INTERNATIONAL TRADE COMMISSION

[Investigation No. 701-TA-312 (Final)]

Softwood Lumber From Canada

AGENCY: United States International Trade Commission

ACTION: Institution and scheduling of a final countervailing duty investigation.

SUMMARY: The Commission hereby gives notice of the institution of final countervailing duty investigation No. 701-TA-312 (Final) under section 705(b) of the Tariff Act of 1930 (19 U.S.C. 1671d(b)) (the act) to determine whether an industry in the United States is materially injured, or is threatened with material injury, or the establishment of an industry in the United States is materially retarded, by reason of imports from Canada of softwood lumber, [1] provided for in subheadings 4407.10.00, 4409.10.10, 4409.10.20, and 4409.10.90 of the Harmonized Tariff Schedule of the United States (HTS).

For further information concerning the conduct of this investigation, hearing procedures, and rules of general application, consult the Commission's Rules of Practice and Procedure, part 201, subparts A through E (19 CFR part 201), and part 207, subparts A and C (19 CFR part 207).

EFFECTIVE DATE: March 6, 1992.

FOR FURTHER INFORMATION CONTACT: Jim McClure (202-205-3191), Office of Investigations, U.S. International Trade Commission, 500 E Street SW., Washington, DC 20436. Hearing-impaired persons can obtain information on this matter by contacting the Commission's TD terminal on 202-205-1810. Persons with mobility impairments who will need special assistance in gaining access to the Commission should contact the Office of the Secretary at 202-205-2000.

SUPPLEMENTARY INFORMATION:

Background: This invesitgation is being instituted as a result of an affirmative preliminary determination by the Department of Commerce that certain benefits which constitute subsidies within the meaning of section 703 of the act (19 U.S.C. 1671b) are being provided to manufacturers, producers, or exporters in Canada of softwood lumber. The investigation was self-initiated on October 31, 1991, by the U.S. Department of Commerce.

Participation in the investigation and Public service list: Persons wishing to participate in the investigation as parties must file an entry of appearance with the Secretary to the Commission, as provided in § 201.11 of the Commission's rules, not later than twenty-one (21) days after publication of this notice in the **Federal Register.** The Secretary will prepare a public service list containing the names and addresses of all persons, or their representatives, who are parties to this investigation upon the expiration of the period for filing entries of appearance.

Limited disclosure of business proprietary information (BPI) under an administrative protective order (APO) and BPI service list: Pursuant to § 207.7(a) of the Commission's rules, the Secretary will make BPI gathered in this final investigation available to authorized applicants under the APO issued in the investigation, provided that the application is made not later than twenty-one (21) days after the publication of this notice in the **Federal Register.** A separate service list will be maintained by the Secretary for those parties authorized to receive BPI under the APO.

Staff report: The prehearing staff report in this investigation will be placed in the nonpublic record on May 11, 1992, and a public version will be issued thereafter, pursuant to § 207.21 of the Commission's rules.

Hearing: The Commission will hold a hearing in connection with this investigation beginning at 9:30 a.m. on May 28, 1992, at the U.S. International Trade Commission Building. Requests to appear at the hearing should be filed in writing with the Secretary to the Commission on or before May 15, 1992. A nonparty who has testimony that may aid the Commission's deliberations may request permission to present a short statement at the hearing. All parties and nonparties desiring to appear at the hearing and make oral presentations should attend a prehearing conference to be held at 9:30 a.m. on May 20, 1992, at the U.S. International Trade Commission Building. Oral testimony and written materials to be submitted at the public hearing are governed by §§ 201.6(b)(2), 201.13(f), and 207.23(b) of the Commission's rules.

Written submissions: Each party is encouraged to submit a prehearing brief to the Commission. Prehearing briefs must conform with the provisions of § 207.22 of the Commission's rules; the deadline for filing is May 21, 1992. Parties may also file written testimony in connection with their presentation at the hearing, as provided in § 207.23(b) of the Commission's rules, and posthearing briefs, which must conform with the provisions of § 207.24 of the Commission's rules. The deadline for filing posthearing briefs in June 5, 1992; witness testimony must be filed no later than three (3) days before the hearing. In addition, any person who has not entered an appearance as a party to the investigation may submit a written statement of information pertinent to the subject of the investigation on or before June 5, 1992. All written submissions must conform with the provisions of § 201.8 of the Commission's rules; any submissions that contain BPI must also conform with the requirements of §§ 201.6, 207.3, and 207.7 of the Commission's rules.

In accordance with §§ 201.16(c) and 207.3 of the rules, each document filed by a party to the investigation must be served on all other parties to the investigation (as identified by either the public or BPI service list), and a certificate of service must be timely filed. The Secretary will not accept a document for filing without a certificate of service.

Authority: This investigation is being conducted under authority of the Tariff Act of 1930, title VII. This notice is published pursuant to § 207.20 of the Commission's rules.

By order of the Commission.

Issued: March 20, 1992.

Stephen McLaughlin,

Acting Secretary.

[FR Doc. 92-6945 Filed 3-25-92; 8:45 am]

BILLING CODE 7020-02-M

[Investigation No. 332-317]

Economy-Wide Modeling of the Economic Implications of a FTA With Mexico and a NAFTA With Canada and Mexico; Hearing

AGENCY: United States International Trade Commission.

ACTION: Cancellation of hearing.

SUMMARY: On October 28, 1991, following receipt of a request from the U.S. Trade Representative (USTR), the Commission instituted Investigation No. 332-317, under section 332(g) of the

[1] For purposes of this investigation, "softwood lumber" means coniferous wood sawn or chipped lengthwise, sliced or peeled, whether or not planed, sanded or finger-jointed, of a thickness exceeding 6 mm, provided for in subheading 4407.10.00 of the HTS; and coniferous wood siding, flooring and other goods (except coniferous wood moldings and wood dowel rods; but including strips and friezes for parquet flooring, not assembled) continuously shaped (tongued, grooved, rebated [rabbeted], chamfered, V-jointed, beaded, molded, rounded or the like) along any of its edges or faces, whether or not planed, sanded or finger-jointed, provided for in HTS subheadings 4409.10.10, 4409.10.20 and 4409.10.90.

Tariff Act of 1930. On February 4, 1992, the Commission scheduled a public hearing in connection therewith for March 26, 1992. On March 17, 1992, the Commission received notice of withdrawal from the only scheduled witness for the hearing scheduled for March 26, 1992. Therefore, the public hearing in connection with this investigation (scheduled to be held beginning at 9:30 a.m. on March 26, 1992, at the U.S. International Trade Commission Building, 500 E Street, SW., Washington DC), is cancelled.

EFFECTIVE DATE: March 20, 1992.

FOR FURTHER INFORMATION CONTACT: Edward Carroll (202–205–1819), Office of Public Affairs, U.S. International Trade Commission. Hearing impaired persons can obtain information on this study by contacting the Commission's TDD terminal on (202–205–1810).

By order of the Commission.

Dated: March 24, 1992.

Kenneth R. Mason,

Secretary.

[FR Doc. 92–7160 Filed 3–25–92; 8:45 am]

BILLING CODE 7020–02–M

INTERSTATE COMMERCE COMMISSION

[Finance Docket No. 32016]

Sioux & Western Railroad Co.—Construction Exemption—Charles County, Mo; Notice

AGENCY: Interstate Commerce Commission.

ACTION: Notice of exemption.

SUMMARY: Pursuant to 49 U.S.C. 10505, the Interstate Commerce Commission conditionally exempts from the prior approval requirements of 49 U.S.C. 10901 the construction by the Sioux & Western Railroad Company of approximately 2 miles of rail line between the Sioux Plant and a Union Pacific Railroad Company line in Charles County, MO.

DATES: The exemption will not become effective until the environmental process is completed. At that time, the Commission will issue a further decision addressing the environmental matters and establishing an effective date for the exemption, if appropriate. Petitions to reopen must be filed by April 15, 1992.

ADDRESSES: Send pleadings referring to Finance Docket No. 32016 to:

(1) Office of the Secretary, Case Control Branch, Interstate Commerce Commission, Washington, DC 20423.

(2) Petitioner's representative: John R. Molm, Esquire, Troutman, Sanders, Lockerman and Ashmore, 1400 Candler Building, 127 Peachtree Street, NE., Atlanta, GA 30303.

FOR FURTHER INFORMATION CONTACT: Joseph H. Dettmar, (202) 927–5660, (TDD for hearing impaired: (202) 927–5712.

SUPPLEMENTARY INFORMATION: Additional information is contained in the Commission's decision. To purchase a copy of the full decision, write to, call, or pick up in person from: Dynamic Concepts, Inc., room 2229, Interstate Commerce Commission Building, Washington, DC 20423. Telephone: (202) 289–4357/4359. (Assistance for the hearing impaired is available through TDD services (202) 927–5721.)

Decided: March 11, 1992.

By the Commission, Chairman Philbin, Vice Chairman McDonald, Commissioners Simmons, Phillips, and Emmett.

Sidney L. Strickland, Jr.,

Secretary.

[FR Doc. 92–7017 Filed 3–25–92; 8:45 am]

BILLING CODE 7035–01–M

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

[Docket No. 86–22]

Marijuana Scheduling Petition; Denial of Petition; Remand

AGENCY: Drug Enforcement Administration, Justice.

ACTION: Final order.

SUMMARY: This is a final order of the Administrator of the Drug Enforcement Administration (DEA) concluding the plant material marijuana has no currently accepted medical use and denying the petition of the National Organization for Reform of Marijuana Laws (NORML) to reschedule marijuana from Schedule I to Schedule II of the Controlled Substances Act.

EFFECTIVE DATE: March 26, 1992.

FOR FURTHER INFORMATION CONTACT: Office of Congressional and Public Affairs, 202–307–7363.

SUPPLEMENTARY INFORMATION:

Background

On December 21, 1989, the former Administrator of DEA, following rulemaking on the record, which included a hearing before an administrative law judge, issued a final order concluding the plant material marijuana has no currently accepted medical use, and denying the petition of NORML to reschedule marijuana from Schedule I to Schedule II of the Controlled Substances Act. 54 FR 63767. On April 26, 1991, the United States Court of Appeals for the District of Columbia Circuit remanded the matter to the Administrator for clarification of DEA's interpretation of the term "currently accepted medical use in treatment in the United States." *Alliance for Cannabis Therapeutics* v. *DEA*, 930 F.2d 936.

Following a review of the entire record in this matter, and a comprehensive re-examination of the relevant statutory standard, I conclude that marijuana has no currently accepted medical use and must remain in Schedule I. Further hearings are unnecessary since the record is extraordinarily complete, all parties had ample opportunity and wide latitude to present evidence and to brief all relevant issues, and the narrow question on remand centers exclusively on this Agency's legal interpretation of a statutorily-created standard.

Summary of the Decision

Does the marijuana plant have any currently accepted medical use in treatment in the United States, within the meaning of the Federal Controlled Substances Act, 21 U.S.C. 801, *et seq.*? Put simply, is marijuana good medicine for illnesses we all fear, such as multiple sclerosis (MS), glaucoma and cancer?

The answer might seem obvious based simply on common sense. Smoking causes lung cancer and other deadly diseases. Americans take their medicines in pills, solutions, sprays, shots, drops, creams and sometimes in suppositories, but never by smoking. No medicine prescribed for us today is smoked.

With a little homework, one can learn that marijuana has been rejected as medicine by the American Medical Association, the National Multiple Sclerosis Society, the American Glaucoma Society, the American Academy of Ophthalmology the American Cancer Society. Not one American health association accepts marijuana as medicine.

For the last half century, drug evaluation experts at the United States Food and Drug Administration (FDA) have been responsible for protecting Americans from unsafe and ineffective new medicines. Relying on the same scientific standards used to judge all other drugs, FDA experts repeatedly have rejected marijuana for medical use.

Yet claims persist that marijuana has medical value. Are these claims true, What are the facts?

Between 1987 and 1988, DEA and NORML, under the guidance of an administrative law judge, collected all relevant information on this subject. Stacked together it stands nearly five feet high. Is there reliable scientific evidence that marijuana is medically

effective. If it has medical value, do its benefits outweight its risks? What do America's top medical and scientific experts say? Would they prescribe it for their patients, their families, their friends?

As the current Administrator of Drug Enforcement, and as a former United States District Judge, I have made a detailed review of the evidence in this record to find the answers.

There are significant short-term side effects and long-term risks linked to smoking marijuana. Marijuana is likely to be more cancer-causing than tobacco; damages brain cells; causes lung problems, such as bronchitis and emphysema; may weaken the body's antibacterial defenses in the lungs; lowers overall blood pressure, which could adversely affect the supply of blood to the head; causes sudden drops in blood pressure (orthostatic hypotension), rapid heart beat (tachycardia), and heart palpitations; suppresses luteinizing hormone secretion in women, which affects the production of progesterone, an important female hormone; causes anxiety and panic in some users because of its mind-altering effects; produces dizziness, trouble with thinking, trougle with concentrating, fatigue, and sleepiness; and impairs motor skills.

As a plant, marijuana can contain bacteria capable of causing serious infections in humans, such as salmonella enteritidis, Klebsiella pneumoniae, group D Streptoccoccus and pathogenic aspergillus.

Several of these risk stand out. The immune systems of cancer patients are weakened by radiation and chemotherapy, leaving them susceptible to infection. If they experiment with marijuana to control nausea, they risk weakening their immune systems further and exposing themselves to the infection-causing bacteria in the plant. It is estimated, for example, that at Memorial Sloan-Kettering Cancer Center 60 patients die each year from pathogenic aspergillus infections.

Glaucoma patients face possible blindness caused by very high fluid pressures within their eyes. If they experiment with marijuana to lower their eye fluid pressure, it can cause dramatic drops in their blood pressure and reduce the blood supply to their heads. Glaucoma experts testified this reduced the blood supply to the optic nerves and could speed up, rather than slow down, their loss of eyesight.

MS, glaucoma and cancer patients who have undiagnosed heart problems risk heart palpitations, very rapid heart beats and sudden dramatic drops in blood pressure if they experiment with marijuana. For MS and glaucoma patients who must take medications for the rest of their lives, experimenting with marijuana poses the additional risks of lung cancer, emphysema, bladder cancer and leukemia.

Many risks remain unknown. Marijuana contains over 400 separately identified chemicals. No one knows all the effects of burning these chemicals together and inhaling the burnt mix. Are these risks outweighed by medical benefits?

There are scientific studies showing pure THC (Delta-9-Tetrahydrocannabinol), one of the many chemicals found in marijuana, has some effect in controlling nausea and vomiting. Pure THC is pharmaceutically made in a clean capsule form, called Marinol, and is available for use by the medical community. More information on Marinol can be found in the "Physicians' Desk Reference," available in most libraries.

Since marijuana contains THC, you might think marijuana also would be effective. However, the effect of taking a drug in combination with other chemicals is seldom the same as taking just the pure drug. As already noted, marijuana contains over 400 other chemicals, not just THC. There are no reliable scientific studies that show marijuana to be significantly effective in controlling nausea and vomiting. People refer to the Sallan study as proving marijuana's effectiveness. They are mistaken. The Sallan study involved pure THC, not marijuana. People refer to the Chang study to support marijuana's effectiveness. They also are mistaken. Doctor Chang tested the combination of pure THC and marijuana to treat nausea and vomiting. The preliminary results he got were probably due to the THC, not the marijuana. Because he tested the combination, we cannot tell just what effects can be attributed to marijuana alone. People cite a third study, done by Doctor Levitt, as proof marijuana is effective. They are mistaken. Doctor Levitt compared marijuana to THC in controlling nausea and vomiting, and he concluded that THC was the more effective drug.

A librarian can help locate copies of thes studies should you want to see them for yourself. Sallan, et al., "Antiemetic Effect of Delta-9-Tetrahydrocannibinol in Patients Receiving Cancer Chemotherapy," 293 New England Journal of Medicine 795–797 (1975); Chang, et al., "Delta-9-Tetrahydrocannabinol as an Antiemetic in Cancer Patients Receiving High-Dose Methotrexate," 91 Annals of Internal Medicine 819–824 (1979); Levitt, et al., "Randomized Double Blind Comparison of Delta-9-Tetrahydrocannabinol (THC) and Marijuana As Chemotherapy Antiemetics," (Meeting Abstract) 3 Proceedings of the Annual Meeting of the American Society of Clinical Oncology 91 (1984).

During the 1970's and 1980's, a number of states set up research programs to give marijuana to cancer and glaucoma patients, on the chance it might help. Some people point to these programs as proof of marijuana's usefulness. Unfortunately, all research is not necessarily good scientific research. These state programs failed to follow responsible scientific methods. Patients took marijuana together with their regular medicines, so it is impossible to say whether marijuana helped them. Observations or results were not scientifically measured. Procedures were so poor that much critical research data were lost or never recorded. Although these programs were well-intentioned, they are not scientific proof of anything.

Some people refer to a study by Doctor Thomas Ungerleider as proof marijuana reduced nausea in bone marrow transplant patients. Unfortunately, Doctor Ungerleider neglected to follow responsible scientific methods in his study. Like the state programs, it proves nothing. Doctor Ungerleider chose not to publish his study evidently because of its serious weaknesses. He admitted as much when questioned under oath.

Those who say there are reliable scientific studies showing marijuana is an effective drug for teating nausea and vomiting are wrong. No such studies exist.

Our nation's top cancer experts reject marijuana for medical use. Doctor David S. Ettinger, a professor of oncology at the Johns Hopkins University School of Medicine, an author of over 100 scholarly articles on cancer treatment, and a nationally respected cancer expert, testified:

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

Doctor Richard J. Gralla, a professor of medicine at Cornell University Medical College, an associate attending physician at the Memorial Sloan-Kettering Cancer Center, and an expert in cancer research, testified:

> Most experts would say, and our studies support, that the cannabinoids in general are not very effective against the major causes of nausea and vomiting.

Doctor Gralla added:

I have found that because of the negative side effects and problems associated with marijuana * * *. most medical oncologists and researchers have little interest in marijuana for the treatment of nausea and vomiting in their patients.

Doctor John Laszlo, Vice President of Research for the American Cancer Society, an expert who has spent 37 years researching cancer treatments, and who has written a leading textbook on the subject, "Antiemetics and Cancer Chemotherapy," testified there is not enough scientific evidence to justify using marijuana to treat nausea and vomiting. Not one nationally-recognized cancer expert could be found to testify on marijuana's behalf.

To be an effective treatment for glaucoma, a drug must: (i) Lower the pressure within the eye (intraocular pressure), (ii) for prolonged periods of time, and (iii) actually preserve sight (visual fields). Five scientific studies are cited as evidence marijuana is an effective glaucoma treatment. Those who cite these studies are mistaken. These studies tested pure THC, not marijuana. W.D. Purnell and J.M. Gregg, "Delta-9-Tetrahydorcannabinol, Euphoria and Intraocular Pressure in Man," 7 Annals of Ophthalmology 921–923 (1975); M. Perez-Reyes, D. Wagner, M.E. Wall, and K.H. Davis, "Intravenous Administration of Cannabinoids on Intraocular Pressure," The Pharmacology of Marijuana 829–832 (M.C. Braude and S. Szara eds. 1976); J.C. Merritt, S.M. McKinnon, J.R. Armstrong, G. Hatem, and L.A. Reid, "Oral Delta-9-Tetrahydrocannabinol in Hyperogeneous Glaucomas," 12 Annals of Ophthalmology 947 (1980); K. Green and M. Roth, "Ocular Effects of Topical Administration of Delta-9-Tetrahydrocannabinol in Man," 100 Archives of Ophthalmology 265–267 (1982); and W.M. Jay and K. Green, "Multiple-Drop Study of Topically Applied 1% Delta-9-Tetrahydrocannabinol in Human Eyes," 101 Archives of Ophthalmology 591–593 (1983).

Threee studies show very heavy doses of marijuana, taken for short periods of time, can reduce eye pressure. R.S. Hepler, I.M. Frank, and T.J. Ungerleider, "Pupillary Constriction After Marijuana Smoking," 74 American Journal of Ophthalmology 1185–1190 (1972); R.S. Hepler, I.M. Frank, and R. Petrus, "Ocular Effects of Marijuana Smoking," The Pharmacology of Marijuana 815–824 (1976); and J.C. Merritt, W.J. Crawford, P.C. Alexander, A.L. Anduze and S.S. Gelbart, "Effect of Marijuana on Intraocular and Blood Pressure in Glaucoma," 87 Ophthalmology 222–228 (1980)

Unusally large doses or marijuana were needed in these three studies to achieve the desired effect. Heavy marijuana use produces dizziness, trouble with thinking, impaired motor skills, fatigue and sleepiness. The 1976 study by Doctors Hepler, Frank and Petrus emphasized "Our subjects were sometimes too sleepy to permit measurement of intraocular pressures * * * 3 hours after intoxication." If a glaucoma patient were to smoke marijuana 8 to 10 times every day for the rest of his life, would he be alert and energetic enough to live a relatively normal life? Would he develop other diseases? No scientific studies exist to answer these questions. Robert Randall claims to have saved his sight by smoking 8 to 10 marijuana cigarettes every day. Under oath he admits he stays at home most days, follows no daily schedule or routine, and has not held a regular job in over 15 years. He also has avoided having a comprehensive medical examination since 1975.

No scientific studies have shown marijuana can reduce eye pressure over long periods of time.

No scientific studies have shown marijuana can save eyesight.

America's top glaucoma experts reject marijuana as medicine. Doctor Keith Green is a professor of Ophthalmology who serves, or has served, on the editorial boards of eight prestigious eye journals (Ophthalmic Research, Oftalmo Abstracto, Current Eye Research, Experimental Eye Research, Investigative Opthalmology, American Journal of Ophthalmology, Archives of Ophthalmology, and Survey of Ophthalmology). Doctor Green has conducted extensive basic and clinical research using marijuana and THC to treat glaucoma patients. He has authored over 200 books or research articles in ophthalmology and is a highly respected expert on this subject. Doctor Green testified:

There is no scientific evidence * * * that indicates that marijuana is effective in regulating the progression of symptoms associated with glaucoma. * * * It is clear that there is no evidence that marijuana use prevents the progression of visual loss in glaucoma. * * * The quantities of the drug required to reduce intraocular pressure in glaucoma sufferers are large, and would require the inhalation of at least six marijuana cigarettes each day. * * * Smoking is not a desirable form of treatment for many reasons * * * [M]arijuana . . . has little potential future as a glaucoma medication.

Doctor George Spaeth is the Director of the Glaucoma Service at Wills Eye Hospital in Philadelphia, the largest service in the United States devoted to researching and treating glaucoma and to teaching other doctors about this disease. Doctor Spaeth is President of the American Glaucoma Society. He is a professor of ophthalmology, the editor of a scholarly eye journal (Ophthalmic Surgery), and the author of over 200 research articles on glaucoma. He testified:

I have not found any documentary evidence which indicates that a single patient has had his or her natural history of the disease altered by smoking marijuana.

Amputees and victims of MS can suffer from extreme muscle spasms. It is claimed marijuana is useful in treating spasticity. Three unusually small, inconclusive studies have tried using pure THC, not marijuana, to treat spasticity. D.J. Petro and C. Ellenberger, "Treatment of Human Spasticity with Delta-9-Tetrahydro-cannabinol," 21 Journal of Clinical Pharmacology 413S–416S (1981) (included only nine patients). Two of the studies are mere abstracts, or short digests, without much detail. Hanigan, Destee & Troung Abstr. B45, Clin. Pharmacol. Ther. 198 (1986) (included only five patients), and Sandyk, Cannoe, Stern and Snider Abstr. PP 331, 36 Neurology 342 (1986) (included only three patients).

No scientific studies exist which test marijuana to relieve spasticity.

National experts on MS reject marijuana as medicine. Doctor Kenneth P. Johnson is Chariman of the Department of Neurology at the University of Maryland School of Medicine. He manages that Maryland Center for MS, one of the most active MS research and treatment centers in the United States. He sits on the editiorial boards of noted medical journals related to MS (Neurology and Journal of Neuroimmunology). He is the author of over 100 scientific and medical articles on MS. Doctor Johnson has spent most of his long career researching MS and has diagnosed and treated more than 6,000 patients with MS. Doctor Johnson testified:

At this time, I am not aware of * * * any legitimate medical research in which marijuana was used to treat the symptoms of multiple sclerosis. * * * To conclude that marijuana is therapeutically effective without conducting rigorous testing would be professionally irresponsible.

Doctor Stephen Reingold is Assistant Vice President of Research for the National Multiple Sclerosis Society, which spends over $7 million each year

on MS research. Only the Federal Government spends more. Doctor Reingold testified:

> I could find no actual published research which has used marijuana * * * In the existing research using THC, the results were inconclusive * * * In the absence of any well-designed, well-controlled research * * *, the National Multiple Sclerosis Society * * * does not endorse or advocate its use * * *.

Doctor Donald H. Silberberg is Chairman of the Department of Neurology at the University of Pennsylvania School of Medicine and Chief of the Neurology Service at the Hospital of Pennsylvania. Doctor Silberberg is on the editorial board of Annals of Neurology and is President of the National Medical Advisory Board for the National Multiple Sclerosis Society. He has been actively researching and treating MS for most of his career, has written over 130 medical articles on MS and is Co-Director of a large MS research center at the University of Pennsylvania. Doctor Silberberg testified:

> I have not found any legitimate medical or scientific works which show that marijuana * * * is medically effective in treating multiple sclerosis or spasticity. * * * The long-term treatment of the symptoms of multiple sclerosis through the use of marijuana could be devastating. * * * [T]he use of (marijuana), especially for long-term treatment * * * would be worse than the original disease itself.

The only favorable evidence that could be found by NORML and DEA consists of stories by marijuana users who claim to have been helped by the drug. Scientists call these stories anecdotes. They do not accept them as reliable proofs. The FDA's regulations, for example, provide that in deciding whether a new drug is a safe and effective medicine, "isolated case reports * * * will not be considered.' 21 CFR 314.126(e). Why do scientists consider stories from patients and their doctors to be unreliable?

First, sick people are not objective scientific observers, especially when it comes to their own health. We all have heard of the placebo effect. Patients have a tendency to respond to drugs as they believe is expected of them. Imagine how magnified this placebo effect can be when a suffering person experiments on himself, praying for some relief. Many stories no doubt are due to the placebo effect, not to any real medical effects of marijuana.

Second, most of the stories come from people who took marijuana at the same time they took prescription drugs for their symptoms. For example, Robert Randall claims marijuana has saved his sight, yet he has taken standard glaucoma drugs continuously since 1972. There is no objective way to tell from these stories whether it is marijuana that is helpful, or the proven, traditional medicines. Even these users can never know for sure.

Third, any mind-altering drug that produces euphoria can make a sick person think he feels better. Stories from patients who claim marijuana helps them may be the result of the mind-altering effects of the drug, not the results of improvements in their conditions.

Fourth, long-time abusers of marijuana are not immune to illness. Many eventually get cancer, glaucoma, MS and other diseases. People who become dependent on mind-altering drugs tend to rationalize their behavior. They invent excuses, which they can come to believe, to justify their drug dependence. Stories of marijuana's benefits from sick people with a prior history of marijuana abuse may be based on rationalizations caused by drug dependence, not on any medical benefits caused by the drug. Robert Randall, for example, admits under oath to becoming a regular user in 1968, four years before he showed the first signs of, and was diagnosed as having, glaucoma. Since then he has smoked marijuana 8 to 10 times every day.

A century ago many Americans relied on stories to pick their medicines, especially from snake oil salesmen. Thanks to scientific advances and to the passage of the Federal Food, Drug and Cosmetic Act (FDCA) in 1906, 21 U.S.C. 301 *et seq.*, we now rely on rigorous scientific proof to assure the safety and effectiveness of new drugs. Mere stories are not considered an acceptable way to judge whether dangerous drugs should be used as medicines

There are doctors willing to testify that marijuana has medical uses NORML found over a dozen to testify in this case. We have a natural tendency to believe doctors. We assume their opinions are entitled to respect. But what if a doctor is giving an opinion beyond his professional competence? Evaluating the safety and effectiveness of drugs is a specialized area. Does the doctor have this specialized expertise? Is he familiar with all the published scientific studies? Or is he improperly basing his opinion on mere stories or anecdotal evidence? Does he really know what he is talking about? Does he have a personal motive to exaggerate or lie? Questions like these led the United States Supreme Court, in 1973, to warn about the opinions of doctors concerning the value of drugs as medicine, when not supported by rigorous scientific testing. *Weinberger* v. *Hynson, Etc.*, 412 U.S. 609, 639:

> [I]mpressions or beliefs of physicians, no matter how fervently held, are treacherous.

Nearly half the doctors who testified for NORML are psychiatrists. They do not specialize in treating or researching cancer, glaucoma or MS. One is a general practitioner who works as a wellness counselor at a health spa. Under oath he admits to using every illegal, mind-altering drug he has ever studied, and he prides himself on recommending drugs that would never be recommended by medical schools or reputable physicians. Another is a general practitioner who quit practicing in 1974. He admits he has not kept up on new medical and scientific information about marijuana for 18 years.

Only one of the doctors called by NORML is a nationally-recognized expert. Doctor John C. Merritt is a board-certified ophthalmologist and researcher who has authored articles on the use of marijuana and cannabinoids to reduce eye pressure. He is in private practice and sees mostly children who suffer from glaucoma. Doctor Merritt testified, "[M]arijuana is a highly effective IOP-lowering drug which may be of critical value to some glaucoma patients who, without marijuana, would progressively go blind." The last scientific study using marijuana in glaucoma patients, published by Doctor Merritt in 1979, concluded:

> It is because of the frequency and severity with which the untoward events occurred that marijuana inhalation is not an ideal therapeutic modality for glaucoma patients.

One year later, in 1980, Doctor Merritt gave the following testimony, under oath, before the United States Congress, House Select Committee on Narcotics Abuse and Control:

> For me to sit here and say that the lowering pressure effects occurred repeatedly, day in and day out, I have no data, and neither does anyone else, and that is the real crux of the matter. When we are talking about treating a disease like glaucoma, which is a chronic disease, the real issue is, does the marijuana repeatedly lower the intraocular pressure? I have shown you no * * * studies, and to my knowledge there is no data to that effect.

Doctor Merritt was unable to explain, under oath, the contradictory positions he has taken on this subject.

Each of NORML's doctors testified his opinion is based on the published scientific studies. With one exception, none of them could identify under oath the scientific studies they swore they relied on. Only one had enough knowledge to discuss the scientific technicalities involved. Eventually, each

one admitted he was basing his opinion on anecdotal evidence, on stories he heard from patients, and on his impressions about the drug.

Sadly, Doctor Ivan Silverberg, an oncologist from San Francisco, exaggerated while on the witness stand. At first he swore "there is voluminous medical research which shows marijuana is effective in easing nausea and vomiting." Pushed on cross-examination to identify this voluminous research, Doctor Silverberg replied, "Well * * *, I'm going to have to back off a little bit from that." How far would Doctor Silverberg back off? Was he aware, at least, of the approximate number of scientific studies that have been done using marijuana to treat nausea? Under oath, he replied, "I would doubt very few. But, no, I'm not."

Beyond doubt, the claims that marijuana is medicine are false, dangerous and cruel.

Sick men, women and children can be fooled by these claims and experiment with the drug. Instead of being helped, they risk serious side effects. If they neglect their regular medicines while trying marijuana, the damage could be irreversible. It is a cruel hoax to offer false hope to desperately ill people.

Those who insist marijuana has medical uses would serve society better by promoting or sponsoring more legitimate scientific research, rather than throwing their time, money and rhetoric into lobbying, public relations campaigns and perennial litigation.

Clarification of Currently Accepted Medical Use

The Controlled Substances Act of 1970 divides the universe of all durgs of abuse into five sets or schedules. Drugs in Schedule I are subject to the most severe controls, because they have a high potential for abuse and no currently accepted medical use in treatment in the United States. 21 U.S.C. 812 (b)(1). Drugs of abuse which have currently accepted medical use in treatment in the United States are placed in Schedules II, III, IV and V. Regrettably, the Controlled Substances Act does not speak directly to what is meant by "currently accepted medical use."

A century before the Controlled Substances Act was enacted, the determination of what drugs to accept as medicine was totally democratic and totally standardless. Each patient and each physician was free to decide for himself, often based on no more than anecdotal evidence. This state of affairs became unsatisfactory to a majority of the American people. In 1906, Congress intervened with the passage of the Food, Drug and Cosmetic Act (FDCA). A shift began away from anecdotal evidence to objectively conducted scientific research, away from uninformed opinions of lay persons and local doctors to expert opinions of specialists trained to evaluate the safety and effectiveness of drugs, and away from totally democratic decision-making to oversight by the Federal Government.

By 1969, Congress had developed detailed Federal statutory criteria under the FDCA to determine whether drugs are acceptable for medical use. Those deemed acceptable can be marketed nationally. Those deemed unacceptable are subject to Federal seizure if marketed interstate. The FDCA is a very complex regulatory scheme not easily summarized. However, it is fair to say that drugs falling into one of four FDCA categories were accepted by Congress for medical use.

First, Congress accepted new drugs which have been approved by FDA's experts as safe and effective for use in treatment, based on substantial scientific evidence. 21 U.S.C. 321(p) and 355 (so-called "NDA-approved drugs").

Second, Congress accepted those drugs "generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective," based on substantial scientific evidence. 21 U.S.C. 321(p) and 355; *Weinberger* v. *Bentex Pharmaceuticals, Inc.*, 412 U.S. 645 (1973). An acronym for this category is "human GRASE drugs" (Generally Recognized As Safe and Effective). These drugs achieve acceptance through rigorous scientific proof, through a past history of widespread use in treatment in the United States, and through recognition by a consensus of drug experts outside the FDA.

Third, Congress accepted for use in veterinary medicine those drugs "generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of animal drugs, as safe and effective," based on substantial scientific evidence. 21 U.S.C. 321(w) and 355. An acronym for these is "animal GRASE drugs." They achieve acceptance through rigorous scientific evidence and through recognition by a consensus of drug experts outside the FDA. Unlike human GRASE drugs, animal GRASE drugs need not have a past history of widespread use.

Finally, Congress accepted those drugs marketed prior to 1938 which had been subject to the 1906 provisions of the FDCA, provided these very old drugs retain their exact formulations and are never promoted for new uses. 21 U.S.C. 321(p) and (w). These are politically "grandfathered" drugs. They need not meet modern standards for safety and effectiveness.

A fifth group of drugs was accepted for research use only, not for use in treatment of patients. 21 U.S.C. 355(i) (so-called "IND or approved investigational new drugs").

Drugs intended for medical use and shipped interstate are subject to Federal seizure under the FDCA if they do not fit within one of the above accepted sets or groupings. It seems fair to say that seizable drugs were rejected by Congress for medical uses.

In enacting the Controlled Substances Act in 1970, could Congress have intended to create a totally new Federal standard for determining whether drugs have accepted medical uses? Or did Congress intend to rely on standards it had developed over the prior 64 years under the FDCA? There is nothing in the Controlled Substances Act, its legislative history, or its purposes that would indicate Congress intended to depart radically from existing Federal law.

Indeed, it seems likely that the core standards developed under the FDCA represent a long-term consensus of expert medical and scientific opinion concerning when a drug should be accepted by anyone as safe and effective for medical use.

Fortunately, there is a way to corroborate what Congress intended. Congress did more than just announce criteria for scheduling drugs of abuse under the Controlled Substances Act; Congress applied those criteria to an initial listing of drugs that it placed into the original five schedules of the Act.

NDA-approved drugs were placed by Congress into Schedules II, III, IV and V of the Act. For example, pethidine (also known as meperidine) received New Drug Application (NDA) approval in 1942. Congress put it into Schedule II(b)(14). Methamphetamine had an approved NDA. Congress put it into Schedule III(a)(3). I am not aware of any drug with an approved NDA that Congress originally put into Schedule I.

Drugs with medical uses, but without approved NDA's also were placed by Congress into Schedules II, III, IV and V. For example, cocaine was put into Schedule II(a)(4). Codeine combinations were put into Schedules III(d)(1) and V. Morphine combinations were put into Schedule III(d)(8). Phenobarbital was put into Schedule IV(11). Barbiturates were put into Schedule III(b)(1). Amphetamines were put into Schedule III(a)(1).

The Court of Appeals for the First Circuit was correct when it decided in

Grinspoon v. *DEA*, 828 F.2d 881 (1987) that NDA approval is not the only method by which drugs can achieve Federal recognition as having medical uses. Congress put both GRASE drugs and pre-1938-grandfathered drugs into Schedules II, III, IV and V of the CSA.

Drugs recognized under the FDCA for research use only, not for use in treatment, such as alphacetylmethadol and marijuana, were placed by Congress into Schedule I.

Unfortunately, Federal records are not complete enough to do a comprehensive mathematical mapping, tracing every drug in the initial Controlled Substances Act schedules back to its legal status under the FDCA. Nevertheless, determining legislative intent does not require mathematical certainty. Probability based on circumstantial evidence, on samplings, and on inductive reasoning can suffice, especially when there is nowhere else to turn.

The pattern of initial scheduling of drugs in the Controlled Substance Act, viewed in light of the prior legal status of these drugs under the FDCA, convinces me that Congress equated the term "currently accepted medical use in treatment in the United States" as used in the Controlled Substances Act with the core FDCA standards for acceptance of drugs for medical use.

This is not to say that every FDCA requirement for GRASE status, or for NDA approval, is pertinent to scheduling determinations under the Controlled Substances Act. There are differences. But the core FDCA criteria appear to have guided the Congress in the decisions it made concerning the initial scheduling of drugs in the Act.

These same core FDCA criteria served as the basis for an eight-point test used by my predecessor as Administrator to describe drugs with currently accepted medical uses. 54 FR 53783 (December 29, 1989):

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

Some uncertainty remains over the precise meaning and application of parts of this test. Therefore, the Court of Appeals for the District of Columbia Circuit remanded these proceedings for a further explanation. In addition to addressing those parts of the test that concerned the Court of Appeals, it would be useful to clarify the entire test, pinpoint its origins, and identify which elements are both necessary and sufficient to establish a prima facie case of currently accepted medical use. This is not an effort to change the substantive law. The statutory meaning of currently accepted medical use remains the same as enacted by Congress in 1970. My purpose simply is to clarify this Agency's understanding of the law.

A. The Drug's Chemistry Must Be Known and Reproducible

The ability to recreate a drug in standardized dosages is fundamental to testing that drug and to using it as a medicine. Knowing the composition, properties, methods of production, and methods of analysis of a drug is essential to reproducing it in standardized dosages. To be GRASE or to receive NDA approval, a drug's chemistry must be known and reproducible. See *e.g.*, 21 CFR 314.50(d)(1) and 314.126(b)(7)(d); *Dorovic* v. *Richardson*, 749 F.2d 242, 251 (7th Cir. 1973). The listing of a drug in a current edition of one of the official compendia normally satisfies this requirement. 21 U.S.C. 321(j); 21 CFR 314.50(d)(1).

The first element of our eight-point test, namely, "scientifically determined and acccepted knowledge of its chemistry," should be clarified to read:

> The substance's chemistry must be scientifically established to permit it to be reproduced into dosages which can be standardized. The listing of the substance in a current edition of one of the official compendia, as defined by section 201(j) of the Food, Drug and Cosmetic Act, 21 U.S.C. 321(j), is sufficient generally to meet this requirement.

Acceptance of this knowledge will be discussed elsewhere.

B. There Must Be Adequate Safety Studies

No drug can be considered safe in the abstract. Safety has meaning only when judged against the intended use of the drug, its known effectiveness, its known and potential risks, the severity of the illness to be treated, and the availability of alternative therapies. *Hess & Clark Division of Rhodia, Inc.* v. *FDA*, 495 F.2d 975, 993 (D.C. Cir. 1974). To know the risks, there must be adequate studies, by all methods reasonably applicable, to show the pharmacological and toxicological effects of the drug. 21 CFR 314.125(b)(2). This includes animal studies and clinical trials in large numbers of humans. 21 CFR 312.21. The studies need not be well-controlled, but they must be adequate. *Edison Pharmaceuticals Co.* v. *FDA*, 600 F.2d 831 (D.C. Cir. 1979). Short term (acute) studies of a drug intended to treat long-term (chronic) illnesses, such as glaucoma or MS, are clearly inadequate. *United States* v. Naremco, Inc., 553 F.2d 1138, 1143 (8th Cir. 1977). The second element of our eight-point test, namely, "the toxicology and pharmacology of the substance in animals," should be clarified as follows:

> There must be adequate pharmacological and toxicological studies, done by all methods reasonably applicable, on the basis of which it could fairly and responsibly be concluded, by experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, that the substance is safe for treating a specific, recognized disorder.

It must be emphasized that while the existence of adequate safety tests is a separate analytical question, the ultimate determination of whether a drug is safe for a specific use is not a distinct issue. Safety and effectiveness are inextricably linked in a risks-benefits calculation. A determination that a drug is ineffective is tantamount to a determination that it is unsafe. *United States* v. *Rutherford*, 442 U.S. 544 (1970).

The scheduling criteria of the Controlled Substances Act appear to treat the lack of medical use and lack of safety as separate considerations. Prior rulings of this Agency purported to treat safety as a distinct factor. 53 FR 5156 (February 22, 1988). In retrospect, this is inconsistent with scientific reality. Safety cannot be treated as a separate analytical question.

C. There Must Be Adequate and Well-Controlled Studies Proving Efficacy

Since 1962, Congress has prohibited the FDA to approve an NDA unless the applicant submits adequate, well-contolled, well-designed, well-conducted, and well-documented studies, performed by qualified investigators, which prove the efficacy of a drug for its intended use. 21 U.S.C. 355(d); 21 CFR 314.126. Similarly, a drug cannot be considered GRASE unless it is supported by this same quantity and quality of scienfitic proof. 21 CFR 314.200(e)(i); *Weinberger* v. *Hynson, Etc.*, 412 U.S. 609, 629 (1973).

Studies involving related, but not identical, drugs are irrelevant. *United States* v. *Articles of Food & Drug*, 518 F.2d 743, 747 (5th Cir. 1975). Studies involving the same drug combined with other drugs are irrelevant. *United States* v. *Articles of Drug * * * Promise Toothpaste, 826 F.2d 564, 570 (7th Cir. 1987). Incomplete studies are insufficient. United States* v. *Articles of Food & Drug, supra.* Uncontrolled studies are insufficient. 21 U.S.C. 355(d); *Cooper Labs* v. *FDA*, 501 F.2d 772, 778 (D.C. Cir. 1974). Statistically insignificant studies are insufficient. 21 CFR 312.21, 314.50(d)(6) and 314.126(b)(7). Poorly designed studies are insufficient. 21 CFR 314.126(b)(2). Poorly conducted studies are insufficient. 21 CFR part 58—Good Laboratory Practices. Poorly documented studies are insufficient. 21 CFR 312.58 and 314.200(e)(4). Studies by investigators who are not qualified, both to conduct and to evaluate them are insufficient. 21 U.S.C. 355(d). Moreover, since scientific reliability requires a double examination with similar results, one valid study is insufficient. There must be two or more valid studies which corroborate each other. See 1 J. O'Reilley "Food and Drug Administration" 13–55 n.12 (1985).

Lay testimonials, impressions of physicians, isolated case studies, random clinical experience, reports so lacking in details they cannot be scientifically evaluated, and all other forms of anecdotal proof are entirely irrelevant. 21 CFR 314.126(e); *Weingerger* v. *Hynson, Etc.*, 412 U.S. 609, 630 (1973).

Element three of our eight-point test, namely, "establishment of its effectiveness in humans through scientifically designed clinical trials," should be restated as:

> There must be adequate, well-controlled, well-designed, well-conducted and well-documented studies, including clinical investigations, by experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, on the basis of which it could fairly and responsibly be concluded by such experts that the substance will have the intended effect in treating a specific, recognized disorder.

D. Acceptance by Qualified Experts Is Required

The opinions of lay persons are totally irrelevant to whether a drug is GRASE or meets NDA requirements. The observations and opinions of medical practioners who are not experts in evaluating drugs also are irrelevant to whether a drug is GRASE or meets NDA requirements. *Weinberger* v. *Hynson, Etc.*, 412 U.S. 609, 619 (1973). By explicit requirements in the FDCA since 1938, the only body of opinion that counts is that of experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs. 21 U.S.C. 321 (p) and (w).

From this, one would conclude that expert acceptance of a drug as safe and effective for its intended use is essential to a drug having a currently accepted medical use under the CSA. How widespread must this expert acceptance be?

To be GRASE, a drug must be "generally recognized" among experts as safe and effective for its intended use. The drug must be known or familiar to the national community of relevant experts. *United States* v. *Articles of Drug* * * *Furestrol Vaginal Suppositories*, 294 F. Supp. 1307, 1309 (N.D. Ga. 1968) *aff'd*, 415 F.2d 390 (5th Cir. 1969). To determine if a drug is known to the community of experts, courts have looked to whether there is widely available scientific literature about the drug, *Premo Pharmaceutical Laboratories, Inc.* v. *United States*, 629 F.2d 795, 803 (2d Cir. 1980), whether it is widely taught in medical schools, *Lemmon Pharmaceuticals Co.* v. *Richardson*, 319 F. Sup. 375, 378 (E.D. Pa. 1970), and whether it is widely discussed by experts. *United States* v. *Bentex Ulcerine*, 469 F. 2d 875, 880 (5th Cir. 1972).

The recognition of a drug as GRASE need not be universal. General recognition is sufficient. *United States* v. *41 Cartons* * * *Ferro-Lac*, 420 F.2d 1126, 1132 (5th Cir. 1970). The Supreme Court has interpreted this to mean a consensus of experts is familiar with and accepts a drug as safe and effective. *Weinberger* v. *Hynson, Etc.*, 412 U.S. 609, 629 (1973). However, if there is a serious dispute among the experts, a drug cannot be considered GRASE. *United States* v. *An Article of Food* * * *Coco Rico*, 752 F.2d 11, 15 (1st Cir. 1985); *Merrit Corp.* v. *Folsom*, 165 F. Supp. 418, 421 (D.D.C. 1958).

During the NDA process, the FDA may reach out to the expert community for its views. 21 CFR 314.103(c)(3). The FDA need not determine that a drug is generally known and accepted by the expert community. Nor must the FDA develop a consensus of opinion among outside experts. The FDA has both the experts and the statutory mandate to resolve conflicts over the safety and efficacy of new drugs. *Weinberger* v. *Bentex Pharmaceuticals, Inc.*, 412 U.S.C 638, 653 (1973).

In drafting the Controlled Substances Act, Congress appears to have accommodated, rather than chosen from these different FDCA standards. Clearly, the Controlled Substances Act does not authorize the Attorney General, nor by delegation the DEA Administrator, to make the ultimate medical and policy decision as to whether a drug should be used as medicine. Instead, he is limited to determing whether others accept a drug for medical use. Any other construction would have the efect of reading the word "accepted" out of the statutory standard. Since Congress recognized NDA-approved drugs as having currently accepted medical uses, without any need for a national consensus of experts, FDA acceptance of a drug through the NDA process would seem to satisfy the Controlled Substances Act. And, since Congress recognized GRASE drugs as having currently accepted medical uses, without the need for NDA approval, acceptance of a drug by a national consensus of experts also would seem to satisfy the Act.

When a drug lacks NDA approval and is not accepted by a consensus of experts outside FDA, it cannot be found by the Attorney General or his delegate to have a currently accepted medical use. To do so would require the Attorney Genral to resolve complex scientific and medical disputes among experts, to decide the ultimate medical policy question, rather than merely determine whether the drug is accepted by others.

Because the recognition of a drug by non-experts is irrelevant to GRASE status, to NDA approval, and to currently accepted medical use under the Controlled Substances Act, points seven and eight of our eight-point test should be combined and restated as follows:

> The drug has a New Drug Application (NDA) approved by the Food and Drug Administration pursuant to the Food, Drug and Cosmetic Act, 21 U.S.C. 355. Or, a consensus of the national community of experts, qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, accepts the safety and effectiveness of the substance for use in treating a specific, recognized disorder. A material conflict of opinion among experts precludes a finding of consensus.

This restatement also incorporates the component of part one of our eight-point test concerning "accepted knowledge of its chemistry."

E. The Scientific Evidence Must Be Widely Available

Nothing in the FDCA, nor in FDA's regulations, requires that scientific evidence supporting an NDA be published. This stems from the fact that a consensus of experts outside FDA is

not required for NDA approval. In contrast, most courts have held that a drug cannot be considered GRASE unless the supporting scientific evidence appears in the published scientific and medical literature. Without published studies, it would be difficult for the community of experts outside FDA to develop an informed acceptance of a drug for medical use. *Cooper Labs Inc. v. FDA*, 501 F.2d 772, 786 (D.C. Cir. 1974).

Point four of the eight-point test focuses, in part, on the "general availability of information regarding the substance and its use." This should be clarified to read:

> In the absence of NDA approval, information concerning the chemistry, pharmacology, toxicology and effectiveness of the substance must be reported, published, or otherwise widely available, in sufficient detail to permit experts, qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, to fairly and responsibly conclude the substance is safe and effective for use in treating a specific, recognized disorder.

F. General Availability of a Drug Is Irrelevant

The second component of point four of the eight--point test involves the "general availability of the substance" for use in treatment. The second component of point eight focuses on "use of the substance by a substantial segment of the medical practitioners in the United States." These elements justifiably concerned the Court of Appeals, leading to the remand in this case.

Under the FDCA, a human GRASE drug must have a material history of past use in treatment in the United States. 21 U.S.C. 321(p)(2) (which has * * *, otherwise than in such investigations, been used to a material extent or a material time); *Weinberger v. Hynson, Etc.*, 412 U.S. 609, 631 (1973). Rigorous scientific proofs and current unanimous acceptance by the medical and scientific community are not enough for a human drug to be GRASE. *Tri-Bio Labs. Inc. v. United States*, 836 F.2d 135, 142 n.8 (3d Cir. 1987). The general availability of a drug for use in treatment is a factor courts have considered to determine if a human drug is GRASE.

In contrast, a drug can achieve current acceptance for human medical use through the NDA process without a past history of use in treatment. Also, animal drugs can become accepted as GRASE without any past history of medical use. Given this conflict in FDCA standards, which did Congress choose when drafting the CSA?

As the Court of Appeals points out, requiring a material history of past use in treatment before recognizing a drug as having a currently accepted medical use, would permanently freeze all Schedule I drugs into Schedule I. 930 F.2d at 940. Clearly, Congress did not intend this result. Moreover, the use of the word "currently" before the term "accepted medical use" would indicate Congress rejected the human GRASE requirement of past material use in treatment. I conclude that the general availability of a drug is irrelevant to whether it has a currently accepted medical use in treatment within the meaning of the Controlled Substances Act.

G. Recognition in Generally Accepted Texts Is Irrelevant

Point five of the eight-point test deals with "recognition of its clinical use in generally accepted pharmacopeia, medical references, journals or textbooks." The listing of a drug in an official compendium is sufficient to show its chemistry is scientifically established. This appears in my clarification to point one. The requirement that information concerning the chemistry, pharmacology, toxicology and effectiveness of the substance be reported, published or otherwise widely available, is explained adequately in revised point four. To the extent the scheduling of a drug directly influences its recognition in publications, this element is subject to the same criticism identified by the Court of Appeals concerning point four. Therefore, this should not be treated as a distinct requirement.

H. Specific, Recognized Disorders Are the Referent

It is impossible to judge the safety and effectiveness of a drug except in relation to a specific intended use. A drug cannot obtain NDA approval or GRASE status except in relation to the treatment of a specific, recognized disorder. This is an essential aspect of whether a drug has currently accepted medical use. Rather than standing alone, this requirement will be more clearly understood by incorporating it into the other critical elements.

To summarize, the five necessary elements of a drug with currently accepted medical use in treatment in the United States are:

(i) The Drug's Chemistry Must Be Known and Reproducible

> The substance's chemistry must be scientifically established to permit it to be reproduced into dosages which can be standardized. The listing of the substance in a current edition of one of the official compendia, as defined by section 201(j) of the Food, Drug and Cosmetic Act, 21 U.S.C. 321(j), is sufficient generally to meet this requirement.

(ii) There Must Be Adequate Safety Studies

> There must be adequate pharmacological and toxicological studies done by all methods reasonably applicable on the basis of which it could fairly and responsibly be concluded, by experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, that the substance is safe for treating a specific, recognized disorder.

(iii) There Must Be Adequate and Well-Controlled Studies Proving Efficacy

> There must be adequate, well-controlled, well-designed, well-conducted and well-documented studies, including clinical investigations, by experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs on the basis of which it could fairly and responsibly be concluded by such experts, that the substance will have its intended effect in treating a specific, recognized disorder.

(iv) The Drug Must Be Accepted by Qualified Experts

> The drug must have a New Drug Application (NDA) approved by the Food and Drug Administration, pursuant to the Food, Drug and Cosmetic Act, 21 U.S.C. 355. Or, a consensus of the national community of experts, qualified by scientific training and experience to evaluate the safety and effectivenss of drugs, must accept the safety and effectiveness of the substance of use in treating a specific, recognized disorder. A material conflict of opinion among experts precludes a finding of consensus.

(v) The Scientific Evidence Must Be Widely Available

> In the absence of NDA approval, information concerning the chemistry, pharmacology, toxicology and effectiveness of the substance must be reported, published, or otherwise widely available in sufficient detail to permit experts, qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, to fairly and responsibly conclude the substance is safe and effective for use in treating a specific, recognized disorder.

Together these five elements constitute prima facie evidence that a drug has currently accepted medical use in treatment in the United States. In the interest of total clarity, let me emphasize those proofs that are irrelevant to the determination of currently accepted medical use, and that will not be considered by the Administrator:

(i) Isolated case reports;

(ii) Clinical impressions of practitioners;

(iii) Opinions of persons not qualified by scientific training and experience to evaluate the safety and effectiveness of the substance at issue;

(iv) Studies or reports so lacking in detail as to preclude responsible scientific evaluation;

(v) Studies or reports involving drug substances other than the precise substance at issue;

(vi) Studies or reports involving the substance at issue combined with other drug substances;

(vii) Studies conducted by persons not qualified by scientific training and experience to evaluate the safety and effectivness of the substance at issue;

(viii) Opinions of experts based entirely on unrevealed or unspecified information;

(ix) Opinions of experts based entirely on theoretical evaluations of safety or effectiveness.

Bad Medicine By Any Standard

My predecessor as DEA Adminstrator developed and relied upon an eight-point test to determine whether marijuana has accepted medical uses. 54 FR 53783 (December 29, 1989):

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

The Court of Appeals remanded the decision of my predecessor for clarification of what role factors (4), (5) and (8) of the initial eight-point test played in his reasoning. For ease of discussion, these factors can be divided as follows:

(4)(a) General availability of the substance * * *;

(4)(b) General availability of * * * information regarding the substance and its use;

(5) Recognition of its clinical use in generally accepted pharmacopeia, medical references, journals or textbooks;

(8)(a) Recognition * * * of the substance by a substantial segment of the medical practitioners in the United States; and

(8)(b) [U]use of the substance by a substantial segment of the medical practitioners in the United States.

I have found no evidence indicating initial factors (4)(a) or (8)(b) played any role in my predecessor's decision. In light of my understanding of the legal standard involved, these factors are irrelevant to whether marijuana has a currently accepted medical use.

My predecessor emphasized the lack of scientific evidence of marijuana's effectiveness, and the limited data available on its risks, as reflected in the published scientific studies. He also emphasized the importance of this data to the conclusions reached by experts concerning the drug. 54 FR 53783. I take this to mean that, under initial factor (4)(b), he believed the information available to experts is insufficient for them responsibly and fairly to conclude the marijuana is safe and effective for use as medicine.

Marijuana is not recognized as medicine in generally accepted pharmacopeia, medical references and textbooks, as noted by my predecessor. 54 FR 53784. I take this to mean, under initial factor (5), that he determined that marijuana's chemistry is neither known, nor reproducible, as evidenced by its absence from the official pharmacopeia. Finally, my predecessor concluded, under initial factor (8)(a), that the vast majority of physicians does not accept marijuana as having medical use. 54 FR 53784. Along the way, he found that highly respected oncologists and antiemetic researchers reject marijuana for use in controlling nausea and vomiting, 54 FR 53777, that experts experienced in researching glaucoma medications reject marijuana for use in treating glaucoma, 54 FR 53779, and that noted neurologists who specialize in treating and conducting research in spasticity reject marijuana for use by MS patients, 54 FR 53780. I take this to mean my predecessor found no national consensus of qualified experts accepts marijuana's value as medicine.

Certainly I cannot know my predecessor's unstated reasoning. However, I have reviewed the entire record *de novo*, and I am convinced that his application of the initial eight-point test to this record correctly resulted in the conclusion that marijuana has no currently accepted medical use in treatment in the United States. Therefore, I adopt in their entirety the findings of facts and conclusions of law reached by the former Administrator in his final order of December 21, 1989, 54 FR 53767.

Pursuant to the remand of the Court of Appeals, I have condensed and clarified the initial standard into a five-point test. My application of the refined, five-point test to this record is set out briefly below.

First, marijuana's chemistry is neither fully known, nor reproducible. Thus far, over 400 different chemicals have been identified in the plant. The proportions and concentrations differ from plant to plant, depending on growing conditions, age of the plant, harvesting and storage factors. THC levels can vary from less than 0.2% to over 10%. It is not known how smoking or burning the plant material affects the composition of all these chemicals. It is not possible to reproduce the drug in dosages which can be considered standardized by any currently accepted scientific criteria. Marijuana is not recognized in any current edition of the official compendia. 21 U.S.C. 321(j).

Second, adequate safety studies have not been done. All reasonably applicable pharmacological and toxicological studies have not been carried out. Most of the chronic animal studies have been conducted with oral or intravenous THC, not with marijuana. Pharmacological data on marijuana's bioavailability, metabolic pathways and pharmacokinetics in inadequate. Studies in humans are too small and too few. Sophisticated epidemiological studies of marijuana use in large populations are required, similar to those done for tobacco use. Far too many questions remain unknown for experts fairly and responsibly to conclude marijuana is safe for any use.

Third, there are no adequate, well-controlled scientific studies proving marijuana is effective for anything.

Fourth, marijuana is not accepted for medical use in treatment by even a respectable minority, much less a consenus, of experts trained to evaluate drugs. The FDA's expert drug evaluators have rejected marijuana for medical use. No NDA has been approved by FDA for marijuana. The testimony of nationally recognized experts overwhelmingly rejects marijuana as medicine, compared to the scientifically empty testimony of the psychiatrists, a wellness counselor and general practitioners presented by NORML.

Fifth, given my conclusions on points one, two and three, it follows that the published scientific evidence is not adequate to permit experts to fairly and responsibly conclude that marijuana is safe and effective for use in humans.

A failure to meet just one of the five points precludes a drug from having a currently accepted medical use. Marijuana fails all five points of the test.

NORML has argued, unsuccessfully, that the legal standard for currently accepted medical use should be whether a respectable minority of physicians accepts the drug. The key to this medical malpractice defense is that the minority opinion must be recognized as respectable, as competent, by members of the profession.

In the absence of reliable evidence adequately establishing marijuana's chemistry, pharmacology, toxicology and effectiveness, no responsible physician could conclude that marijuana

is safe and effective for medical use. To quote Doctor Kenneth P. Johnson, Chairman of the Department of Neurology at the University of Maryland, and the author of over 100 scientific and medical articles on MS: "To conclude that marijuana is therapeutically effective without conducting rigorous testing would be professionally irresponsible."

By any modern scientific standard, marijuana is no medicine.

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

Dated: March 18, 1992.

Robert C. Bonner,

Administrator.

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NUCLEAR REGULATORY COMMISSION

ENVIRONMENTAL PROTECTION AGENCY

Proposed Guidance Document on the Testing of Mixed Radioactive and Hazardous Waste

AGENCIES: Nuclear Regulatory Commission, Environmental Protection Agency.

ACTION: Notice of availability and request for public comment.

SUMMARY: The Nuclear Regulatory Commission (NRC) and the Environmental Protection Agency (EPA) are jointly issuing a proposed guidance document on the testing of mixed radioactive and hazardous waste (mixed waste). This guidance document was developed to assist mixed waste generators in identifying and performing the testing required under the Federal regulations that implement the Resource Conservation and Recovery Act Subtitle C hazardous waste program and to ensure that employee radiation exposures are maintained As Low As Reasonably Achievable (ALARA). The agencies are soliciting comments from interested members of the regulated community, the States, and the public.

Interested individuals may provide the agencies with their comments on the proposed guidance document by forwarding their written comments to the NRC at the address listed in the "**ADDRESSES**" section. Interested parties may also participate in a public meeting being held to solicit oral comments on the proposed guidance document. Interested individuals will be given an opportunity to speak for fifteen minutes at this meeting. This time allowance may be extended, on request for good cause, if the schedule of speakers permits this extension.

DATES: The agencies will accept written comments until May 26, 1992. Individuals submitting comments after this date cannot be assured that the agencies will be able to afford their comments full consideration in any revisions that may be made to the proposed guidance document.

The public meeting to solicit oral comments on the proposed guidance document will be held on April 14, 1992, from 8:30 a.m. until 4:30 p.m. at the Mayflower/Stouffer Hotel, New York Room 1127 Connecticut Avenue NW., Washington, DC 20036, telephone (202) 347-3000.

ADDRESSES: Copies of the proposed guidance document may be obtained by contacting Dominick A. Orlando, NRC Mixed Waste Project Manager, Division of Low-Level Waste Management and Decommissioning, Office of Nuclear Material Safety and Safeguards, U.S. Nuclear Regulatory Commission, Washington, DC 20555, telephone (301) 504-2566.

Written comments on the proposed guidance document should be directed to David L. Meyer, Chief, Regulatory Publications Branch, Division of Freedom of Information and Publications Service, Office of Administration, U.S. Nuclear Regulatory Commission, Washington, DC 20555 or hand delivered to the Commission's offices at 7920 Norfolk Avenue, Bethesda, MD between the hours of 7:45 a.m. and 4:14 p.m. on Federal workdays.

Requests to speak at the public meeting should be submitted, in writing, to EPA. The written request should be addressed to Reid Rosnick, Mixed Waste Coordinator, Permits and State Programs Branch, Office of Solid Waste (OS-342), U.S. Environmental Protection Agency, 401 M Street SW., Washington, DC 20460. Interested speakers should include in the written request a statement identifying the topics to be addressed in their presentations, the names and affiliations of the individual(s) that will speak, and the amount of time the speaker(s) will require. A transcript of the oral proceedings will be included in the record for this action.

FOR FURTHER INFORMATION CONTACT: Dominick A. Orlando, Mixed Waste Project Manager, Division of Low-Level Waste Management and Decommissioning, Office of Nuclear Material Safety and Safeguards, U.S. Nuclear Regulatory Commission, Washington, DC 20555, telephone (303) 504-2566 or; Reid Rosnick, Mixed Waste Coordinator, Permits and State Programs Division, Office of Solid Waste, U.S. Environmental Protection Agency, 401 M Street SW., Washington, DC 20460, telephone (202) 260-4755.

Dated at Rockville, MD this 19th day of March, 1992.

For the U.S. Nuclear Regulatory Commission.

Robert M. Bernero,

Director, Office of Nuclear Material Safety and Safeguards.

For the U.S. Environmental Protection Agency.

Sylvia K. Lowrance,

Director, Office of Solid Waste.

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OFFICE OF MANAGEMENT AND BUDGET

Circular No. A-76: Performance of Commercial Activities; Amendment

AGENCY: Office of Management and Budget.

ACTION: Issuance of Transmittal Memorandum No. 11, amending OMB Circular No. A-76, "Performance of Commercial Activities."

SUMMARY: This notice contains Transmittal No. 11, dated February _____, 1992, to OMB Circular No. A-76, "Performance of Commercial Activities."

This Transmittal Memorandum updates the Federal pay raise assumptions and inflation factors used for computing the Government's in-house personnel and non-pay cost increases for Fiscal Years 1992 through 1997. The Federal pay raise assumptions and the non-pay category rates are contained in the President's Budget for Fiscal Year 1993. The factors contained in OMB Circular No. A-76, Transmittal Memorandum No. 10, dated February 28, 1991, are outdated.

The revision does not require any agency to (1) create or maintain a duplicate control/monitoring/reporting system or (2) adopt any additional controls, not presently in compliance with Federal Acquisition Regulations (FAR).

FOR FURTHER INFORMATION CONTACT: Mr. David Childs, Federal Services Branch, General Management Division,