their patients for which the patients are charged, either separately or together with charges for other professional services.

This is designed to require such practitioners, primarily "diet doctors" to keep records since under those circumstances they are acting

in the same capacity as a pharmacy and accounting for large distribution of the amphetamines and barbiturates.

We have agreed with the other subcommittee to include additional language to subsection 307(a), that will carry forward this intent, while at the same time requiring practitioners who administer or dispense controlled dangerous substances listed in Schedules I or II and narcotic substances listed in Schedule III of this act also to keep records. It should be noted that they are presently required to keep records under the existing narcotic laws.

(*c*) *Education and research*

In recognition of the concern that I mentioned when discussing the Department of Justice's role in education and research, we have drafted some alternate language (which, I might add, was suggested by the House Committee on Interstate and Foreign Commerce's Subcommittee on Public Health and Welfare), which we consider to be adequate as an alternative to the existing language in section 602. It is in effect a combination of the language in H.R. 17463 and subsections 602 (a) and (b) of the Working Print of the Interstate and Foreign Commerce Committee Subcommittee on Public Health and Welfare.

What it does in effect is set out in greater detail the specific areas of education and research to be undertaken by the Department of Justice. It is the Department's feeling that this language sufficiently allows us to conduct the kind of programs that we feel are necessary for effective implementation of the act, and, therefore, we have no objection to such changes in section 602, should the committee consider this language more appropriate.

These matters plus those discussed under the heading of controversial issues (i.e. the control decision authority, registration of researchers and Department of Justice research), Mr. Chairman, I feel can be improved upon with the changes that are being suggested. We hope resolution will succeed in the interest of getting the very best law possible to help reverse the present skyrocketing drug abuse problem.

CONCLUSION

The Department of Justice firmly supports H.R. 17463 and suggests the above mentioned alternate language to the committee for its consideration, in addition to changes that we shall offer during the week.

As the Attorney General has just stated, and as I have stated on numerous occasions, this legislation deals with the law enforcement aspects of the problem. It does not attempt to deal with the rehabilitative or long-range education and research areas. Those areas, important as they are, are left to other legislation and other approaches that we feel are not within the ambit of this bill.

This bill gives us the necessary law enforcement tools to conduct effective drug investigations and to exercise meaningful regulatory controls over the legitimate industry from a law enforcement point of view.

By that I mean the bill provides penalties that are realistic and enforceable, and it contains a regulatory system that will help identify the flow of drugs legitimately produced and hopefully pinpoint the sources of diversion so that they can be dealt with by the Bureau of Narcotics and Dangerous Drugs.

The bill further allows us to react quickly as new drugs of abuse create problems in our society, or have the potential to create such problems. With its scheduling system and the Attorney General's ability to bring drugs under control, we believe that H.R. 17436 will be as timely in 1980 as it is in 1970.

The bill is designed to give us good, efficient law enforcement and regulatory controls over a problem that is with us now, that must be resolved now, that must be acted upon now. While not intending to offend anyone, I must state that many people have lost sight of the ultimate objective of the bill, which is to provide meaningful enforcement and penalty controls over the narcotic and dangerous drug problem that is with us now and will probably be with us in the future.

I feel that Congress must move with speed to give us what we need to get on with the job at hand. The illicit drug problem is growing, diversion is continuing, and the citizenry of the United States is suffering as a result of the present posture of the laws. While law enforcement alone cannot stop the drug problem or eradicate its causes, it can, if properly armed with the necessary legislative tools and with trained manpower and adequate funding, do a better job of containing it. The public safety and the Federal Government's law enforcement credibility are at stake. I urge swift passage of H.R. 17463.

Thank you very much, Mr. Chairman, for your patience and indulgence.

The CHAIRMAN. We thank you, Mr. Ingersoll, for your very fine statement.

(A section-by-section analysis and the comparison between H.R. 17463 and present law referred to follow:)

SECTION-BY-SECTION ANALYSIS AND COMPARISON BETWEEN THE CONTROLLED DANGEROUS SUBSTANCES ACT, H.R. 17463, AND EXISTING FEDERAL NARCOTIC, MARIHUANA, AND DANGEROUS DRUG LAWS

Introduction

The following materials contain a section-by-section digest of H.R. 17463, the Controlled Dangerous Substances Act, and a comparison of the provisions of H.R. 17463 with those found in existing Federal narcotic, marihuana, and dangerous drug laws. Those provisions of H.R. 17463 which differ substantively from the provisions of S. 3246, the Senate-passed version of the Controlled Dangerous Substances Act, will be footnoted where appropriate.

TITLE I—FINDINGS AND DECLARATIONS, DEFINITIONS, REPEALERS, AND CONFORMING AMENDMENTS

Section 102.—Definitions

Subsection 102(a) sets out a definition of "addict" which is substantially similar to the definition of "addict" found in Titles I and II of the Narcotic Addict Rehabilitation Act of 1966, 28 U.S.C. 2901(a) and 18 U.S.C. 4251(a) respectively.

Subsection 102(b) sets out a definition of "administer" not found under existing Federal law. The language incorporated in this definition reflects the word's commonly accepted usage among the medical, scientific, and pharmacy professions.

Subsection 102(c) sets out a definition of "agent" not found under existing Federal law. The definition specifies those persons who are to be deemed agents of manufacturers, distributors, and dispensers of controlled dangerous substances for purposes of invoking the principal-agent doctrine and determining exemptions from the registration requirements.

Subsection 102(d) defines "Bureau of Narcotics and Dangerous Drugs" in language similar to that found in 21 CFR 320.1(f).

Subsection 102(e) sets out a definition of "control" not found in existing Federal law. The definition sets out the activities relating to the drugs listed in the

schedules contained in Title II of the Act which are to be deemed "control." Such activities include addition, removal, or change in the placement of a controlled substance within the various schedules.

Subsection 102(f) sets out the definition of "controlled dangerous substance." The definition is an adaptation of the definition of "controlled substance" found in 21 CFR 320.1(j), relating to the Drug Abuse Control Amendments of 1965. Included in this definition are all drugs, substances, and immediate precursors listed in the four schedules contained in Title II. The definition utilizes the word "substance" rather than "drug," since the word "substance" is broader in scope than "drug" and thus will encompass precursor chemicals as well as actual drugs.

Subsection 102(g) defines "counterfeit substance" in language similar to that used for defining "counterfeit drug" in the Drug Abuse Control Amendments of 1965, 21 U.S.C. 321(g)(2).

Subsection 102(h) defines "Department of Justice" in language identical to that found in 21 CFR 320.1(b).

Subsection 102(i) defines "depressant or stimulant drug" in language identical to that found in the Drug Abuse Control Amendments, 21 U.S.C. 321(v).

Subsection 102(j) sets out a definition of "dispense" not found under existing Federal law. The definition designates those drug-related activities which are to be deemed "dispensing" for purposes of determining the types and degree of regulatory controls applicable.[1]

Subsection 102(k) sets out a definition of "distribute" not found under existing Federal law. The definition designates the drug-related activities which are to be deemed "distribution" for purposes of determining the regulatory controls applicable and the imposition of criminal sanctions.[2]

Subsection 102(l) defines "drug" in language identical to that contained in the Drug Abuse Control Amendments, 21 U.S.C. 321(g)(1).

Subsection 102(m) defines "marihuana" in language identical to that contained in the Marihuana Tax Act of 1937, 26 U.S.C. 4761(2).

Subsection 102(n) defines "manufacture" in language similar to that found in the Narcotic Manufacturing Act of 1960, 21 U.S.C. 502(f).

Subsection 102(o) defines "narcotic drug" in language substantially similar to that found in the Harrison Narcotic Act of 1914, 26 U.S.C. 4731(a).

Subsection 102(p) defines "net disposal" in language identical to that found in the Narcotic Manufacturing Act of 1960, 21 U.S.C. 503(h).

Subsection 102(q) defines "opiate" in language substantially similar to that found in the Harrison Narcotic Act, 26 U.S.C. 4731(g)(1).

Subsection 102(r) defines "opium poppy" in language identical to that found in the Opium Poppy Control Act, 21 U.S.C. 188a(c).

Subsection 102(s) sets out a definition of "poppy straw" not found under existing Federal law. This definition carries over the definition of "poppy straw" found in the Single Convention on Narcotic Drugs, 1961.

Subsection 102(t) defines "practitioner" in language similar to that found under Federal regulations applicable to the Harrison Narcotic Act, 26 CFR 151.11(h). The definition in H.R. 17463 is broader than existing definitions in that it includes pharmacies, hospitals, clinics, and medical and non-medical researchers, as well as physicians, dentists, and veterinarians.

Subsection 102(u) defines "production" in language similar to that found in the Opium Poppy Control Act, 21 U.S.C. 188a(b).

Subsection 102(v) sets out a definition of "immediate precursor" not found under existing Federal law. This definition is a modification of the definition of "narcotic precursor" found in the Narcotic Manufacturing Act of 1960, 21 U.S.C. 502(i), but is broader in scope in that it encompasses precursors of both narcotic and non-narcotic drugs.

Subsection 102(w) sets out the standard statutory definition of "State."

Subsection 102(x) sets out a definition of "ultimate user" not found under existing Federal law. The subsection is a codification of the language commonly accepted and used to define the term.

Subsection 102(y) sets out the standard statutory definition of "United States."

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[1] This definition differs to a limited extent from the definition of "dispense" contained in S. 3246 in that prescribing or administering, as well as packaging or labeling substances in preparation for distribution, is to be deemed "dispensing."

[2] This definition incorporates the definition of "deliver" contained in S. 3246. The S. 3246 definition of "deliver" has been deleted from H.R. 17463.

TITLE II—STANDARDS AND SCHEDULES

Section 201.—Authority to control

This section authorizes the Attorney General, with the advice of the Secretary of Health, Education, and Welfare, to add, delete, or reschedule any substance as a controlled dangerous substance, and sets forth the criteria to be considered in making such decision. Some of these are the drug's potential for abuse, scientific knowledge regarding the substance, the history and scope of abuse, risks to public health, psychic or physiological dependence liability, and treaty requirements. The Attorney General may control such drugs pursuant to the procedures established by Subchapter II of Chapter 5 of Title 5 of the United States Code.

Section 504 of Title 21 of the United States Code empowers the Attorney General to modify the list of basic narcotic drugs based on the drug's chemical structure, content and addiction liability or convertibility into an addicting drug. It does not detail further criteria, except that the drug must be a narcotic drug as defined by section 4731(a) of Title 26.

Section 321(v) of Title 21 United States Code (the Drug Abuse Control Amendments of 1965), provides that the Attorney General may, after investigation, issue regulations according to the proceedings established by section 371(e), (f), and (g) of Title 21, and thereby include other drugs under the definition of "depressant and stimulant drug." The definition requires that the investigation reveal that the drug have a potential for abuse because of its depressant or stimulant effect on the central nervous system or its hallucinogenic effect.

The primary changes instituted by the new Bill include requiring the Attorney General to seek the advice of the Secretary of Health, Education, and Welfare and the Scientific Advisory Committee before adding, deleting, or rescheduling a substance; setting forth in detail the specific elements to be considered in making such a decision; and applying the procedures set out in the Administrative Procedures Act, Subchapter II of Chapter 5, to that process.

Section 202.—Schedules of controlled substances

This section sets forth the four basic schedules to be used in determining the level of control of dangerous substances. Before each schedule is a list of criteria to be used by the Attorney General in determining the drugs which will fit into that schedule. Some drugs are initially included in the bill. Generally, Schedule I contains opiates, opium derivatives, and hallucinogenic substances. Schedule II contains medically usable opiates, opium derivatives, and coca leaf derivatives. Schedule III contains the central nervous system stimulants (amphetamines), and depressants (barbiturates), as well as low-narcotic mixtures and compounds. Schedule IV contains certain exempt narcotic preparations.

The existing law has no such definite scheduling system. Each type of substance is dealt with by different. separate laws. Section 4731(a) of Title 26 of the Internal Revenue Code defines narcotic drugs so as to include both vegetable-origin drugs and those produced by chemical synthesis from opium and coca leaves. Section 4731(g) includes as an "opiate" any substance found by the Attorney General to have an addiction-forming or addiction-sustaining liability similar to morphine or cocaine. These substances are controlled under the Harrison Narcotic Law (Tax), section 4701 et seq. of Title 26; by the Narcotic Drugs Import and Export Act, sections 171–185 of Title 21; and by the Narcotic Manufacturing Act of 1960, section 501 et seq. of Title 21. In addition, heroin is specificially treated under the criminal laws of sections 1401–1407 of Title 18. Marihuana is defined by section 4761(2) of Title 26 (Marihuana Tax Act) and is controlled under those laws and under the Narcotic Drugs Import and Export Act, sections 171–185 of Title 21. The depressant, stimulant, and hallucinogenic drugs are defined and controlled by the Drug Abuse Control Amendments of 1965 in Title 21 of the Food Drug, and Cosmetic Act. Under these amendments, regulations have been written which list specific controlled substances and set out the criteria used in determining the selection of these drugs (Title 21, Code of Federal Regulations).

The major change in the existing law made by this section of the bill is the collecting of all the narcotics, opiates, and dangerous drugs into one comprehensive law and placing them into specific schedules. The requisite criteria for each schedule is set out in the Bill, and every type of drug or dangerous substance to be controlled can be classified accordingly. The drugs listed in the schedules in the Bill have almost all been controlled by name under the existing

law, either by proclamation, regulation, or under the Drug Abuse Control Amendments. The only exceptions are three new drugs listed in Schedule III: (4) Chlordiazepoxide; (6) Diazepam; and (12) Meprobamate, all derivatives of barbituric acid. Meprobamate was controlled as of July 6, 1970.[3]

TITLE III—REGULATION OF MANUFACTURE, DISTRIBUTION, AND DISPENSING OF CONTROLLED DANGEROUS SUBSTANCES

Section 301.—Rules and regulations

Section 301 authorizes the Attorney General to promulgate rules and regulations and charge reasonable fees relating to the registration of manufacturers, distributors, and dispensers of controlled dangerous substances. While no identical counterpart to this section exists under present Federal law, provisions of the Harrison Narcotic Act, 26 U.S.C. 4721, provide for the imposition of an occupational tax, varying from one to 24 dollars, on manufacturers, importers, wholesale and retail distributors, and physicians and other practitioners dealing in or handling narcotic drugs. Provisions of the Marihuana Tax Act, 26 U.S.C. 4751, provide for the imposition of a similar occupational tax on such individuals dealing in or handling marihuana. No provisions are made under the Drug Abuse Control Amendments for the assessment of fees relating to the registration of manufacturers and distributors of stimulant and depressant drugs.

Section 302.—Registration requirements

Section 302(a) requires all persons manufacturing, distributing, or dispensing controlled dangerous substances to register annually with the Attorney General.

Under the Harrison Narcotic Act, persons dealing in narcotic drugs who are required to pay the occupational tax under 26 U.S.C. 4721 must register annually pursuant to the provisions of 26 U.S.C. 4722. The Marihuana Tax Act requires that persons required to pay the occupational tax under 26 U.S.C. 4751 must register annually pursuant to the provisions of 26 U.S.C. 4753. These persons, who include manufacturers, importers, wholesale and retail distributors, and practitioners, generally submit an application for registration to a district office of the Internal Revenue Service, which in turn is forwarded to the Bureau of Narcotics and Dangerous Drugs for investigation and approval. Upon approval, the district director of the Internal Revenue Service is then authorized to issue a registration.

Provisions of the Narcotic Manufacturing Act of 1960, 21 U.S.C. 506, require all persons manufacturing any basic class of narcotic drug to be licensed on an annual basis with the Attorney General.

Under the Drug Abuse Control Amendments, persons manufacturing or distributing stimulant or depressant drugs must register annually pursuant to 21 U.S.C. 360(b). Application for registration is presently made to the Food and Drug Administration of the Department of Health, Education, and Welfare, as the result of an agreement between the Department of Justice and the Department of Health, Education, and Welfare subsequent to the 1968 Presidential Reorganizational Plan vesting narcotic, marihuana, and dangerous drug enforcement and regulatory authority in the Department of Justice.

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[3] The following differences are noted in section 202 of this bill and section 202 of S. 3246, the Senate-passed Controlled Dangerous Substances Act:

(a) Under (a)(3), page 24, line 1, the words "in treatment" have been added to this version.

(b) Under (a)(3)(a), page 24, line 5, the word "opiates" has been substituted for the word "substances" in S. 3246.

(c) Under (a)(3)(a), page 24 and 25, two chemical spellings have been corrected, that of (15) Diethylthiambutene and (18) Dimethylthiambutene.

(d) Six new drugs and one amended spelling are added to this bill in (a)(3)(b):
(1) Acetorphine
(2) Acetyldihydrocodeine (corrected spelling)
(6) Cyprenorphine
(8) Dihydro codeine
(9) Dihydro morphine
(10) Etorphine
(22) Pholcodine

(e) Under (b) schedule II, the listing of substances included under (a), page 28, line 13 to page 29, line 2, has been slightly reworded from the Senate Act.

(f) Under (c) schedule III (2), page 30, line 13, the words "currently accepted" were substituted for the words "well documented and approved."

(g) Under (d) schedule IV(a)(3), page 35, line 17, the words "one hundred" were substituted for the word "fifty" used in the Senate Act.

(h) In (d) schedule IV, page 36, line 2, the words "or not more than five milligrams per dosage unit" have been deleted from the Senate version.

Subsection 302(b) exempts agents of registrants acting in the usual course of business, common and contract carriers, warehousemen, and ultimate users from the registration requirements, and authorizes the possession of controlled dangerous substances by these individuals in the ordinary course of business.

Under the present Federal narcotic laws, 26 U.S.C. 4724(c) authorizes the possession of narcotic drugs by employees of registrants, ultimate users, warehousemen, and common carriers, and exempts them from the occupational tax and registration requirements. Under the Marihuana Tax Act, 26 U.S.C. 4772 exempts employees of registrants acting in the usual course of business from the occupational tax and registration requirements.

Under the Drug Abuse Control Amendments, 21 U.S.C. 360a(a) and (b) authorizes the sale, delivery, disposal, or possession of stimulant and depressant drugs by employees of registrants acting in the usual course of business, common and contract carriers, warehousemen, and ultimate users.

Subsection 302(c) permits the Attorney General to waive by regulation the requirement for registration of certain manufacturers, distributors, or dispensers if he finds it consistent with the public health and safety.

While no comparable provisions are to be found under existing Federal law, the Harrison Narcotic Act, the Marihuana Tax Act, and the Drug Abuse Control Amendments all specifically exempt State and local officials from the registration and/or occupational tax requirements. [26 U.S.C. 4772(b) and 21 U.S.C. 360a(a)(6).]

Subsection 302(d) requires a separate registration for each principal place of business or practice where a registrant manufactures, distributes, or dispenses controlled dangerous substances.

The registration provisions of the Harrison Narcotic Act, 26 U.S.C. 4722, require an applicant to register his place of business and place or places where such business is carried on. The Marihuana Tax Act requires likewise under 26 U.S.C. 4751. The registration provisions of the Drug Abuse Control Amendments, 21 U.S.C. 360, require that an applicant register his places of business and establishments wherein stimulant and depressant drugs are manufactured.

Subsection 302(e) authorizes the Attorney General to inspect the establishment of any registrant or applicant for registration. This provision is designed to enable the Attorney General to ascertain prior to registration, or after registration as the case may be, whether the registrant has undertaken adequate precautions to safeguard the physical security of controlled drugs.

Under the regulations promulgated under the Harrison Narcotic Act, 26 CFR 151.23, authorization is granted for the inspection of plant facilities to ascertain the adequacy of security measures taken to safeguard narcotic drugs. Such inspections are conducted to determine, in part, the qualifications of an applicant for registration under 26 U.S.C. 4722. Similar inspections are authorized under 26 CFR 151.21 and 26 CFR 151.22 for persons applying for registration under the Marihuana Tax Act.

Under the Drug Abuse Control Amendments, 21 U.S.C. 360(h), registered establishments are subject to inspections on a biennial basis starting from the date of registration.

Section 303.—Registration

Subsection 303(a) authorizes the Attorney General to register an applicant to manufacture schedules I and II substances if he determines that such registration would be consistent with the public interest and the international obligations of the United States. In determining the public interest, the Attorney General must consider six criteria, such as effective controls against diversion; compliance with State and local law; the applicant's prior conviction record; and the applicant's past experience in the manufacture of these substances. The Attorney General must also take into consideration the effect of registration on necessary domestic drug supplies and competition between domestic manufacturers.

Under the Narcotic Manufacturing Act of 1960, the Attorney General is authorized to license manufacturers of basic classes of narcotic drugs pursuant to 21 U.S.C. 506. In determining whether to issue a license, the Attorney General must consider such criteria as maintenance of effective controls against diversion; compliance with international obligations; and the applicant's reputation and experience in the manufacture of narcotic drugs.

Under the Marihuana Tax Act, there are no statutory criteria which must be considered prior to registration under 26 U.S.C. 4751. By regulation, 26 CFR

152.23, an applicant wishing to handle marihuana must show that under the laws of the jurisdiction in which he is operating or practicing that he is legally qualified to engage in the activities for which registration is sought.

Under the Drug Abuse Control Amendments, the only criteria which must be considered for registration purposes is compliance by the applicant with appropriate State and local law.

Subsection 303(b) requires the Attorney General to register an applicant to distribute schedules I and II drugs unless he makes a finding that issuance of such registration would be inconsistent with the public interest. In determining the public interest, the Attorney General must consider such criteria as adequate safeguards against diversion; compliance with applicable State and local law; the applicant's prior conviction record; and the applicant's past experience in the distribution of controlled drugs.

With the exception of compliance with applicable State and local law, no statutory criteria are provided for under existing Federal law relating to the registration of distributors of narcotic drugs, marihuana, and stimulant and depressant drugs.

Subsection 303(c) prohibits persons registered under subsections 303(a) and 303(b) from manufacturing or distributing Schedules I and II controlled drugs other than those specified in their registrations or in excess of the quota assigned pursuant to section 306.

Under provisions of the Narcotic Manufacturing Act of 1960, 21 U.S.C. 506(c), a license authorizing the manufacture of any one basic class of narcotic drugs does not authorize the licensee to manufacture any other basic class of narcotic drug.

Under the Harrison Narcotic Act and the Marihuana Tax Act, there are no provisions restricting a registrant to particular classes of narcotic drugs, nor are specific classes of narcotic drugs designated in a registration. No restrictions in terms of the types or classes of stimulant or depressant drugs which a manufacturer or distributor may deal in are imposed under the Drug Abuse Control Amendments.

Subsections 303(d) and 303(e) require the Attorney General to register manufacturers and distributors of schedules III and IV substances unless he determines that the issuance of such registration would be inconsistent with the public interest. In determining the public interest, the Attorney General must consider such criteria as maintenance of effective controls against diversion; compliance with applicable State and local law; the applicant's prior conviction record; and the applicant's past experience in the manufacture or distribution of schedules III and IV substances.

The licensing criteria under the Narcotic Manufacturing Act of 1960 discussed earlier, 21 U.S.C. 506, are applicable to manufacturers of narcotic drugs contained in schedules III and IV of H.R. 17463. The Drug Abuse Control Amendments contain no criteria for the registration of manufacturers and distributors of stimulant and depressant drugs contained in schedule III of H.R. 17463, with the exception that the applicant must comply with applicable State and local law.

Subsection 303(f) provides that practitioners, which includes by definition pharmacies, shall be registered to dispense substances in schedules II through IV if they are authorized to dispense under the laws of the State in which they practice. This subsection further provides for the registration of persons wishing to conduct research using schedule I substances. If the applicant's qualifications and protocol are approved by the Secretary of Health, Education, and Welfare, the Attorney General can deny registration only upon a finding that the applicant falsified his application; the applicant has been convicted of a felony relating to controlled dangerous substances; the applicant's State license has been revoked; or the applicant's proposed procedures give reason to believe that the drugs being used will not be adequately safeguarded against diversion.

Under the Harrison Narcotic Act, practitioners administering or dispensing narcotic drugs are permitted to pay the occupational tax and register under 26 U.S.C. 4721(4) and 26 U.S.C. 4722. Retail dealers, which includes pharmacists, are permitted to register and pay the occupational tax under 26 U.S.C. 4722 and 26 U.S.C. 4721(3).

The Drug Abuse Control Amendments specifically exempt pharmacies dispensing stimulant and depressant drugs from the registration requirements under 21 U.S.C. 360, although physicians dispensing stimulant and depressant drugs are required to register pursuant to that section.

Persons using the narcotic drugs listed in schedule I for research purposes may pay the occupational tax and register either as practitioners under 26 U.S.C. 4721(4) and 26 U.S.C. 4722, or as researchers under 26 U.S.C. 4721(5) and 26 U.S.C. 4722. No criteria, other than compliance with State law, need be met by persons registering under these sections.

Persons using stimulant and depressant drugs for research purposes, including the hallucinogenic drugs listed in schedule I of H.R. 17463, are presently exempted from registration under the Drug Abuse Control Amendments by virtue of 21 U.S.C. 360a(a)(5).

Section 304.—Denial, revocation, or suspension of registration

Subsection 304(a) authorizes the Attorney General to revoke a registration uopn a finding that the registrant falsified his application; has been convicted of a felony relating to controlled dangerous substances; or has had his State license revoked and is no longer authorized to manufacture, distribute, or dispense controlled dangerous substances.

Under the Narcotic Manufacturing Act of 1960, 21 U.S.C. 507, the Attorney General is authorized to revoke or suspend a narcotic manufacturing license upon a finding that the licensee has been convicted of a felony relating to narcotic drugs, or that the licensee has violated or failed to comply with regulations relating to narcotic drugs.

No specific provisions are made for the suspension or revocation of registrations under the Harrison Nartotic Act, the Marihuana Tax Act, or the Drug Abuse Control Amendments.

Subsection 304(b) authorizes the Attorney General to limit suspension or revocation to those particular controlled dangerous substances with respect to which grounds for revocation or suspension exist.

Under the Narcotic Manufacturing Act of 1960, 21 U.S.C. 507, the Attorney General may restrict revocation or suspension to the basic narcotic drug class for which grounds for revocation or suspension exist, or the Attorney General may extend revocation or suspension to all basic classes of narcotic drugs for which the manufacturer holds licenses.

Subsection 304(c) requires the Attorney General to serve on the applicant or registrant a show cause order as to why registration should not be denied, revoked, or suspended. Furthermore, the applicant must be afforded a hearing under the provisions of the Administrative Procedures Act.

Similar provisions are provided for under the Narcotics Manufacturing Act of 1960, 21 U.S.C. 506(e), and 21 U.S.C. 507(b), in the case of denial, suspension, or revocation of a narcotic manufacturing license.

Subsection 304(d) permits the Attorney General to suspend a registration simultaneously with the institution of proceedings bearing on the denial, revocation, or suspension of registration if he finds there is an imminent danger to the public health or safety.

There exists no comparable counterpart to this subsection under existing Federal narcotic, marihuana, or dangerous drug laws.

Subsection 304(e) provides that the suspension or revocation of a registration shall automatically suspend or revoke any production quota applicable under section 306.

No comparable counterpart to this subsection exists under the Narcotics Manufacturing Act of 1960.

Subsection 304(f) authorizes the Attorney General to place under seal, at the time of suspension or the effective date of a revocation order, all controlled dangerous substances owned or possessed by a registrant. Upon a revocation order becoming final, all controlled dangerous substances shall be forfeited to the Government.

Similar provisions are made with regard to narcotic drugs under the Narcotic Manufacturing Act of 1960, 21 U.S.C. 507.

Section 305.—Marking of containers

Section 305 provides that all commercial containers of controlled dangerous substances must be identified by a symbol as specified in regulations to be promulgated by the Attorney General.

Under the Harrison Narcotic Act, 26 U.S.C. 4703 requires that all packages containing narcotic drugs have affixed to them the appropriate tax stamps issued pursuant to 26 U.S.C. 4771.

Under the Marihuana Tax Act, 26 U.S.C. 4743 requires that all packages containing marihuana have affixed to them the appropriate tax stamps issued pursuant to 26 U.S.C. 4771.

The regulations promulgated under the Drug Abuse Control Amendments, 21 CFR 320.18, require that all packages of controlled stimulant and depressant drugs bear a symbol specified in the regulation.

Section 306.—Quotas

Section 306 authorizes the Attorney General to determine and establish production quotas for the manufacture of substances listed in schedules I and II. These quota provisions are drawn for the most part from the quota provisions of the Narcotic Manufacturing Act of 1960, 21 U.S.C. 509, although a number of technical modifications have been added to the quota provisions of H.R. 17463.

Section 307.—Records and reports of registrants

Section 307 requires that upon the effective date of the Act, all registrants manufacturing, distributing, or dispensing controlled dangerous substances must make a record of all controlled drug stocks on hand. These records must be maintained for a period of two years. Each two-year period after the Act's effective date, registrants must make an inventory of all dangerous substance stocks on hand. These recordkeeping and inventory requirements are not applicable to the practitioner who prescribes or administers, but not otherwise dispenses, controlled dangerous substances listed in schedules II through IV.

The general recordkeeping provision for narcotic drugs under the Harrison Narcotic Act is found in 26 U.S.C. 4732. Under this section, registrants, upon demand, are required to submit a statement setting forth the quantity of narcotic drugs received over a designated period, and the persons from whom the drugs were received. By virtue of 26 CFR 151.400, persons who fill prescriptions for narcotic drugs are required to maintain them in a separate file and make them accessible to inspection for a period of not less than two years.

Under the Drug Abuse Control Amendments, 21 U.S.C. 360a(d) provided that on the effective date of the Act, all persons manufacturing, selling, delivering, or otherwise disposing of stimulant and depressant drugs were required to make a record of all such drugs on hand and maintain the record for at least three years. This provision further required manufacturers to record the kinds and quantities of stimulant and depressant drugs manufactured or compounded and to keep such records for at least three years. Persons selling, delivering, or otherwise disposing of stimulant and depressant drugs were required to record the kind and quantity of each such drug received, sold, delivered, or otherwise disposed of and to keep such record for at least three years. At the present time, these recordkeeping and inventory requirements are no longer in force, due to the expiration of the three-year period from the effective date of the Drug Abuse Control Amendments, which was February 1, 1966.

Section 308.—Order forms

Section 308 provides that controlled dangerous substances listed in schedules I and II must be distributed pursuant to order forms as prescribed by the Attorney General. Practitioners administering or dispensing such drugs to patients or research subjects, and pharmacists distributing such drugs to ultimate users, are specifically exempted from the order form requirements.

This section is for the most part a carry-over of the order form requirements imposed for the distribution of narcotic drugs under the Harrison Narcotic Act. Under 26 U.S.C. 4705(a), narcotic drugs must be distributed pursuant to a written order of the purchaser. Under subsection (c) of that provision, practitioners and pharmacists are specifically exempted from the order form requirements. Similar order form requirements and exemptions are made for the distribution of marihuana under 26 U.S.C. 4742. No order form requirements are imposed for the distribution of stimulant and depressant drugs under the Drug Abuse Control Amendments.

Section 309.—Prescriptions

Subsection 309(a) provides that no substance listed in schedule II may be dispensed without a written prescription from a practitioner, with the exception of a practitioner other than a pharmacist dispensing directly to an ultimate user. The subsection further provides, however, that in emergency situations, a schedule II drug may be dispensed upon the oral prescription of a practitioner so long as the applicable provisions of the Federal Food, Drug, and Cosmetic Act bearing

on oral prescriptions are complied with. The subsection further provides that no prescription for a schedule II substance may be refilled.

This subsection carries over the provisions in the existing Federal narcotic laws with respect to the dispensing of narcotic drugs pursuant to a written prescription, as required by 26 U.S.C. 4705(c)(2). Under 26 CFR 151.411, practitioners may dispense narcotic drugs to bona fide patients without prescriptions or order forms. However, under other regulations promulgated under the Harrison Act, oral prescriptions for the narcotic drugs listed in schedule II of H.R. 17463 are prohibited [26 CFR 151.397].

Subsection 309(b) provides that, except when dispensed by a practitioner other than a pharmacist, no controlled dangerous substance listed in schedule III which is a prescription drug may be dispensed without a written prescription. The subsection further provides that such prescriptions may not be filled or refilled more than six months after date and may not be refilled more than five times after the date of the prescription, unless renewed by the practitioner.

This subsection carries over the existing provisions of the Drug Abuse Control Amendments and the regulations promulgated thereunder with respect to stimulant and depressant drugs. Under 21 U.S.C. 360a (e), no prescription for any stimulant or depressant drug may be filled or refilled more than six months after date and no prescription may be refilled more than five times after date, unless renewed by a practitioner either in writing or orally.

With respect to the naroctic drugs listed in schedule III, under the provisions of the Harrison Narcotic Act discussed with respect to subsection 309(a), a prescription for a class B narcotic drug cannot be refilled.

TITLE IV—IMPORTATION AND EXPORTATION

Section 401.—Importation of controlled dangerous substances

In this section, it is declared unlawful to import any schedule I or II drugs or any narcotic drugs listed in schedules III or IV except with the special consent of the Attorney General. This includes the opiates, narcotic drugs, coca leaf derivatives, and hallucinogenics. In addition, this section requires that the non-narcotic controlled substances under schedule III be imported only for medical and other legitimate uses pursuant to notification requirements to be established by regulation.[4]

Existing law provides similar controls for the narcotics and marihuana. Section 173 of Title 21 bans the importation of narcotic drugs, opium, and coca leaves except under special regulations for medical and legitimate use. Section 176a of Title 21 forbids the importing of marihuana specifically, while this substance is included under the general controls of section 401 in the bill because it is listed under schedule I. However, the importation of non-narcotic dangerous substances is controlled only indirectly under existing law by the Drug Abuse Control Amendments of 1965. Section 381 of Title 21 requires that foreign establishments that wish to import drugs into the United States register pursuant to Section 360(i) of the same Title. A drug imported may be reviewed, but only as to the sanitariness of the conditions under which it was manufactured; whether or not its sale was forbidden in its country of origin; or whether or not it was adulterated.

The primary changes instituted by this section include providing for importation of narcotics for medical or scientific needs during an emergency situation when United States supplies are inadequate or when the competition among domestic manufacturers is inadequate. Under current laws, finished narcotic drugs may not be imported. Also new is the requirement of notification before any controlled schedule III stimulant and depressant drugs may be imported.

Section 402.—Importation of coca leaves

This section provides for the importation of coca leaves for use in this country providing that the cocaine and cocaine source material is removed and destroyed.

Section 173a of Title 21 is a substantially identical provision.

[4] In section 401(a), page 51, line 6, the phrase "continental United States, State of Hawaii, or Puerto Rico or any insular possession or other place subject to the jurisdiction of the United States" has replaced the words "United States" as used in the Senate Act

Section 403.—Exportation of controlled dangerous substances

Subsection 403(a) restricts the exporting of narcotic drugs from the United States except as is provided under existing treaty obligations, including the most recent, the 1961 Single Convention. It sets forth the requirements to be met to insure that these treaty obligations are fulfilled, and requires that a permit be obtained from the Attorney General before exporting under the acceptable circumstances.

Section 182 of Title 21 is substantially the same as this proposed law, except for a few minor modifications in wording. The only substantive changes made by this bill are to include the 1961 Single Convention parties as qualified nations for export, and to specifically require the permit for permission to export under these provisions.

Subsection 403(b) permits the Attorney General to authorize the exporting of any narcotic drug to any of those nations party to the listed treaties, notwithstanding the requirements of subsection (a) if the drug is to be applied to a special scientific purpose and authorities of that nation will permit that importation.

This provision is substantially the same as Section 182(c) of Title 21.

Subsection 403(c) forbids the exportation of any non-narcotic controlled dangerous substance listed in schedule I and II (the hallucinogenic substances) from the United States unless the destination country has a system for the control of imports of such substances deemed adequate by the Attorney General; the export is consigned to a properly licensed receiver; evidence has been furnished to the Attorney General that the drug is to be used in the receiving country for a legitimate need and purpose; and a permit to export the substance has been issued.

This is a new provision. The only control exerted over the exporting of these types of substances under existing law is under 21 U.S.C. 381(d), which defines the standards to be applied for determining adulteration or misbranding of the substances to be exported.

The new provision will provide direct supervision, for the first time, of the exporting of these non-narcotic schedule I and II substances, and will require a permit for export from the Attorney General.

Subsection 403(d) permits the Attorney General to authorize the export of any non-narcotic dangerous substance notwithstanding subsection 403(c), if the drug is to be applied to a special scientific purpose and is approved for that use by the authorities of the recipient nation.

This is a new provision, but is comparable to a similar provision applicable to narcotic drugs, Section 182(c) of Title 21.

Subsection 403(e) controls the export of all other controlled dangerous substances which do not require an export permit under the rest of this section. These substances may not be exported unless the recipient nation by law permits the importation of such drugs and evidence of these laws is presented to the Attorney General. A special invoice will be required for a shipment of these substances under this subsection.

There is no comparable law now in force.

Section 404.—Transshipment and in-transit shipment of controlled dangerous substances

This section forbids the admission into the United States of any schedule I substance being transported to another nation, except when it is being exported to that nation for scientific, medical, or other legitimate purposes. The prior written approval of the Attorney General is necessary and will be granted or denied within twenty-one days of the request. Substances controlled under schedules II and III may be admitted for such transportation or transshipment only after advance notice is given to the Attorney General.

A similar provision is in effect under current law as applied to smoking opium, Section 180 of Title 21. That product is totally banned from the United States and, except when prior approval is given, no other narcotic drug may be admitted, transferred, or transshipped.

The new provision extends the ban against such shipments to all schedule I drugs, but provides that exceptions may be granted for scientific, medical, or other legitimate purposes in the country of destination. However, dangerous substances listed in schedules II and III may be transshipped only with advance notice to the Attorney General.

Section 501.—Prohibited acts A—Penalties

Subsection 501(a) makes it unlawful, except as authorized by this Act, for anyone to knowingly (1) manufacture, distribute, or dispense, or possess with intent to manufacture, distribute, or dispense, a controlled dangerous substance; (2) import into the United States schedules III or IV substances; (3) export any schedules I or II substances or a schedule III narcotic drug; (4) bring or possess on board any vessel, vehicle or aircraft in the United States any schedules I or II substances or any schedule III narcotic drug not constituting part of the cargo entered in the manifest or part of the official supplies of the vehicle; and (5) create, distribute, or possess with intent to distribute a counterfeit controlled dangerous substance.

Existing law provides that it is unlawful, except where provided otherwise by law, to manufacture, sell, or dispense depressant and stimulant drugs (21 U.S.C. 360a); sell or smuggle marihuana (21 U.S.C. 176a); or sell, dispense or give away narcotic drugs (26 U.S.C. 4704, 26 U.S.C. 4705), or manufacture narcotic drugs (21 U.S.C. 505). It is unlawful, except as provided otherwise by law, to import any narcotic drug (21 U.S.C. 173). The importation of depressant and stimulant drugs is only controlled as far as investigating the sanitariness of the manufacturing; the legality of its sale in the producing nation; and the purity of the product (21 U.S.C. 381). The exportation of narcotic drugs is controlled by 21 U.S.C. 182, and 49 U.S.C. 781 makes it illegal to bring or possess contraband narcotic drugs on board a vessel, vehicle, or aircraft. Section 331 of Title 21 prohibits the manufacture or sale of a counterfeit drug.

Subsection 501(a) of the bill will therefore only alter the effects of existing law by tightening the controls on the importation of depressant and stimulant drugs by forbidding their importation altogether except when the requirements of Title IV are met.[5]

Subsection 501(b) makes it unlawful to manufacture or distribute any schedules I or II substance intending or knowing that it will be unlawfully imported into the United States. This subsection further states that it is intended to apply to acts of manufacture or distribution of these substances outside the territorial jurisdiction of the United States. It establishes that any person who violates this subsection shall be tried in the United States district court at the point of entry of such person into the United States, or in the United States district court for the District of Columbia.

There is no comparable law for narcotic or dangerous drug law violations currently in effect.

Subsection 501(c) establishes the penalties to be applied to violations of subsections 501(a) and 501(b). The penalties are applied according to the schedule of the substance illegally handled:

(1) Schedule I or II narcotic drugs: imprisonment for not more than 12 years and/or a $25,000 fine, with a special parole term of at least 3 years required.

(2) Other schedules I, II, or III (except for (4) below) substances: imprisonment for not more than 5 years and/or $15,000 fine, including a special parole term of at least 2 years.

(3) Schedule IV substances: imprisonment for not more than 1 year and/or a fine of not more than $5,000.

(4) Distributing a small amount of marihuana for no remuneration, first offense under this Act: imprisonment for not more than 1 year and/or a fine of not more than $5,000.

The laws currently impose punishments based on the substance which is illegally handled:

(1) For knowingly importing, transporting, or selling any narcotic drug (including marihuana): imprisonment of 5 to 20 years and a fine of not more than $20,000. 21 U.S.C. 174.

(2) For the manufacture, sale or delivery of depressant or stimulant drugs: imprisonment for not more than 5 years or fine of not more than $10,000. 21 U.S.C. 333(b).

(3) There is no law in effect comparable to the one proposing special treatment for distributing a small amount of marihuana or for the special parole terms provided.

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[5] In section 501(a)(2), the Senate bill, S. 3246, simply uses the term "United States," while this version expands that term somewhat.

The new bill will alter existing laws in this area by reducing the maximum prison term and abolishing the mandatory five-year sentence. It will provide for the special parole term to be applied to the sentence, and will establish the special punishment for distributing marihuana for no remuneration.

Subsection 501(d) describes the special parole terms which are to be applied to sentences under this Act. It may be revoked if its terms are violated. If so, the original term of imprisonment shall be increased by the period of the special parole term. The resulting new term of imprisonment is not diminished by the time spent on special parole. If the parole is revoked, the defendant may be required to serve all or part of the remainder of the new term. This special parole term is in addition to and not in lieu of any other parole provisions.

This special parole term is a new program, and there are no comparable laws now in force for narcotic drug law convictions. However, this provision conforms to suggested changes proposed by Section 4303 of the Study Draft of a New Federal Criminal Code drawn up by the National Commission on Reform of Federal Criminal Laws.

Subsection 501(e) makes it unlawful to knowingly or intentionally possess a controlled dangerous substance, unless it was lawfully obtained by prescription or as otherwise authorized by the Act. A violator of this section shall be sentenced to a term of imprisonment for not more than one year and/or fined not more than $5,000.

Under existing law, a conviction for possession of marihuana or narcotic drugs would result in a sentence of imprisonment from two to ten years and may also be fined not more than $20,000 (26 U.S.C. 7237). In addition, the possession of illegal narcotic drugs or marihuana may serve as a presumption under 21 U.S.C. 174 and 21 U.S.C. 176a that the defendant knew the substance was illegally imported, and subject him to a penalty of imprisonment for five to twenty years plus a fine up to $20,000. The illegal simple possession of depressant and stimulant drugs may be punished by a sentence of imprisonment for not more than one year and/or a fine up to $1,000.

Section 502.—Prohibited acts B—penalties

Subsection 502(a) applies to those persons registered under this Act to handle the controlled dangerous substances. It is unlawful for these registrants to (1) distribute or dispense without a proper prescription; (2) manufacture or distribute beyond the specific authorization of their registration; (3) violate the regulations controlling transshipment through this country to another; (4) omit the required symbols from containers; (5) remove, alter, or obliterate such symbols; (6) refuse or fail to maintain all required records and forms; or (7) refuse entry to any inspection authorized by this Act.

Current law prohibits these same acts to registrants under Title 21 of the United States Code, Chapter 11, Sections 501 through 517, concerned with the Manufacture of Narcotic Drugs, except that this section contains no regulations as to the transshipment through the United States; the removal or alteration of required symbols; or the failure to attach such symbol. 21 U.S.C. 180 requires official approval before such transshipment of narcotic drugs will be permitted. The Drug Abuse Control Amendments at 21 U.S.C. 331 prohibit all these acts in dealing with depressant and stimulant drugs, except for the prohibition against transshipment.

This subsection simply codifies existing prohibitions relating to those persons registered under the Narcotic Manufacturing Act and the Drug Abuse Control Amendments. It extends control over dangerous substances being shipped through the United States to a third country.

Subsection 502(b) prohibits registrants from manufacturing any controlled dangerous substance unless they are properly registered to do so and produce only their allowed quota.

Under existing law, 21 U.S.C. 505 and 26 U.S.C. 4722 prohibit the manufacture of narcotic drugs without proper registration and beyond the given quota. 21 U.S.C. 331 declares it unlawful to manufacture stimulant and depressant drugs unless properly registered, and declares it unlawful to fail to keep the required records.

This new provision will have the same effect as existing laws already have.

Subsection 502(c) provides punishment for violations of the prohibitions set forth by this section. A civil fine of not more than $25,000 may be imposed, except that if the violation is presented by indictment or information alleges, and the trier of fact finds, that the violation was committed knowingly or inten-

tionally, then the act may be punished by imprisonment for not more than one year and/or a fine of not more than $25,000.

Under existing law, anyone who violates the registration, manufacturing, or recordkeeping requirements of the Narcotic Manufacturing Act is guilty of a felony and, under 21 U.S.C. 515, may be punished by imprisonment of not more than five years and/or fined up to $10,000. 21 U.S.C. 333 provides that violation of these provisions under the Drug Abuse Control Amendments generally subjects the guilty to imprisonment for not more than one year and/or a fine of not more than $1,000, although some specific violations are subject to penalties of up to five years and/or $10,000 fine. A violation of the general provision with the intent to defraud or mislead will be punished by imprisonment of up to three years and/or a $10,000 fine.

The new law would place greater emphasis on utilizing a civil fine to punish these procedural violations by registrants unless it is provide that the act was clearly intentional.

Section 503.—Prohibited acts C—Penalties

Subsection 503(a) refers to registrants who knowingly or intentionally distribute a schedules I or II substance not pursuant to an order form; use a fictitious, revoked, or suspended registration number, or one belonging to someone else; obtain possession of a controlled substance through fraud, forgery, misrepresentation, deception, or subterfuge; furnish fraudulent records, or information; or use any communication facility to facilitate the commission of any offense under this Act. Each separate use of a communication facility is a separate violation under this last phrase and it includes any public or private communication instrumentalities. It is also prohibited for these registrants to make, distribute, or possess any equipment used to make any substance or container into a counterfeit controlled dangerous substance.

Existing law requires the use of an order form for the distribution of narcotic drugs (26 U.S.C. 4705). It declares that the use of a false or fraudulent statement in obtaining a license, registering, producing, supplying quota information, or keeping records is a misdemeanor (21 U.S.C. 515). 18 U.S.C. 1403 provides that it is illegal to use any communication facilities to commit an offense listed in specified laws pertaining to narcotic drug law violations. The wording is substantially the same as that used in this Act. The Drug Abuse Control Amendments in 21 U.S.C. 331(i) prohibit making, selling, or possessing the materials used in making or labeling a drug into a counterfeit drug. The wording used in that law is substantially the same as that used in this bill.

This subsection expands existing law only by extending these various prohibitions to registrants dealing in both narcotic and non-narcotic dangerous substances.

Subsection 503(b) provides that the penalty imposed for the violation of the prohibitions in the above subsection is imprisonment for not more than three years and/or a fine of not more than $30,000.

Under existing law, the penalties imposed vary greatly with the specific violation. For a registrant to distribute not pursuant to an order form, he may receive a punishment under 26 U.S.C. 7237 of from two to ten years in prison and be fined up to $20,000. For using fraud for various purposes under the Manufacturing Act, 21 U.S.C. 515(b) imposes a penalty of up to one year and/or $2,000 fine. For illegal use of communications facilities under 18 U.S.C. 1403, a registrant may be imprisoned from two to five years and fined up to $5,000. For making, distributing, or possessing materials to use to make counterfeit drugs, 21 U.S.C. 333(b)(1) imposes a punishment of imprisonment for not more than five years and/or a fine of $10,000.

The new bill makes uniform the penalty to be applied to registrants for these types of violations, and generally speaking, softens existing penalties, especially by abolishing the mandatory minimum prison terms imposed by some.

Section 504.—Endeavor and conspiracy

This section provides that a person may be punished for endeavoring or conspiring to commit an offense under this Act. Upon conviction, his sentence may not exceed the punishment prescribed for the offense which was the object of the attempt or the conspiracy.

Existing laws for conspiring to commit the offenses of illegal sale or importation of narcotic drugs or marihuana provide that the punishment will be the same as that provided for the actual offense [21 U.S.C. 174, 21 U.S.C. 176a, 26 U.S.C. 7237(a).] Attempts to commit an offense are not punishable under current law.

Section 505.—Additional penalties

Any penalty imposed for violation of this bill will be in addition to any civil or administrative penalty.

This wording is substantially in agreement with existing Federal law.

Section 506.—Distribution to persons under age eighteen.

This section provides punishment for any person who is at least eighteen years of age who distributes a narcotic drug to a person under age eighteen who is at least three years his junior. The prison term may be up to twenty-four years and/or a fine of up to $50,000. The distribution of any non-narcotic controlled drug from schedules I, II, III, or IV to a person under eighteen at least three years his junior by a person over eighteen may be punished by twice the penalty authorized under subsection 501(c)(2), (3), or (4). Probation and suspension of sentence are not permitted.

Under 26 U.S.C. 7237(b), if a person over age eighteen distributes narcotic drugs or marihuana to a person under age eighteen, the offender may be imprisoned from ten to forty years and fined up to $20,000. Such sentence cannot be suspended and probation may not be granted, and if a narcotic drug is involved, the parole provisions under Federal law cannot apply. Under the Drug Abuse Control Amendments, 21 U.S.C. 333(b)(2) provides that in the case of any person eighteen years or older who distributes a controlled dangerous drug to a person under age twenty-one, punishment shall be imposed by imprisonment for not more than ten years and/or a fine not exceeding $15,000. A second offense shall be punished by imprisonment for not more than fifteen years and/or a fine not exceeding $20,000.[6]

Section 507.—Conditional discharge for possession as first offense and expunging of records

This section[7] provides special first offender treatment for a person found guilty of possession of a controlled dangerous substance who has never been previously convicted for a narcotic or dangerous drug violation. The court may, without entering judgment of guilty, place the person on probation under such terms and conditions as the court might require. If these are violated, the court may enter an adjudication of guilt and proceed with the sentencing. However, if the terms are met, the court shall discharge such person and dismiss the proceedings against him without an adjudication of guilt or a conviction. However, this discharge and dismissal may only be applied once to each person. If the person given this treatment was under age twenty-one at the time of the offense, after the probation term is successfully concluded, the court may expunge the record of this treatment and return the person's record to its status prior to this arrest and trial. That person may not thereafter be found guilty of perjury or of giving a false statement by reason of his failure to acknowledge such arrest or trial.

Under existing Federal laws concerning narcotic drugs and marihuana, there are no first offender provisions. Under the Drug Abuse Control Amendments, 21 U.S.C. 333(b)(3)(B), a person who is convicted of possession of a dangerous drug may receive a suspended sentence and be placed on probation for up to one year. The court may unconditionally discharge the person from the probation and set aside the conviction. If the probation term is completed, the conviction is automatically set aside.

Section 508.—Second or subsequent offenses

This section[8] provides that the imprisonment and fine provisions of this bill be doubled in the case of a second or subsequent commission of an offense. If a special parole term is provided, it also will be doubled. A second or subsequent offense is a conviction either under this Act or any Federal law relating to narcotic drugs, marihuana, or dangerous drugs. Enhancement of the sentence under this section comes only after the defendant is convicted and the United States Attorney presents evidence of the prior conviction, and the identity of the accused is affirmed as that of the person with the prior conviction.

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[6] Under this section, S. 3246 does not include doubling the term of imprisonment for a second conviction under 501(c)(4), which this version does, at page 65, lines 3 and 4.

[7] In this section, a minor wording change has been made from S. 3246, replacing the words "of this section or for purposes" in lines 1 and 2 on page 66 for the word "purposes."

[8] In this section one change has been made from S. 3246 by changing the wording "the commission of the offense" and stating, on lines 13 and 14 on page 67, "his conviction for that offense."

Under current Federal law, greater punishments are generally provided in the case of second or subsequent offenses by the penalty statutes for each offense. These penalties are frequently nearly twice the original penalty, but there is no one provision for these penalties. In 26 U.S.C. 7237, penalties for second or subsequent offenses involving narcotic drugs or marihuana are provided. Under 21 U.S.C. 33, penalties for convictions for second or subsequent offenses are set out for violations of the Drug Abuse Control Amendments.

Section 509.—Continuing criminal enterprise

Section 509[9] provides for the determination of the existence of a continuing criminal enterprise in conjunction with a conviction for a violation under this Act. After a plea or a determination of guilty to a violation of this Act which carries a sentence of more than one year, the court may consider evidence that the defendant has been involved in such a continuing criminal enterprise. This section sets out the procedure to be followed in raising and determining this issue. Upon a finding that the defendant has been so involved, the court shall sentence him to prison for five years to life, and fine him $50,000. All the profits obtained through violations of this Act, any interest acquired or maintained through violations, and any interest in any enterprise established or operated in violation of the Act will be forfeited to the United States. For a second or subsequent conviction under this provision, the same forfeitures will be made and a prison term of from ten years to life and a fine of $100,000 will be imposed.

This section further sets out the criteria to be considered in determining if the accused has been involved in a continuing criminal enterprise and the appellate review procedures to be followed. There are no limitations on the information which may be considered by the court concerning the background, character, and conduct of a person accused of violating this section in order to determine an appropriate sentence.

There is currently no provision of this nature under existing law.

TITLE VI—ADMINISTRATIVE PROVISIONS

Section 601.—Delegation of authority—rules, regulations, and procedures—bequests and gifts

This section provides that the Attorney General may delegate his functions under this Act to employees of the Department of Justice. He may promulgate regulations and rules for the enforcement of this Act, as well as accept gifts for the Department for the purpose of preventing or controlling the abuse of dangerous substances.

This provision is substantially the same as comparable administrative provisions under existing Federal acts, for example, 21 U.S.C. 514.

Section 602.—Education and research

This section authorizes the Attorney General to carry out educational and research programs relating to the effects of and potential for abuse of controlled dangerous substances. He may enter into contracts with public or private individuals or organizations to obtain research on these substances, without requiring performance bonds. He may authorize these researchers to withhold the names and identities of persons who are subject of such research, and may authorize the possession and distribution of dangerous substances.

Similar programs are currently being conducted under broad administrative provisions, but no one specific Federal law details authorization for education and research programs as does this section.

Section 603.—Cooperative arrangements

Section 603 provides that the Attorney General shall cooperate with local, State, and Federal agencies in discharging the national and international obligations concerning narcotics and dangerous substances. Through such cooperation, he may arrange for the exchange of information; cooperate in the prosecution of cases; conduct law enforcement training programs; maintain information and statistics on addicts and violators; and conduct eradication programs against wild or illicit plant life from which controlled dangerous substances may be extracted. At the request of the Attorney General, any Federal agency must furnish assistance or advice for the purposes of carrying out this Act.

[9] The term "United States" was added before the word "Attorney" on line 11, page 68 of this Act, thus altering the wording used in this section in S. 3246.

Sections 197 and 198 of Title 21, United States Code, currently provide for such cooperative arrangements in language substantially similar to that used in this Act; however, there is currently no specific law providing for programs of eradication of wild or illicit plant life.

Section 604.—Scientific Advisory Committee

This section establishes a Scientific Advisory Committee to advise the Attorney General with respect to the classification and control of substances. The section sets forth the general qualifications for members of the Committee, their payment, and their duties. Other committees may be created as needed to advise the Attorny General with respect to prevention and control of the abuse of dangerous substances.

Existing Federal law provides for an advisory committee under the Drug Abuse Control Amendments to help in the determination of whether or not a substance is a "depressant or stimulant drug." [21 U.S.C. 360a(g).]

Section 605.—Administrative hearings

This section authorizes the Attorney General to use administrative procedures in order to carry out his functions under this Act. Any hearings will be conducted under the Administrative Procedures Act.

This provision is similar to administrative provisions used under existing Federal law, such as 21 U.S.C. 506 and 21 U.S.C. 198a.

Section 606.—Subpoenas

This section authorizes the Attorney General to subpoena witnesses and records and sets forth the procedure to be used. In the event of a refusal to obey such a subpoena, this section would authorize court action.

This section is substantially the same as the provisions under Sections 198a, 198b, and 198c of Title 21 of the United States Code.

Section 607.—Judicial review

This section provides that judicial review will be available for final determinations of the Attorney General under this Act and sets forth the courts of proper jurisdiction.

This provision is substantially the same as the procedure available under 21 U.S.C. 371 and 21 U.S.C. 516 and is in agreement with the aim of the Administrative Procedures Act, Subchapter II of Chapter 5, Title 5, United States Code.

TITLE VII—ENFORCEMENT PROVISIONS

Section 701.—Powers of enforcement personnel

Subsection 701(a) permits those officers and employees of the Bureau of Narcotics and Dangerous Drugs designated by the Attorney General to carry firearms; execute and serve warrants and subpoenas; make arrests without warrants for offenses committed against the United States in their presence; and to make seizures of property.

Under the Harrison Narcotic Act, 26 U.S.C. 7607, Special Agents of the Bureau of Narcotics and Dangerous Drugs are authorized to carry firearms; execute and serve warrants and subpoenas; and make arrests without a warrant for offenses committed against the United States relating to narcotic drugs and marihuana.

Under the Drug Abuse Control Amendments, 21 U.S.C. 372(e), Special Agents of the Bureau of Narcotics and Dangerous Drugs are authorized to carry firearms; execute and serve warrants; make executive seizures; and make arrests without a warrant for offenses committed under the Act.

Subsection 701(b) provides that no provision contained in the Act shall derogate from the authority of the Secretary of the Treasury under the customs and related laws. No comparable counterpart to this subsection exists in current Federal law since this subsection is designed only to insure that the Act will in no way affect the authority of the Treasury Department to enforce the customs laws.

Section 702.—Search warrants

Subsection 702(a) provides that search warrants relating to offenses involving controlled dangerous substances may be served at any time of the day or night so long as there is probable cause to believe that grounds exist for the warrant and for its service at such time.

Under 18 U.S.C. 1405, search warrants relating to offenses involving narcotic drugs may be served at any time of the day or night so long as there is probable cause to believe that grounds exist for the warrant.

Search warrants relating to offenses involving stimulant and depressant drugs must presently be served in the daytime unless the positivity requirement of Rule 41(c) of the Federal Rules of Criminal Procedure is met.

Subsection 702(b) authorizes the execution of search warrants relating to felony offenses involving controlled dangerous substances without knocking or announcing authority and purposes if the judge or magistrate issuing the warrant is satisfied that there is probable cause to believe that if the officers knocked and announced their authority and purpose, either the evidence sought would be quickly or easily destroyed or disposed of, or the officers would be placed in danger of physical harm. Additional provisions require that the search warrant state on its face that an unannounced entry is authorized and that the officers identify themselves as soon as is practicable after gaining entry.

No provisions are made under existing Federal law for the authorization of unannounced entries in the execution of search warrants. Under the common law, unannounced entries are permitted in those instances where the officer executing a search warrant has probable cause to believe that if he knocked and announced his authority and purpose, either the evidence sought would be destroyed or his life would be placed in danger.

Section 703.—Administrative inspections and warrants

Section 703 sets out the provisions for the administrative inspections authorized by the Act and provides for the issuance and execution of administrative inspection warrants.

Subsection 703(a) sets out the criteria which must be met to give rise to the requisite probable cause for the issuance and execution of administrative inspection warrants; the procedures for obtaining such warrants; and the mode and manner in which such warrants are to be executed.

No provisions are made under existing Federal law for the issuance and execution of administrative inspection warrants. However, a number of recent Supreme Court decisions have held that in the absence of consent or imminent danger to the public health and safety, the Fourth Amendment requires that warrants must be obtained for conducting administrative inspections. [*Camara* v. *Municipal Court of the City and County of San Francisco*, 387 U.S. 523 (1967); *See* v. *City of Seattle*, 387 U.S. 541 (1967); and *Colonnade Catering Corp.* v. *United States*, 90 S. Ct. 774 (1970).]

Subsection 703(b) sets out those premises which are to be deemed "controlled premises" for the purpose of administrative inspections, and the types of materials which are subject to inspection. The subsection further sets out those instances where inspection warrants are not required and those materials which are specifically excluded from the scope of inspection authority.

These provisions are, in part, an adaptation of the inspection provisions contained in the Drug Abuse Control Amendments, 21 U.S.C. 360a(d)(2)(A) & (B), and 21 U.S.C. 374, which authorize inspections for the purpose of inspecting the records required under the Act and inspecting the premises in which stimulant and depressant drugs are manufactured, processed, or held for introduction into interstate commerce.

Section 704.—Forfeitures

Section 704 sets out the types of property which are subject to forfeiture under the Act. These include controlled dangerous substances manufactured or obtained in violation of the Act; raw materials, products, and equipment used in the manufacture or conveyance of controlled dangerous substances in violation of the Act; conveyances used to transport or conceal controlled dangerous substances, with certain exceptions; and books, records, and other documents used in violation of the Act.

Under the Harrison Narcotics Act, 26 U.S.C. 4706, unstamped packages of narcotic drugs are subject to seizure and forfeiture. Under 49 U.S.C. 782, any vehicle, vessel, or aircraft which is used to transport, conceal, or facilitate the transportation or concealment of a narcotic drug or marihuana is subject to seizure or forfeiture. Certain exceptions, similar to those contained in subsection 704(a) of H.R. 17463, are made with respect to common carriers.

Under the Drug Abuse Control Amendments, 21 U.S.C. 334(a)(2), stimulant and depressant drugs used in violation of the Act; counterfeit drugs; equipment used to manufacture or process stimulant or depressant drugs in violation of

the Act; and any punch, die plate, stone, labeling, container, or other thing used in making counterfeit drugs are all subject to libel proceedings and condemnation in United States district courts. However, there are no provisions allowing for the seizure and forfeiture of conveyances used to transport, conceal, or facilitate the transportation or concealment, of stimulant or depressant drugs in violation of the Drug Abuse Control Amendments.

Section 704 also carries over a number of provisions contained in existing Federal law with respect to the procedures for seizure and forfeiture and disposal of forfeited property.

Section 705.—Injunctions

Section 705 provides that the district courts of the United States shall have jurisdiction in proceedings to enjoin violations of the Act. The section further provides that violations of injunctions or restraining orders are to be tried by jury upon demand of the accused, in accordance with the Federal Rules of Civil Procedure.

The language of this section is substantially similar to the language of the injunction provision contained in the Drug Abuse Control Amendments, 21 U.S.C. 332.

Section 706.—Enforcement proceedings

Section 706 permits the Director of the Bureau of Narcotics and Dangerous Drugs, prior to the institution of criminal proceedings, to require that the person against whom such a proceeding is contemplated be given notice and an opportunity to present his views with regard to the proceeding contemplated. This section has the effect of enabling a person to explain the circumstances surrounding a suspected violation and thus possibly avoid the institution of criminal proceedings.

The language of this section is substantially similar to language contained in the Drug Abuse Control Amendments, 21 U.S.C. 335.

Section 707.—Immunity and privilege

Section 707 authorizes a United States Attorney, with the approval of the Attorney General, to make application to the court to order any witness in a case brought under the provisions of the Act to testify or produce evidence in his possession. Such witnesses cannot be prosecuted or subjected to any penalty or forfeiture because of this compelled testimony or production of evidence, provided that the witness has claimed his privilege against self-incrimination. This exemption does not preclude prosecution for perjury or contempt.

Under existing Federal narcotic, marihuana, and dangerous drug law, there are no provisions allowing for grants of specific immunity in cases involving narcotic, marihuana, or dangerous drug violations.

Section 708.—Burden of proof; liabilities

Section 708 provides that there shall be no burden on the Government to negate any exemption under the Act and that the burden of showig such an exemption shall be on the person claiming its benefit. The section further provides that in the absence of proof that a person is a registrant or a holder of an order form, it shall be presumed that he is not, and the burden shall be on the person to show that he is. Other provisions of section 708 relieve Federal officers from liability while enforcing the Act.

This section is for the most part a codification of the current Federal case law and is not reflected in existing Federal narcotic, marihuana, or dangerous drug statutes.

Section 709.—Payments and advances

Section 709 authorizes the Attorney General to make payments to persons who furnish information relating to violations of the Act in such sums as he deems appropriate.

This subsection is an adaptation of the provisions contained in the Narcotic Drugs Import and Export Act, 21 U.S.C. 199, authorizing the Attorney General to make payments for information concerning violations of the Federal narcotic laws.

TITLE VIII—ADVISORY COMMITTEES

Section 801.—Committee on Marihuana

Section 801 calls for the establishment of a Committee on Marihuana jointly appointed by the Attorney General and the Secretary of Health, Education, and

Welfare. The Committee, consisting of no less than five persons, is to undertake a 24-month study into the various phases of marihuana use, including such things as the identification of the existing gaps in our knowledge of marihuana; the medical and social aspects of marihuana use; surveys on the extent and nature of marihuana use; studies into the relationship between marihuana use and crime; and an evaluation of the efficacy of existing marihuana laws.

No comparable counterpart to section 801 exists under current Federal law.

Section 802.—Committee on Nongovernmental Drug Abuse Prevention and Control

Section 802 calls for the establishment of a Committee on Nongovernmental Drug Abuse Prevention and Control to study the extent to which nongovernmental organizations are involved in the prevention and control of drug abuse and to advise as to how such organizations can best be fostered and encouraged. The Committee is to consist of twenty-one members appointed by the President and it is to submit its findings to the President and Congress within one year after the effective date of the Act.

TITLE IX—MISCELLANEOUS

Title IX contains a number of miscellaneous provisions normally found in an act of this type. These include: repealers; conforming amendments; continuation of pending proceedings; continuation of regulations; severability clause; saving clause; republishing of schedules; and an effective date.

COMPARISON OF PENALTY STRUCTURES BETWEEN H.R. 17463 (CONTROLLED DANGEROUS SUBSTANCES ACT OF 1969) AND PRESENT LAW

Violation	Law applicable	Maximum fine	Sentence	Special parole term	Probation or suspended sentence permitted	Parole permitted
Unlawful distribution, possession with intent to distribute, manufacture, importation, and exportation, etc.:						
1st offense	Present law:					
	Narcotics	$20,000	5 to 20 years	No	No	No.
	Marihuana	20,000	do	No	No	Yes.
	Dangerous drugs	10,000	Up to 5 years	No	Yes	Yes.
	H.R. 17463:					
	I and II narcotics	25,000	Up to 12 years	(1)	Yes	Yes.
	I and II nonnarcotic and III substances.	15,000	Up to 5 years	(2)	Yes	Yes.
	IV substances	5,000	Up to 1 year	No	Yes	Yes.
2d offense	Present law:					
	Narcotics	20,000	10 to 40 years	No	No	No.
	Marihuana	20,000	do	No	No	Yes.
	Dangerous drugs	20,000	Up to 5 years	No	Yes	Yes.
	H.R. 17463:					
	I and II narcotics	50,000	Up to 24 years	(3)	Yes	Yes.
	I and II nonnarcotic and III substances.	30,000	Up to 10 years	(4)	Yes	Yes.
	IV substances	10,000	Up to 2 years	No	Yes	Yes.
Simple possession:						
1st offense	Present law:					
	Narcotics	20,000	2 to 10 years		Yes	Yes.
	Marihuana	20,000	do		Yes	Yes.
	Dangerous drugs	1,000	Up to 1 year		Yes	Yes.
	H.R. 17463:					
	I and II narcotics	5,000	do		Yes	Yes.
	I and II nonnarcotics and III substances	5,000	do		Yes	Yes.
	IV substances	5,000	do		Yes	Yes.
2d offense	Present law:					
	Narcotics	20,000	5 to 20 years		No	No.
	Marihuana	20,000	do		No	Yes.
	Dangerous drugs	1,000	Up to 1 year		Yes	Yes.
	H.R. 17463:					
	I and II narcotics	10,000	Up to 2 years		Yes	Yes.
	I and II nonnarcotics and III substances	10,000	do		Yes	Yes.
	IV substances	10,000	do		Yes	Yes.

See footnotes at end of table.

COMPARISON OF PENALTY STRUCTURES BETWEEN H.R. 17463 (CONTROLLED DANGEROUS SUBSTANCES ACT OF 1969) AND PRESENT LAW—Continued

Violations	Law applicable	Maximum fine	Sentence	Probation or suspended sentence permitted	Parole permitted
Distribution of small amounts of marihuana for no profit.	Present law: No applicable provisions. H.R. 17463:				
1st offense		$5,000	1 year	Yes	Yes.
2d offense		15,000	Up to 10 years	Yes	Yes.
Continuing criminal enterprise.	Present law: No applicable provisions. H.R. 17463:				
1st offense		50,000	5 years to life	No	No.
2d offense		100,000	10 years to life	No	No.
Conditional discharge for possession as 1st offense	[5]				
Endeavor and conspiracy	[6]				
Distribution of persons under the age of 18	[7]				

[1] At least 3 years.
[2] At least 2 years.
[3] At least 6 years.
[4] At least 4 years.

[5] H. R. 17463 provides that a court may, upon finding any person guilty of possessing a controlled dangerous substance without intent to distribute, and who has not previously been convicted under any Federal or State law relating to narcotic drugs, marihuana, stimulant, depressant, or hallucinogenic drugs, defer further proceedings and place the person on probation upon such reasonable terms and conditions as it may require. Upon violation of the terms of probation, the court may enter an adjudication of guilt and proceed as provided by the respective acts. Upon fulfillment of the terms of probation, the court shall discharge the person and dismiss the proceedings. Such discharge shall not be deemed a conviction for the purposes of the disabilities imposed by law upon persons convicted of crimes. However, such discharge and dismissal under these sections is available only once with respect to any person.

There are no provisions for 1st offender treatment under the present Federal law for offenses involving possession of narcotics or marihuana. There is a provision allowing for 1st offender treatment under the Drug Abuse Control Amendments of 1965, but it is applicable only to cases involving possession of dangerous drugs.

[6] H.R. 17463 provides that any person who endeavors or conspires to commit any offense under the act may be punished by imprisonment and/or fine, which may not exceed the maximum punishment proscribed for committing the offense.

Present Federal law provides that any person who conspires to commit an offense under any of the acts may be punished by imprisonment and/or fine not exceeding the maximum punishment proscribed for committing the offense. Attempt to commit an offense under any of the existing acts is not punishable as an offense.

[7] H.R. 17463 provides that any person over 18 who knowingly and intentionally violates subsec. 501(a)(1) by distributing a substance classified in schedules I or II which is a narcotic to a person under 18 years of age who is at least 3 years his junior is punishable by a term of imprisonment twice that authorized by subsec. 501(c)(1), by a fine of $25,000, or both. Distribution of any other controlled dangerous substance classified in schedules I, II, III, or IV by a person over 18 to a person under 18 who is at least 3 years his junior is punishable by a term of imprisonment up to twice that authorized under subsec. 501(c) (2) or (3), by the fine authorized under subsec. 501(c) (2) or (3) or both. For any of these offenses, imposition or execution of sentences cannot be suspended and probation cannot be granted.

Under existing Federal law, distribution of narcotics or marihuana by a person over 18 to a person under 18 years of age is punishable by imprisonment for not less than 10 years nor more than 40 years and, in addition, may be fined not more than $20,000. Imposition or execution of such sentence cannot be suspended and probation cannot be granted. In addition, if the offense involves a narcotic drug, the parole provisions under Federal law shall not apply. Under the Drug Abuse Control Amendments of 1965, a person over 18 who distributed dangerous drugs to a person under 21 years of age is punishable by imprisonment for not more than 10 years, a fine not exceeding $15,000, or both. A 2d offense is punishable by imprisonment for not more than 15 years, a fine not exceeding $20,000, or both.

Note: Under existing Federal law, possession with intent to distribute is not a separate offense.

CITATION OF EACH SECTION OF H.R. 17463 TO EXISTING LAWS AND REGULATIONS

H.R. 17463	Narcotic law	Marihuana law	Dangerous drug law
102(a)	28 U.S.C. 2901 (a) 18 U.S.C. 4251 (a)	Not available	Not available.
102(b)	Not available	do	Do.
102(c)	do	do	Do.
102(d)	do	do	21 CFR 320.1(f).
102(e)	do	do	Not available.
102(f)	do	do	21 CFR 320.1(j).
102(g)	do	do	21 U.S.C. 321 (g)(2).
102(h)	do	do	21 CFR 320.1(b).
102(i)	do	do	21 U.S.C. 321 (v).
102(j)	do	do	Not available.
102(k)	do	do	Do.
102(l)	do	do	21 U.S.C. 321(g)(1).
102(m)	do	26 U.S.C. 4761(2)	Not available.
102(n)	21 U.S.C. 502(f)	Not available	Do.
102(o)	26 U.S.C. 4731(a)	do	Do.
102(p)	21 U.S.C. 503(h)	do	Do.
102(q)	26 U.S.C. 4731(g)(1)	do	Do.
102(r)	21 U.S.C. 188a(c)	do	Do.
102(s)	Not available	do	Do.
102(t)	26 CFR 151.11(h)	26 CFR 151.11(h)	Do.
102(u)	21 U.S.C. 188a(b)	Not available	Do.
102(v)	21 U.S.C. 502(i)	do	Do.
102(w)	Not available	do	Do.
102(x)	do	do	Do.
102(y)	do	do	Do.
201	21 U.S.C. 504	do	21 U.S.C. 321 (v).
202	Not available	do	Not available.
301	26 U.S.C. 4721	26 U.S.C. 4751	Do.
302(a)	26 U.S.C. 4722 21 U.S.C. 506	26 U.S.C. 4753	21 U.S.C. 360(b).
302(b)	26 U.S.C. 4724(c)	26 U.S.C. 4772	21 U.S.C. 360a(a), (b).
302(c)	26 U.S.C. 4772(b)	26 U.S.C. 4772(b)	21 U.S.C. 360a(a)(6).
302(d)	26 U.S.C. 4722	26 U.S.C. 4751	21 U.S.C. 360.
302(e)	26 CFR 151.23	26 CFR 151.21 26 CFR 151.22	21 U.S.C. 360(h).
303(a)	21 U.S.C. 506	Not available	Not available.
303(b)	Not available	do	Do.
303(c)	21 U.S.C. 506(c)	do	Do.
303(d), (e)	21 U.S.C. 506(c)	do	Do.
303(f)	26 U.S.C. 4722 26 U.S.C. 4721(3) 26 U.S.C. 4721(4) 26 U.S.C. 4721(5)	26 U.S.C. 4753 26 U.S.C. 4751(3) 26 U.S.C. 4751(4)	21 U.S.C. 360. 21 U.S.C. 360a(a)(5).
304(a)	21 U.S.C. 507	Not available	Not available.
304(b)	21 U.S.C. 507	do	Do.
304(c)	21 U.S.C. 506(e) 21 U.S.C. 507(b)	do	Do.
304(d)	Not available	do	Do.
304(e)	do	do	Do.
304(f)	21 U.S.C. 507	do	Do.
305	26 U.S.C. 4703	26 U.S.C. 4743	21 CFR 320.18.
306	21 U.S.C. 509	Not available	Not available.
307	26 U.S.C. 4732 21 U.S.C. 511	26 U.S.C. 4754	21 U.S.C. 360a(d).
308	26 U.S.C. 4705	26 U.S.C. 4742	Not available.
309(a)	26 U.S.C. 4705(c)(2) 26 CFR 151.411 26 CFR 151.397	Not available	Do.
309(b)	26 U.S.C. 4705(c)(2) 26 CFR 151.411 26 CFR 151.397	do	21 U.S.C. 370a(e).
401	21 U.S.C. 173	21 U.S.C. 176a	21 U.S.C. 381.
402	21 U.S.C. 173a	Not available	Not available.
403(a)	21 U.S.C. 182	do	Do.
403(b)	21 U.S.C. 182(c)	do	Do.
403(c)	Not available	do	Do.
403(d)	21 U.S.C. 182(c)	do	Do.
403(e)	Not available	do	Do.
404	21 U.S.C. 189	do	Do.
501(a)(1)	26 U.S.C. 4705(a) 26 U.S.C. 4704 21 U.S.C. 174 21 U.S.C. 505	26 U.S.C. 4742 26 U.S.C. 4744 21 U.S.C. 176a	21 U.S.C. 360a 21 U.S.C. 331(q)
501(a)(2)	21 U.S.C. 173	21 U.S.C. 176a	Not available
501(a)(3)	21 U.S.C. 182	Not available	Do.
501(a)(4)	49 U.S.C. 781	49 U.S.C. 781	Do.
510(a)(5)	Not available	Not available	21 U.S.C. 331.
501(b)	do	do	Not available
501(c)(1)	26 U.S.C. 7237 21 U.S.C. 174 21 U.S.C. 515 21 U.S.C. 183	do	Do.

CITATION OF EACH SECTION OF H.R. 17463 TO EXISTING LAWS AND REGULATIONS—Continued

H.R. 17463	Narcotic law	Marihuana law	Dangerous drug law
501(c)(2)	26 U.S.C. 7237 21 U.S.C. 174 21 U.S.C. 515 21 U.S.C. 183	26 U.S.C. 7237 21 U.S.C. 176a	21 U.S.C. 333.
501(c)(3)	Not available	Not available	Not available.
501(c)(4)	do	do	Do.
501(d)	do	do	Do.
501(e)	26 U.S.C. 4704 26 U.S.C. 7237	26 U.S.C. 4744 26 U.S.C. 7237	21 U.S.C. 331(q)(3). 21 U.S.C. 333.
502(a)(1)	26 U.S.C. 4705(c)(2)	Not available	21 U.S.C. 331(q)(7).
502(a)(2)	21 U.S.C. 505(a)(2)	do	21 U.S.C. 360a(a)(1)(A).
502(a)(3)	21 U.S.C. 180	do	Not available.
502(a)(4)	Not available	do	21 U.S.C. 331(k).
502(a)(5)	do	do	21 U.S.C. 331(k).
502(a)(6)	26 U.S.C. 4732	26 U.S.C. 4754	21 U.S.C. 331(q)(4).
502(a)(7)	Not available	Not available	21 U.S.C. 331(q)(5), (6).
502(b)(1), (2)	21 U.S.C. 505(a) 21 U.S.C. 505(c)(2)	do	Not available.
502(c)	21 U.S.C. 515 26 U.S.C. 7237 21 U.S.C. 174	21 U.S.C. 7237	21 U.S.C. 333.
503(a)(1)	26 U.S.C. 4705(a)	26 U.S.C. 4742	Not available.
503(a)(2)	Not available	Not available	Do.
503(a)(3)	do	do	Do.
503(a)(4)	21 U.S.C. 515 26 U.S.C. 7207	26 U.S.C. 7207	21 U.S.C. 331(q)(4).
503(a)(5)	18 U.S.C. 1403	18 U.S.C. 1403	Not available.
503(a)(6)	Not available	Not available	21 U.S.C. 331(i)(2).
503(b)	21 U.S.C. 515 26 U.S.C. 7207 18 U.S.C. 1403	26 U.S.C. 7207 18 U.S.C. 1403	21 U.S.C. 333.
504	26 U.S.C. 7237 21 U.S.C. 174	26 U.S.C. 7237 21 U.S.C. 176(a)	18 U.S.C. 371.
505	Not available	Not available	Not available.
506	26 U.S.C. 7237 21 U.S.C. 176b	26 U.S.C. 7237	21 U.S.C. 333.
507	Not available	Not available	21 U.S.C. 333(b)(3)(B).
508	26 U.S.C. 7237(c) 21 U.S.C. 174	26 U.S.C. 7237(c) 21 U.S.C. 176a	21 U.S.C. 333.
509	Not available	Not available	Not available.
601	21 U.S.C. 514 26 U.S.C. 7805	26 U.S.C. 7805	21 U.S.C. 371(a).
602	Not available	Not available	Not available.
603	21 U.S.C. 198	do	Do.
604	Not available	do	21 U.S.C. 360a(g).
605	21 U.S.C. 506 21 U.S.C. 198a	21 U.S.C. 198a	21 U.S.C. 371.
606	21 U.S.C. 198a	21 U.S.C. 198a	Not available.
607	21 U.S.C. 516	Not available	21 U.S.C. 371.
701(a)	26 U.S.C. 7607	26 U.S.C. 7607	21 U.S.C. 372(e).
701(b)	Not available	Not available	Not available.
702(a)	18 U.S.C. 1405	18 U.S.C. 1405	Do.
702(b)	Not available	Not available	Do.
703(a)	do	do	Do.
703(b)	do	do	21 U.S.C. 360a(d)(2). 21 U.S.C. 374.
704	26 U.S.C. 4706 49 U.S.C. 782	26 U.S.C. 4745 49 U.S.C. 782	21 U.S.C. 334(a)(2).
705	Not available	Not available	21 U.S.C. 332.
706	do	do	21 U.S.C. 335.
707	do	do	Not available.
708	21 U.S.C. 516	do	Do.
709	21 U.S.C. 199	do	Do.
801	Not available	do	Do.
802	do	do	Do.

The CHAIRMAN. Mr. Burke will inquire.

Mr. BURKE. With respect to the statements the Attorney General made on inventory keeping, I believe you indicated that the law expired in 1965.

Attorney General MITCHELL. In 1969.

Mr. BURKE. Has there been a recommendation by the Department of Justice that that law be continued?

Mr. INGERSOLL. Mr. Burke, the inventory controls expired in 1969 and up until that time, between 1965 and 1969, a 3-year inventory was required, but that provision of the law expired in 1969.

In recognition of that, we prepared for an inventory procedure in the bill that is before you.

Mr. BURKE. As of this moment, there is no law requiring an inventory bookkeeping?

Mr. INGERSOLL. In the dangerous drug area, that is true. The same controls as always still apply to the narcotics drugs.

Mr. BURKE. In your concluding statement, you pointed out the need for legislative tools, trained manpower, and adequate funding. What has the Department of Justice done during the past year to secure the services of additional narcotics agents? How many agents have they added to their staff?

Mr. INGERSOLL. In 1968, Mr. Congressman, we had in the neighborhood of 600 agents. Today we have about 900 agents. We have asked the President to include in his budget plans for another 150 agents for fiscal year 1971.

In addition to that, we have established a comprehensive forensic laboratory system which presently employs about 90 chemists, and then the balance of our present ceiling of approximately 1,400 is made up of other professional, clerical, and support groups.

We have asked and obtained in resources an increase from about $18 million, a little over $18 million with supplemental requests in fiscal 1969, to $27.5 million in fiscal 1970 and our pending request is in the neighborhood of $36 million, as I recall.

Mr. BURKE. Is there any program in the Department of Justice to train customs inspectors to detect the devious methods that are used in smuggling drugs into the country?

Mr. INGERSOLL. The Bureau of Customs has its training program for its personnel. This is a matter of a separate budget. I think we provide, as I recall, people in their training sessions to get them just generally acquainted with the functions of the Bureau of Narcotics and Dangerous Drugs.

Mr. BURKE. Thank you.

The CHAIRMAN. Mr. Byrnes will inquire.

Mr. BYRNES. Mr. Chairman, Mr. Attorney General, I believe it was last week that I read in the paper of a court of appeals case dealing with possession, and the general conclusion was that possession of at least some drugs was without any penalty, or that the law had been considerably changed from what we thought it was.

Does the new possession definition as contained in the legislation take into consideration this latest case, or am I mistaken about there being a recent case that made rather considerable changes?

Attorney General MITCHELL. I believe you have reference to the *Watson* case that came out of the District Court of Appeals here in the District of Columbia.

Mr. BYRNES. I believe so. That was within the last 2 or 3 weeks.

Attorney General MITCHELL. The decision is subject to appeal and we do not believe the decision will hold up in view of prior decisions of the Supreme Court. I think your characterization of it is correct to the point that it relates to possession. It does not affect the validity or constitutionality of the statute, but it does create the possibility of an affirmative defense to the charges of unlawful possession when the addict possesses it solely for his own use.

As I say, there have been other decisions relating to alcohol and

other substances which are contrary to this decision. We do not believe that it will be sustained.

The statute that we have here relating to possession I do not believe has to be changed in order to accommodate this decision whether it is sustained or otherwise.

Mr. BYRNES. In other words, your point is that further changes in this legislation would not be required if that decision were sustained?

Attorney General MITCHELL. That is our current opinion. We still have the matter under consideration.

Mr. BYRNES. Can you give me a general picture of what the Federal and State responsibilities will be in trying to get at this abuse problem? If this legislation should be enacted, will there be large areas where there will be dual responsibility with a dual system and dual and varying penalties?

It seems to me one of the problems that we have today lies in determining who is taking jurisdiction in terms of what the penalties may be and even as to whether an offense has been committed.

Is there anything in this legislation that will clarify that problem, or do you consider it a problem?

Attorney General MITCHELL. Mr. Byrnes, part of the President's program we are now implementing is the Uniform State Controlled Dangerous Substances Act which has been enacted in three States and Guam and is under consideration in a number of other States. This will help immeasurably in trying to provide a uniform approach to this problem including, we hope, the penalty questions.

Since we have been in office, we have changed our law enforcement approach and have concentrated our efforts against the major traffickers. The major law enforcement effort against the street pusher and the middleman has been left to the jurisdiction of the State and local governments. We are now experimenting with a task force of combined Federal, State and local law enforcement in the State of New York, and hope to expand this to other areas of the country where the jurisdictional questions in this area can be resolved and where the forces of the respective law enforcement agencies can be more appropriately directed at the total problem—in other words, the theory that two plus two plus two will equal eight instead of five or four when law enforcement are running along separate lines of attack.

We are meeting with some success in this area as we have in the organized crime area. Our entire effort is to bring to bear the total resources of all of the governmental structures on this problem. It does take some sorting out because we are starting from scratch, but between the uniform law and the cooperative efforts we are undertaking, including, of course, the extensive training that the Bureau of Narcotics and Dangerous Drugs is doing on behalf of local law enforcement agencies, I anticipate even greater successes. I guess there will be some 22,000 State and local police officers this fiscal year who will have been trained.

Mr. BYRNES. How many jurisdictions would that cover?

Attorney General MITCHELL. Can you sort the State and local out of that?

Mr. INGERSOLL. If you would like a definitive answer we can provide it.

Mr. BYRNES. I thought you might have a general idea. These are both local and, in some cases, State law enforcement agencies.