

UNITED STATES DEPARTMENT OF JUSTICE  
Drug Enforcement Administration

In The Matter Of

MARIJUANA RESCHEDULING PETITION

Docket No. 86-22

OPINION AND RECOMMENDED RULING, FINDINGS OF  
FACT, CONCLUSIONS OF LAW AND DECISION OF  
ADMINISTRATIVE LAW JUDGE

FRANCIS L. YOUNG, Administrative Law Judge

APPEARANCES:

KEVIN B. ZEESE, Esq.  
ARNOLD S. TREBACH, Esq.  
for National Organization For The Reform of  
Marijuana Laws

FRANK B. STILWELL, III, Esq.  
for Alliance for Cannabis Therapeutics

DAVID C. BECK, Esq.  
for Cannabis Corporation of America

CARL ERIC OLSEN, Pro Se

CHARLOTTE J. MAPES, Esq.  
MADELEINE R. SHIRLEY, Esq.  
for the Government

KARL BERNSTEIN  
for National Federation of Parents for Drug-Free Youth

VIRGINIA PELTIER, Esq.  
for the International Association of Chiefs of Police

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## VIII.

### ACCEPTED SAFETY FOR USE UNDER MEDICAL SUPERVISION

With respect to whether or not there is "a lack of accepted safety for use of [marijuana] under medical supervision", the record shows the following facts to be uncontroverted.

#### Findings of Fact

1. Richard J. Gralla, M.D., an oncologist and Professor of Medicine who was an Agency witness, accepts that in treating cancer patients oncologists can use the cannabinoids with safety despite their side effects.

2. Andrew T. Weil, M.D., who now practices medicine in Tucson, Arizona and is on the faculty of the College of Medicine, University of Arizona, was a member of the first team of researchers to perform a Federal Government authorized study into the effects of marijuana on human subjects. This team made its study in 1968. These researchers determined that marijuana could be safely used under medical supervision. In the 20 years since then Dr. Weil has seen no information that would cause him to reconsider that conclusion. There is no question in his mind but that marijuana is safe for use under appropriate medical supervision.

3. The most obvious concern when dealing with drug safety is the possibility of lethal effects. Can the drug cause death?

4. Nearly all medicines have toxic, potentially lethal effects. But marijuana is not such a substance. There is no record in the extensive medical literature describing a proven, documented cannabis-induced fatality.

5. This is a remarkable statement. First, the record on marijuana encompasses 5,000 years of human experience. Second, marijuana is now used daily by enormous numbers of people throughout the world. Estimates suggest that from twenty million to fifty million Americans routinely, albeit illegally, smoke marijuana without the benefit of direct medical supervision. Yet, despite this long history of use and the extraordinarily high numbers of social smokers, there are simply no credible medical reports to suggest that consuming marijuana has caused a single death.

6. By contrast aspirin, a commonly used, over-the-counter medicine, causes hundreds of deaths each year.

7. Drugs used in medicine are routinely given what is called an LD-50. The LD-50 rating indicates at what dosage fifty percent of test animals receiving a drug will die as a result of drug induced toxicity. A number of researchers have attempted to determine marijuana's LD-50 rating in test animals, without success. Simply stated, researchers have been unable to give animals enough marijuana to induce death.

8. At present it is estimated that marijuana's LD-50 is around 1:20,000 or 1:40,000. In layman terms this means that in order to induce death a marijuana smoker would have to consume 20,000 to 40,000 times as much marijuana as is contained in one marijuana cigarette. NIDA-supplied marijuana cigarettes weigh approximately .9 grams. A smoker would theoretically have to consume nearly 1,500 pounds of marijuana within about fifteen minutes to induce a lethal response.

9. In practical terms, marijuana cannot induce a lethal response as a result of drug-related toxicity.

10. Another common medical way to determine drug safety is called the therapeutic ratio. This ratio defines the difference between a therapeutically effective dose and a dose which is capable of inducing adverse effects.

11. A commonly used over-the-counter product like aspirin has a therapeutic ratio of around 1:20. Two aspirins are the recommended dose for adult patients. Twenty times this dose, forty aspirins, may cause a lethal reaction in some patients, and will almost certainly cause gross injury to the digestive system, including extensive internal bleeding.

12. The therapeutic ratio for prescribed drugs is commonly around 1:10 or lower. Valium, a commonly used prescriptive drug, may cause very serious biological damage if patients use ten times the recommended (therapeutic) dose.

13. There are, of course, prescriptive drugs which have much lower therapeutic ratios. Many of the drugs used to treat patients with cancer, glaucoma and multiple sclerosis are highly toxic. The therapeutic ratio of some of the drugs used in antineoplastic therapies, for example, are regarded as extremely toxic poisons with therapeutic ratios that may fall below 1:1.5. These drugs also have very low LD-50 ratios and can result in toxic, even lethal reactions, while being properly employed.

14. By contrast, marijuana's therapeutic ratio, like its LD-50, is impossible to quantify because it is so high.

15. In strict medical terms marijuana is far safer than many foods we commonly consume. For example, eating ten raw potatoes can result in a toxic response. By comparison, it is physically impossible to eat enough marijuana to induce death.

16. Marijuana, in its natural form, is one of the safest therapeutically

active substances known to man. By any measure of rational analysis marijuana can be safely used within a supervised routine of medical care.

17. Some of the drugs most widely used in chemotherapy treatment of cancer have adverse effects as follows:

Cisplatin, one of the most powerful chemotherapeutic agents used on humans - may cause deafness; may lead to life-threatening kidney difficulties and kidney failure; adversely affects the body's immune system, suppressing the patient's ability to fight a host of common infections.

Nitrogen Mustard, a drug used in therapy for Hodgkins disease - nauseates; so toxic to the skin that, if dropped on the skin, this chemical literally eats it away along with other tissues it contacts; if patient's intravenous lead slips during treatment and this drug gets on or under the skin the patient may suffer serious injury including temporary, and in extreme cases, permanent, loss of use of the arm.

Procarbazine, also used for Hodgkins disease - has known psychogenic, i.e., emotional, effects.

Cytosin, also known as Cyclophosphamide - suppresses patient's immune system response; results in serious bone marrow depletion; studies indicate this drug may also cause other cancers, including cancers of the bladder.

Adriamycin, has numerous adverse effects; is difficult to employ in long term therapies because it destroys the heart muscle.

While each of these agents has its particular adverse effects, as indicated above, they also cause a number of similar, disturbing adverse effects. Most of these drugs cause hair loss. Studies increasingly indicate all of these drugs may cause other forms of cancer. Death due to kidney, heart or respiratory failure is a very real possibility with all of these agents and the margin for error is minimal. Similarly, there is a danger of overdosing a patient weakened by his cancer. Put simply, there is very great risk associated with the medical

use of these chemicals agents. Despite these high risks, all of these drugs are considered "safe" for use under medical supervision and are regularly administered to patients on doctor's orders in the United States today.

18. There have been occasional instances of panic reaction in patients who have smoked marijuana. These have occurred in marijuana-naive persons, usually older persons, who are extremely anxious over the forthcoming chemotherapy and troubled over the illegality of their having obtained the marijuana. Such persons have responded to simple person-to-person communication with a doctor and have sustained no long term mental or physical damage. If marijuana could be legally obtained, and administered in an open, medically-supervised session rather than surreptitiously, the few instances of such adverse reaction doubtless would be reduced in number and severity.

19. Other reported side effects of marijuana have been minimal. Sedation often results. Sometimes mild euphoria is experienced. Short periods of increased pulse rate and of dizziness are occasionally experienced. Marijuana should not be used by persons anxious or depressed or psychotic or with certain other health problems. Physicians could readily screen out such patients if marijuana were being employed as an agent under medical supervision.

20. All drugs have "side effects" and all drugs used in medicine for their therapeutic benefits have unwanted, unintended, sometimes adverse effects.

21. In medical treatment "safety" is a relative term. A drug deemed "safe" for use in treating a life-threatening disease might be "unsafe" if prescribed for a patient with a minor ailment. The concept of drug "safety" is relative. Safety is measured against the consequences a patient would confront in the absence of therapy. The determination of "safety" is made in terms of

whether a drug's benefits outweigh its potential risks and the risks of permitting the disease to progress.

22. In the context of glaucoma therapy, it must be kept in mind that glaucoma, untreated, progressively destroys the optic nerve and results in eventual blindness. The danger, then, to patients with glaucoma is an irretrievable loss of their sight.

23. Glaucoma is not a mortal disease, but a highly specific, selectively incapacitating condition. Glaucoma assaults and destroys the patient's most evolved and critical sensory ability, his or her vision. The vast majority of patients afflicted with glaucoma are adults over the age of thirty. The onset of blindness in middle age or later throws patients into a wholly alien world. They can no longer do the work they once did. They are unable to read a newspaper, drive a car, shop, walk freely and do all the myriad things sighted people take for granted. Without lengthy periods of retaining, adaptation and great effort these individuals often lose their sense of identity and ability to function. Those who are young enough or strong-willed enough will regain a sense of place, hold meaningful jobs, but many aspects of the life they once took for granted cannot be recaptured. Other patients may never fully adjust to their new, uncertain circumstances.

24. Blindness is a very grave consequence. Protecting patients from blindness is considered so important that, for ophthalmologists generally, it justifies the use of toxic medicines and uncertain surgical procedures which in other contexts might be considered "unsafe." In practice, physicians often provide glaucoma patients with drugs which have many serious adverse effects.

25. There are only a limited number of drugs available for the

treatment of glaucoma. All of these drugs produce adverse effects. While several government witnesses lightly touched on the side effects of these drugs, none provided a full or detailed description of their known adverse consequences.

26. The adverse physical consequences resulting from the chronic use of commonly employed glaucoma control drugs include a vast range of unintended complications from mild problems like drug induced fevers, skin rashes, headaches, anorexia, asthma, pulmonary difficulties, hypertension, hypotension and muscle cramps to truly serious, even life-threatening complications including the formation of cataracts, stomach and intestinal ulcers, acute respiratory distress, increases and decreases in heart rate and pulse, disruption of heart function, chronic and acute renal disease, and bone marrow depletion.

27. Finally, each FDA-approved drug family used in glaucoma therapy is capable of producing a lethal response, even when properly prescribed and used. Epinephrine can lead to elevated blood pressure which may result in stroke or heart attack. Miotic drugs suppress respiration and can cause respiratory paralysis. Diuretic drugs so alter basic body chemistry they cause renal stones and may destroy the patient's kidneys or result in death due to heart failure. Timolol and related beta-blocking agents, the most recently approved family of glaucoma control drugs, can trigger severe asthma attacks or cause death due to sudden cardiac arrhythmias often producing cardiac arrest.

28. Both of the FDA-approved drugs used in treating the symptoms of multiple sclerosis, Dantrium and Lioresal, while accepted as "safe" can, in fact, be very dangerous substances. Dantrium or dantrolene sodium carries a boxed warning in the Physician's Desk Reference (PDR) because of its very high toxicity. Patients using this drug run a very real risk of developing sympto-

matic hepatitis (fatal and nonfatal). The list of sublethal toxic reactions also underscores just how dangerous Dantrium can be. The PDR, in part, notes Dantrium commonly causes weakness, general malaise and fatigue and goes on to note the drug can also cause constipation, GI bleeding, anorexia, gastric irritation, abdominal cramps, speech disturbances, seizure, visual disturbances, diplopia, tachycardia, erratic blood pressure, mental confusion, clinical depression, renal disturbances, myalgia, feelings of suffocation and death due to liver failure.

29. The adverse effects associated with Lioresal baclofen are somewhat less severe, but include possibly lethal consequences, even when the drug is properly prescribed and taken as directed. The range of sublethal toxic reactions is similar to those found with Dantrium.

30. Norman E. Zinberg, M.D., one of Dr. Weil's colleagues in the 1968 study mentioned in finding 2, above, accepts marijuana as being safe for use under medical supervision. If it were available by prescription he would use it for appropriate patients.

31. Lester Grinspoon, M.D., practicing psychiatrist, researcher and Associate Professor of Medicine at Harvard Medical School, accepts marijuana as safe for use under medical supervision. He believes its safety is its greatest advantage as a medicine in appropriate cases.

32. Tod H. Mikuriya, M.D., a psychiatrist practicing in Berkley, California who treats substance abusers as inpatients and outpatients, accepts marijuana as safe for use under medical supervision.

33. Richard D. North, M.D., who has treated Robert Randall for glaucoma with marijuana for nine years, accepts marijuana as safe for use by his patient

under medical supervision. Mr. Randall has smoked ten marijuana cigarettes a day during that period without any evidence of adverse mental or physical effects from it.

34. John C. Merritt, M.D., an expert in ophthalmology, who has treated Robert Randall and others with marijuana for glaucoma, accepts marijuana as being safe for use in such treatment.

35. Deborah B. Goldberg, M.D., formerly a researcher in oncology and now a practicing physician, having worked with many cancer patients, observed them, and heard many tell of smoking marijuana successfully to control emesis, accepts marijuana as proven to be an extremely safe anti-emetic agent. When compared with the other, highly toxic chemical substances routinely prescribed to cancer patients, Dr. Goldberg accepts marijuana as clearly safe for use under medical supervision. (See finding 17, above.)

36. Ivan Silverberg, M.D., board certified in oncology and practicing that specialty in the San Francisco area, has accepted marijuana as a safe anti-emetic when used under medical supervision. Although illegal, it is commonly used by patients in the San Francisco area with the knowledge and acquiescence of their doctors who readily accept it as being safe for such use.

37. It can be inferred that all of the doctors and other health care professionals referred to in the findings in Sections V, VI and VII, above, who tolerate or permit patients to self-administer illegal marijuana for therapeutic benefit, accept the substance as safe for use under medical supervision.

## Discussion

The Act, at 21 U.S.C. § 812(b)(1)(C), requires that marijuana be retained in Schedule I if "[t]here is a lack of accepted safety for use of [it] under medical supervision." If there is no lack of such safety, if it is accepted that this substance can be used with safety under medical supervision, then it is unreasonable to keep it in Schedule I.

Again we must ask - "accepted" by whom? In the MDMA proceeding the Agency's first Final Rule decided that "accepted" here meant, as in the phrase "accepted medical use in treatment", that the FDA had accepted the substance pursuant to the provisions of the Food, Drug and Cosmetic Act. 51 Fed. Reg. 36555 (1986). The Court of Appeals held that this was error. On remand, in its third Final Rule on MDMA, the Agency made the same ruling as before, relying essentially on the same findings, and on others of similar nature, just as it did with respect to "accepted medical use." 53 Fed. Reg. 5156 (1988).

The administrative law judge finds himself constrained not to follow the rationale in that MDMA third Final Order for the same reasons as set out above in Section V with respect to "accepted medical use" in oncology. See pages 30 to 33. Briefly, the Agency was looking primarily at the results of scientific tests and studies rather than at what physicians had, in fact, accepted. The Agency was wrongly basing its decision on a judgement as to whether or not doctors ought to have accepted the substance in question as safe for use under medical supervision. The criteria the Agency applied in the MDMA third Final Rule are inappropriate. The only proper question for the Agency here is: Have a significant minority of physicians accepted marijuana as safe for use under medical supervision?

The gist of the Agency's case against recognizing marijuana's acceptance as safe is to assert that more studies, more tests are needed. The Agency has presented highly qualified and respected experts, researchers and others, who hold that view. But, as demonstrated in the discussion in Section V above, it is unrealistic and unreasonable to require unanimity of opinion on the question confronting us. For the reasons there indicated, acceptance by a significant minority of doctors is all that can reasonably be required. This record makes it abundantly clear that such acceptance exists in the United States.

Findings are made above with respect to the safety of medically supervised use of marijuana by glaucoma patients. Those findings are relevant to the safety issue even though the administrative law judge does not find accepted use in treatment of glaucoma to have been shown.

Based upon the facts established in this record and set out above one must reasonably conclude that there is accepted safety for use of marijuana under medical supervision. To conclude otherwise, on this record, would be unreasonable, arbitrary and capricious.