TAKE TWO PUFFS AND CALL ME IN THE MORNING

Proponents of marijuana's medical benefits take their case to court

By RICK WEISS

Once a month, Robert Randall strolls into his neighborhood pharmacy in Washington, D.C. He chats with the pharmacist while his prescription is filled, and a few minutes later walks out the door with a 30-day supply of the medicine he needs — 300 prerolled marijuana cigarettes.

Such has been Randall's routine for the past 10 years, ever since he won a court order that recognized his medical need to smoke marijuana. Marijuana lowers the pressure that builds up in his eyes as a result of his having glaucoma. He is the only glaucoma patient in the United States to have won such an order. But if he and others have their way — that is, if Federal Administrative Law Judge Francis Young Jr. rules in their favor later this year — thousands of patients may get easier access to the drug for a variety of ailments ranging from chemotherapy-induced nausea to spasticity.

Such a decision would be the climax of a tedious, decade-long battle by a coalition of groups convinced that pot's therapeutic potential has been unjustly ignored. "It's been like a play by Ionesco with footnotes by Kafka," Randall says of the unusual legal struggle. "It's been absurd, venal and bizarre."

Such surrealism is not a part of his everyday experience, Randall assures. Although he smokes eight to 10 "joints" per day, he says he developed a tolerance to marijuana's psychoactive effects many years ago. Meanwhile, he says, a "fixation" on marijuana as a drug of abuse has kept the Drug Enforcement Administration (DEA) from appreciating the drug's medical merits.

Marijuana (*Cannabis spp.*) is classified by the DEA as a "Schedule 1" drug — one that has "no currently accepted medical use as a treatment in the United States" and is considered unsafe even under medical supervision. A prescription version of delta-9-tetrahydrocannabinol (THC), the primary active ingredient in marijuana, is less tightly restricted and was approved by the Food and Drug Administration in 1985 as an antinausea agent for cancer patients. But its effectiveness is hotly disputed; many patients and physicians claim that purified THC is not nearly as effective as a puff of pot.

As part of a campaign to reverse what they believe is a political bias against marijuana, the Alliance for Cannabis Therapeutics and the National Organization for the Reform of Marijuana Laws, both based in Washington, D.C., have challenged the drug's Schedule 1 status. The groups contend that, at minimum, marijuana should be classified as a Schedule 2 drug — a status that would keep it illegal but would ease the restrictions on research into its medical applications. Although researchers can apply for permission to perform human trials with Schedule 1 drugs, few applications are ever granted. Proponents of reform say a schedule change would speed the recognition, acceptance and availability of marijuana as medicine.

In one of the final stages of the rescheduling challenge, completed earlier this month, court-ordered hearings were held in New Orleans, San Francisco and Washington, D.C. Closing briefs are now being prepared by attorneys on both sides and should be completed by May. After reviewing the briefs and scores of volumes of testimony, Judge Young is expected to make a recommendation to the chief administrator of the DEA before the end of the year.

But even then the battle may not be over. The DEA is not bound by the judge's recommendation, and in either case the DEA's decision can be appealed.

The case may get even more complicated because the DEA is expected within the next few weeks to announce its decision in a similar case involving MDMA — an illegal drug that some believe has potential as an adjunct to psychotherapy. Last year, after lengthy hearings, Judge Young recommended that the DEA drop MDMA from Schedule 1 to Schedule 3. Schedule 3 drugs are illegal to possess except with a DEA license, but are acknowledged as having medical potential.

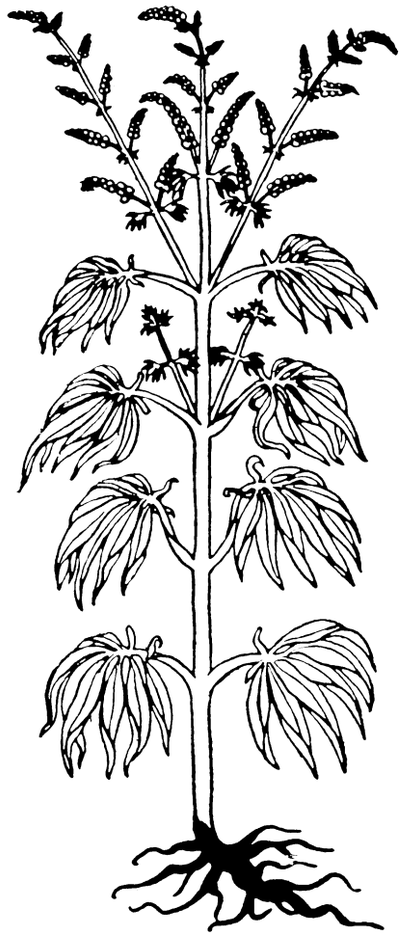

Illustration of Cannabis *from the works of Dioscorides, a first-century physician.*

The DEA ignored that recommendation, kept MDMA in Schedule 1 and was subsequently sued by one of the drug's proponents, Harvard psychiatry professor Lester Grinspoon. Grinspoon claimed that Schedule 1 was an overly restrictive status for a drug that had, he said, "been taken in a therapeutic setting by thousands of people, apparently with few complications." Grinspoon won his case in the U.S. Court of Appeals and the DEA is now reconsidering its stand. Among other things, the case is forcing the DEA to redefine some of its schedule definitions, which may have an impact on the marijuana decision.

A central issue in both cases is the DEA's definition of the "no accepted medical use" clause that relegates a drug to Schedule 1 status.

"The original definition was that in order for a drug to have an accepted medical use it had to be lawfully marketed in the United States under the Food, Drug and Cosmetic Act," says Charlotte Mapes, a DEA attorney. "What the court said [in the MDMA case] is that the administrator cannot rely exclusively on lack of marketing approval as a condition

for no accepted medical use."

Indeed, proponents of rescheduling say a simple lack of FDA approval hardly counterbalances marijuana's long record as a therapeutic agent. Chinese herbal catalogues have listed the plant as an aid to digestion for thousands of years, and as many as 30 marijuana preparations were listed in the *U.S. Pharmacopoeia* as recently as 1937. "It appears that every society that encounters marijuana acknowledges its therapeutic properties," says Alice O'Leary, a cofounder of the Alliance for Cannabis Therapeutics.

In the United States, researchers have been most interested in marijuana's usefulness as an anti-emetic for cancer patients suffering from chemotherapy-induced nausea. Several FDA-approved Investigational New Drug studies have demonstrated its value as such, and in some cases its advantages over THC pills.

"Never mind the absurdity of giving an oral medicine to someone who is throwing up all the time," Randall says of the FDA-approved pills. The tablets have negative side effects of their own, he says, adding that in one study "50 percent of the patients said they'd rather throw up."

According to testimony by John Morgan, a professor of medicine at City College of New York, "Marijuana's use in reducing nausea appears to be quite widespread and generally, albeit discretely, accepted within the oncologic community and among patients. Physicians confront profoundly difficult ethical, legal and moral questions because of marijuana's inappropriate classification."

Marijuana may also be useful for reducing some of the neurological complications inherent to multiple sclerosis, Parkinson's disease and paraplegia. Preliminary studies show that it seems to work quickly and effectively against severe episodes of muscle spasticity, according to testimony by Denis Petro, director of clinical research at Fidia Pharmaceuticals, a major Italian drug company that specializes in neurological therapeutics. Other studies have suggested that marijuana may be useful in the treatment of asthma, anxiety and eating disorders and for improving the quality of life in terminally ill patients.

The DEA says that most such studies have been poorly designed, are fraught with subjective errors and represent little more than collections of anecdotal evidence. Proponents of rescheduling concede that few case-controlled, double-blind studies have been performed on marijuana in its natural form. However, they add, that shortage exists in large part because it is so difficult to get research approval for Schedule 1 drugs.

In addition to the controversy over marijuana's "accepted medical use," there is considerable debate over the issue of its safety and how to apply the "lack of accepted safety" clause in the Schedule 1 definition.

"Marijuana has not killed anyone in 5,000 years," Randall says flatly. But the DEA is not convinced.

"Our perception of safety is different from theirs," DEA attorney Mapes told SCIENCE NEWS. "They're saying it's safe because nobody's died. We're saying that it has to be shown to be safe."

Fitz Hugh Ludlow Memorial Library

Broadsides such as this one characterized the campaign against marijuana in the 1930s and 1940s.

Research has suggested that marijuana can suppress the body's immune system (SN: 7/18/87, p.46), and deficits in short-term memory among users have been reported. According to the most thorough U.S. examination of the health-related effects of marijuana, a 15-month study by the Institute of Medicine of the National Academy of Sciences published in 1982, "marijuana impairs motor coordination and affects tracking ability and sensory and perceptual functions important for safe driving and the operation of other machines." However, the report adds, "we have no convincing evidence thus far of any effects persisting in human beings after cessation of drug use. . . ."

Perhaps most significantly, marijuana has a variety of psychological effects. Depending on the individual, the dose and the setting, it has been known to produce everything from sensory enhancement and euphoria to intense anxiety and paranoia.

"Most doctors do not want to give a psychoactive drug to someone when they can give a nonpsychoactive one that is more effective," says Madeleine Shirley, a DEA attorney working with Mapes in the current case. With so many new drugs being created, she says, "Frankly, there's not a lot of interest in marijuana any more."

The debate goes on. The government says marijuana is notoriously variable in potency, containing dozens of active ingredients in unpredictable concentrations. Randall counters that the marijuana he buys at his local pharmacy – grown on a government pot plantation in Oxford, Miss. – is routinely blended to a uniform potency, tested and certified by the National Institute of Drug Abuse.

In addition, the DEA claims that smoking is a poor way to get a measured dose of a drug, since depth of inhalation and the length of time before exhaling can affect the amount of drug that gets into the bloodstream. But other experts note that inhalation has many benefits as a means of drug delivery, providing rapid absorption and avoiding gastric complications (see related story, p.120).

Given the lack of scientific consensus on such issues, the discussion ultimately turns to politics. Statements from the Alliance for Cannabis Therapeutics clearly suggest that the government's hard line on marijuana is motivated by political considerations.

But if Alliance members believe there is a federal cabal aimed at nipping marijuana research in the bud, federal officials are equally suspicious of the reformers' motivations.

"I think this whole thing has got more to it than meets the eye," says Paul Leber, director of the FDA's division of neurological and pharmacological drug products. "I'm not interested in suppressing a drug just because somebody says it's bad. But I do have to ask myself, 'Is it likely to benefit the patient? Or is this being used by someone in an unscrupulous attempt to foster some nonsense?' "

Proponents of reform note that pot would still be illegal and tightly controlled under Schedule 2 or 3. Rescheduling would simply encourage much-needed research, they say, and might open the door to "compassionate use." Under its compassionate use rule, the FDA allows unapproved drugs to be prescribed when effective alternatives are not available. In addition, if the number of studies begins to increase, hundreds of patients might gain long-sought access to the drug as subjects in licensed studies.

In any case, neither of the parties to the marijuana dispute foresees immediate or widespread availability of the drug. Even if the current rescheduling effort is successful, the government may still be slow to approve new research and to appropriately scale up its marijuana accounting and distribution mechanisms. Because of marijuana's potential for abuse, says the DEA, it would be important to keep careful inventories of the drug.

Happily, sighs Shirley, drug approval and distribution are not the DEA's responsibilities. "We just decide what schedule it's in. Getting the drug to the people is the FDA's problem." □