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]

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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-311-248/6014.
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