Medical Marijuana: The Conflict Between Scientific Evidence and Political Ideology. Part Two of Two

Peter J. Cohen

ABSTRACT. In Part I of this article, I examined the role of the Food and Drug Administration (FDA) in drug approval and then detailed the known risks of medical marijuana (any form of Cannabis sativa used—usually by smoking—to treat a wide variety of pathologic states and diseases). Part II of the article will begin by reviewing the benefits of Cannabis sativa as documented by well designed scientific studies that have been published in the peer-reviewed literature. I will then propose that ability of scientists to conduct impartial studies designed to answer the question of marijuana’s role in medical therapy has been greatly hampered by political considerations. I will posit that in spite of the considerable efforts of policymakers, it is becoming apparent that marijuana’s benefits should be weighed against its well-described risks. I will conclude that political advocacy is a poor substitute for dispassionate analysis and that neither popular votes nor congressional “findings” should be permitted to trump scientific evidence in deciding whether or not marijuana is an appropriate pharmaceutical agent to use in modern medical practice. Whether or not marijuana is accepted as a legitimate medical therapy should remain in the hands of the usual drug-approval process and that the statutory role of the Food and Drug Administration should be dispositive.

KEYWORDS. cannabis, law, marijuana, medical, nausea, pain, policy

Peter J. Cohen, MD, JD, is Adjunct Professor of Law at the Georgetown University Law Center. He is Chair of the Physicians Health Program of the District of Columbia Medical Society and Former Vice Chair of the Institutional Review Board of the Intramural Research Program of the National Institute on Drug Abuse. Formerly, he was Professor of Anesthesiology at the University of Pennsylvania Medical Center and Professor and Chairman of Anesthesiology at the Universities of Colorado and Michigan Medical Centers.

Address correspondence to: Dr. Peter Cohen, 10703 Clermont Avenue, P.O. Box 569, Garrett Park, MD 20896. (E-mail: ccohenp@aol.com).

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PART IV: POTENTIAL BENEFITS OF MEDICAL MARIJUANA

The medical use of marijuana, once officially recognized by the United States Pharmacopoeia (based on anecdotal rather than scientific evidence), was eventually made illegal by Congressional legislation. In this section, I will provide a brief historical background to the medical use of marijuana and will then address the current state of knowledge of its medical benefits based on scientific evidence.

EARLY HISTORY OF MEDICAL MARIJUANA

Marijuana has not always been a pariah drug within the community of healers. In 1851, the United States Pharmacopoeia granted marijuana the status of a legitimate medical compound. In the same year, another government-recognized publication declared (supported more by anecdotal input than scientific data): “The complaints in which it [marijuana] has been specially recommended are neuralgia, gout, rheumatism, tetanus, hydrophobia, epidemic cholera, convulsions, chorea, hysteria, mental depression, delirium tremens, insanity and uterine hemorrhage.”

The Fourth Edition of the United States Pharmacopoeia (1864) described the preparation of Extractum Cannabis Purificatum:

Take of extract of hemp two troy ounces; alcohol a sufficient quantity. Rub the Extract with two fluidounces of Alcohol until they are thoroughly mixed; and, having added twelve fluidounces of Alcohol, allow the mixture to macerate for twenty-four hours. Then filter the tincture through paper, passing sufficient Alcohol through the filter to exhaust the dregs completely. Lastly, by means of a water-bath, at a temperature not exceeding 160°, evaporate to dryness.

More recently, in 1982, an herbal medical text proposed (again without evident supporting scientific evidence):

The principal use of Hemp in medicine is for easing pain and inducing sleep, and for soothing influences in nervous disorders. It does not cause constipation nor affect the appetite like opium. It is useful in neuralgia, gout, rheumatism, delirium tremens, insanity, infantile convulsions, insomnia, etc. The tincture helps parturition, and is used in senile catarrh, gonorrhea, menorrhagia, chronic cystitis and painful urinary affections. An infusion of the seed is useful in after pains and prolapsus uteri. The resin may be combined with ointments [to remedy] inflammatory and neuralgic complaints.

Anecdotal reports of marijuana’s safety and efficacy are not confined to the past. George Annas provides an especially telling description of its use by Stephen Jay Gould, a respected scientist, who had smoked marijuana to alleviate the nausea and discomfort he experienced during chemotherapy for abdominal mesothelioma:

Absolutely nothing in the available arsenal of anti-emetics worked at all. I was miserable and came to dread the frequent treatments with an almost perverse intensity... Marijuana worked like a charm... The sheer bliss of not experiencing nausea—and not having to fear it for all the days intervening between treatments—was the greatest boost I received in all my year of treatment, and surely the most important effect upon my eventual cure.

SCIENTIFIC EVIDENCE OF THE BENEFITS OF MEDICAL MARIJUANA

It is not unreasonable to believe that a botanical remedy whose successful use has been part of numerous cultures for thousands of years might have some healing properties. Nonetheless, although history and anecdotal reports are suggestive, they do not constitute the firm scientific proof that is essential to justify the approval of medical marijuana as a legitimate pharmaceutical agent. The standard of review, as set forth by the FD&C (Food, Drug, and Cosmetic) Act, demands “evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved.” Therefore, it is appropriate to detail some of the scientifically validated and peer-reviewed published evidence...
Regarding the safety and efficacy of medical marijuana.

Severe and unremitting pain is a major cause of morbidity in those suffering from human immunodeficiency virus–acquired immunodeficiency syndrome (HIV-AIDS). Although anecdotal reports from the AIDS community have proclaimed the efficacy of smoked marijuana, it was not until 2007 (the long delay in performing adequate studies is discussed in Part V) that these claims were clearly verified when the efficacy of smoked marijuana in treating such pain was reported in a scientific peer-reviewed publication by Donald Abrams and coworkers.8 In this investigation, a prospective randomized placebo-controlled trial involving adults with painful HIV-associated sensory neuropathy, volunteers were randomly assigned to smoke either marijuana (3.56% Δ9-tetrahydrocannabinol) or identical placebo cigarettes9 three times daily for 5 days. The investigators evaluated both the individual subjects’ quantitative description of chronic pain intensity and the percentage of subjects who reported more than a 30% reduction in pain intensity. They found that smoked marijuana reduced daily pain by an average of 34%. Over twice as many of the subjects who smoked marijuana reported a significant reduction in pain compared with the placebo group. Pain relief was rapid; the first marijuana cigarette reduced chronic pain by 72% whereas only 15% of the placebo group reported immediate relief. No serious adverse events occurred during the study. The authors concluded that “smoked cannabis was well tolerated and effectively relieved chronic neuropathic pain from HIV-associated sensory neuropathy.”10

Abrams’ study involved volunteers with symptoms of pathologic (disease-related) pain. Another approach to measuring the analgesic potency of a drug is to evaluate its ability to mitigate artificially induced pain. In 2007, Wallace and colleagues reported the effect of smoked marijuana on pain that had been produced by the injection of capsaicin (similar to injecting an extract of jalapeno peppers) under the skin in a randomized, double-blind, placebo trial involving 15 healthy volunteers.11 Three doses of marijuana were administered: low (2%), medium (4%), and high (8% Δ9-tetrahydrocannabinol by weight). Although the low dose had no analgesic effect, there was a significant decrease in capsaicin-induced pain within 45 minutes after the medium dose was smoked. However, as with some other analgesic agents, the highest dose actually produced an increase in subjective pain perception. An important observation was that there was no significant impairment of performance among volunteers in the study as evaluated by neuropsychological testing.

Marijuana’s analgesic potency may not be universally acceptable to all patients; this is a phenomenon similar to that observed with other approved medications. In 2008, Wilsey and colleagues12 reported the results of a double-blinded, placebo-controlled, crossover (one group received active and the other group placebo in the first phase; this was then reversed in the second phase of the investigation) study evaluating the analgesic efficacy of smoking marijuana for neuropathic pain. Thirty-eight patients with central and peripheral neuropathic pain smoked a high-dose (7%), low-dose (3.5%), or placebo marijuana. Smoked marijuana produced a dose-related analgesic response. Minimal and well-tolerated psychoactive effects were observed with the lower dose. However, higher doses were associated with some acute cognitive effects, particularly with regard to memory.13 The authors concluded that although marijuana may be useful in mitigating severe pain, cognitive dysfunction may prove a drawback in some patients:

This study adds to a growing body of evidence that cannabis may be effective at ameliorating neuropathic pain, and may be an alternative for patients who do not respond to, or cannot tolerate, other drugs. However, the use of marijuana as medicine may be limited by its method of administration (smoking) and modest acute cognitive effects, particularly at higher doses.14

These findings were recently corroborated by investigators working in the Department of Neurosciences of the University of California San Diego who compared the ability of smoked marijuana (1% to 8% THC) to alleviate HIV-associated neuropathic pain with that of a placebo.15 Active and placebo cigarettes were administered four times daily for 5 consecutive days, followed by a 2-week “washout” period. Another 5-day period was then reinstated with the control and active group reversed. Subjects and investigators were blinded regarding the safety and efficacy of medical marijuana.
whether they had received placebo or active drug. Active marijuana produced a statistically significant decrement in the subjects’ pain score while their mood and daily functioning improved. Side effects were mild and self-limited; however, 2 of the 34 subjects dropped out of the investigation because of unpleasant symptoms. The authors concluded that “smoked cannabis was generally well tolerated and effective [in treating] patients with medically refractory pain due to HIV.”

A recent study suggests that marijuana may be a useful addition to the often-debilitating chemotherapy for hepatitis C (HCV), a potentially deadly viral infection. Although drugs used to treat HCV are effective, their severe side effects—extreme fatigue, nausea, muscle aches, loss of appetite, and depression—often lead patients to stop treatment. Sylvestre and colleagues found that smoked marijuana significantly ameliorated these symptoms, thereby enabling 42% more patients to complete therapy than those who did not use marijuana. The investigators concluded that marijuana use may offer symptomatic and virological benefit (a diminished number of disease-producing viruses in the blood) to some patients undergoing treatment for HCV by helping them to adhere to the challenging medication regimen. An accompanying editorial provided strong support for the necessity of dispassionate scientific evaluation in analyzing the potential efficacy of medical marijuana’s effects:

While further research is required on the biological and clinical aspects of the benefits of cannabis use for HCV treatment, and the effectiveness of cannabis use for HCV treatment needs to be explored in larger study populations, we advocate that in the interim existing barriers to marijuana use are removed for drug users undergoing HCV treatment until the conclusive empirical basis for evidence-based guidance is available.

These scientific data strongly suggest that marijuana has medical utility. Therefore, its designation as a Schedule I controlled substance should be reevaluated to determine whether the evidence supports the concept that marijuana now “has a currently accepted medical use in treatment in the United States” under the Controlled Substance Act (CSA). However, despite such studies, medical marijuana remains illegal under federal law. The next section will address this disconnect between scientific data and federal policy.

PART V: THE BATTLE BETWEEN SCIENCE AND POLITICS

This section will discuss the pervasive intrusion of politics into what should have been a scientifically-based determination of marijuana’s status as a safe and efficacious drug for the treatment of certain medical conditions. I will consider why it took so long for peer-reviewed studies evaluating the medical use of marijuana to appear in the scientific literature. I will then ask why, in face of the documented safety and efficacy of medical marijuana, the Congress continues to designate it as a Schedule I controlled substance and therefore illegal for medical use. I will also explore the question of why the medical use of marijuana was legitimized by popular vote in California and 12 other states rather than by “experts qualified by scientific training and experience.” Finally, I will query whether the legalization of the use of marijuana for medical purposes will inevitably result in its inappropriate use, i.e., will it result in “gaming the system”?

PEER-REVIEWED SCIENTIFIC STUDIES OF MEDICAL MARIJUANA HAVE BEEN PUBLISHED ONLY RECENTLY

As discussed in Part IV, the first objective study of the safety and efficacy of smoked marijuana was published less than two years ago. Why did it take so long for this study to appear in the peer-reviewed scientific literature? Why did the pharmaceutical industry fail to show any interest in this promising compound? Some might prefer a simple answer: since marijuana is a naturally-occurring botanical, it cannot be patented, thus removing any incentive for investing the considerable amount of corporate funds required when seeking Food and Drug Administration (FDA) approval. This consideration does not apply to the purified derivatives or extracts of marijuana, which have either been approved or are currently undergoing clinical evaluation (infra, Part VI).
I will argue that this is far too a facile an explanation for the inordinate delay in bringing information of the medical efficacy of marijuana into the scientific literature. I will demonstrate how one scientist, attempting to conduct “science, not ideology,” was stymied by overwhelming political considerations. The history of his numerous attempts to engage in a well-designed scientific study of the efficacy (or its lack) of smoked marijuana in alleviating serious pain secondary to HIV-AIDS exemplifies the dominant role of politics in this issue.

In 1992, Dr. Donald Abrams, a clinical pharmacologist, Professor of Medicine at the University of California San Francisco, and Chair of the Bay Area’s Community Consortium on HIV research, proposed a study designed to provide objective data about whether or not smoked marijuana could ease subjective symptoms of AIDS wasting thereby producing gains in body weight. The University of California planned to fund the study, the FDA approved the IND, and the ethics of the study protocol were approved by the University Hospital’s Institutional Review Board. However, Dr. Abrams was denied permission to import marijuana from the Netherlands as he had originally planned or to use illegal marijuana that had been seized by the Drug Enforcement Agency (DEA).

Because the National Institute on Drug Abuse (NIDA) grows marijuana and was its only domestic source for scientific investigators, Dr. Abrams requested their assistance, a request that would have involved only a minimum expense to NIDA. However, it was then the policy of the National Institutes of Health (NIH) to restrict its provision of marijuana only to investigators who had received a peer-reviewed NIH grant to conduct a study requiring this drug. Because Abrams’ funding had originated at his university, and not the NIH of which NIDA is a part, he was refused access to NIH’s marijuana.

In May of 1996, hoping that the NIH had changed its policies, Dr. Abrams resubmitted his study proposal to the NIH. At that time, the study had again been approved and funded at the university level; thus, NIH approval was required not for funding, but to allow him to obtain federally grown marijuana. In October 1996, 4 years after he had first initiated requests to obtain marijuana legally, he was again informed that the NIH would not supply it.

In 1998, after 6 years of frustrating attempts to obtain marijuana either in the United States or abroad, the NIH finally approved Dr. Abrams’ request and he was able to obtain marijuana legally. Abrams then initiated the first federally funded effort to study the effects of marijuana on patients with AIDS, an investigation that was eventually published in the peer-reviewed scientific literature.

This was not the only instance in which the federal government appeared to place significant roadblocks in the way of university-sponsored research directed towards obtaining information about the possible medical uses of marijuana. Because of difficulties in obtaining marijuana from NIDA’s “marijuana farm,” Lyle E. Craker, PhD, a professor in the Department of Plant and Soil Sciences at the University of Massachusetts Amherst, petitioned the Drug Enforcement Agency (DEA) in 2003 for permission to cultivate marijuana to use in university-approved clinical studies that would evaluate marijuana’s ability to provide pain relief and control nausea in patients with cancer, as well as to alleviate some of the symptoms of multiple sclerosis in other patients. His petition was denied by the DEA in spite of DEA Administrative Law Judge Mary Ellen Bittner’s nonbinding opinion that it would be in the public interest to grant it. She stated in that opinion that the federal government’s system for evaluating requests for marijuana for clinical study had hindered investigation of the drugs safety and effectiveness.

As of mid-2008, the case is still pending. Four years after the petition was filed, DEA spokesman Steve Robertson told the American Medical News that the agency was reviewing the decision but he declined to comment other than to declare that the government maintains that no sound scientific studies exist to support marijuana’s medical value.

The federal government’s stance regarding scientific investigation of medical marijuana has, however, been far from monolithic. Although those individuals within the NIH who acted on Dr. Abrams’ request appeared to reject even minimal support of scientific study of the medical use of marijuana, other NIH personnel appeared to take an opposite stance. After considerable “wide-ranging public discussion on the potential medical use of marijuana, particularly smoked marijuana,” the National Institutes of Health convened a conference “to review the scientific...
data concerning the potential therapeutic uses for marijuana and the need for and feasibility of additional research" on February 19–20, 1997.37

At this forum,38 a group of experts in anesthesiology, internal medicine, neurology, oncology, ophthalmology, pharmacology, and psychiatry maintained that there was a need for accurate and nonbiased scientific investigation of medical marijuana.39 The participants suggested that although Δ9-tetrahydrocannabinol, the major psychoactive component of marijuana, is currently available as a separate and approved medication, this should not obviate the need to study the efficacy of smoked marijuana itself. They noted the plant may also contain other compounds with important therapeutic properties. Moreover, "the bioavailability and pharmacokinetics of THC derived from smoked marijuana are substantially different than those of the oral dosage form."40

The expert group proposed the possibly beneficial (or even superior41) role of smoked marijuana cannot be delineated without proper investigation. They maintained that studies of marijuana should not be precluded because effective approved therapy was currently available for the diseases in which it might also be efficacious. The members proposed that:

For at least some potential indications, marijuana looks promising enough to recommend that there be new controlled studies done. The indications in which varying levels of interest were expressed are the following:

- Appetite stimulation and cachexia
- Nausea and vomiting following anticancer therapy
- Neurological and movement disorders
- Analgesia
- Glaucoma42

The expert group’s recommendations presented a statement of the overarching goals and principles of scientific investigation in general and the scientific rationale of studying smoked marijuana in particular:

In summary, the testing of smoked marijuana to evaluate its therapeutic effects is a difficult, but not impossible, task. Until studies are done using scientifically acceptable clinical trial design and subjected to appropriate statistical analysis, the questions concerning the therapeutic utility of marijuana will likely remain much as they have to date—largely unanswered. To the extent that the NIH can facilitate the development of a scientifically rigorous and relevant database, the NIH should do so.43

This was not the only expert discussion suggesting that the use of medical marijuana should not be dismissed out of hand. A meeting sponsored by the National Academies of Sciences Institute of Medicine (IOM) to discuss the medical use of marijuana (Workshop: “Prospects for Cannabinoid Drug Development, National Academies of Sciences-Institute of Medicine”) was held on February 23–24, 1998; the proceedings were published in 1999.44 Discussion at this meeting centered on both the adverse effects and potential benefits of smoked marijuana. Participants indicated that smoked marijuana could be a valuable agent in the treatment of chemotherapy-induced nausea and vomiting, HIV-related gastrointestinal disorders, AIDS wasting, severe pain, and some forms of spasticity. Some participants stressed—as had those at the NIH conference held the preceding year—that because the whole marijuana plant contains many possibly active cannabinoids besides THC, its possible efficacy may not be replicated by medications containing only THC (e.g., dronabinol, see infra, Part VI).

Nonetheless, the suggestion that marijuana might have some medical utility that should be discussed at an impartial conference of experts and that its properties should be subjected to scientific investigation evoked a forceful but inaccurate response from the federal government:

A past evaluation by several Department of Health and Human Services (HHS) agencies, including the Food and Drug Administration (FDA), Substance Abuse and Mental Health Services Administration (SAMHSA) and National Institute for Drug Abuse (NIDA), concluded that no sound scientific studies supported medical use of marijuana for treatment in the United States, and no animal or human data supported the safety or efficacy of marijuana for general medical use.45
This “authoritative” statement did not go unnoticed by the media. A reporter for the New York Times observed that:

The Food and Drug Administration said Thursday that “no sound scientific studies” supported the medical use of marijuana, contradicting a 1999 review by a panel of highly regarded scientists. The announcement [which] inserts the health agency into yet another fierce political fight . . . directly contradicts a 1999 review by the Institute of Medicine [IOM], a part of the National Academy of Sciences, the nation’s most prestigious scientific advisory agency. That review found marijuana to be “moderately well suited for particular conditions, such as chemotherapy-induced nausea and vomiting and AIDS wasting.”

Dr. John Benson, co-chairman of the IOM committee and professor of internal medicine at the University of Nebraska Medical Center, whose report had suggested that smoked marijuana could have therapeutic value strongly disputed the FDA’s stance. The federal government “loves to ignore our report,” said Dr. Benson. “They would rather it never happened.”

Dr. Jerry Avorn, a medical professor at Harvard Medical School declared: “Unfortunately, this is yet another example of the F.D.A. making pronouncements that seem to be driven more by ideology than by science.”

More recently, the American College of Physicians (ACP) issued a position paper emphasizing the importance of sound scientific study to evaluate the role of marijuana in modern medical therapy. The ACP paper stressed that this agent was neither devoid of potentially harmful effects nor universally effective. Nonetheless, it strongly recommended that marijuana should not be summarily rejected as a bona fide therapeutic agent and “urged review of marijuana’s status as a Schedule I controlled substance and its reclassification into a more appropriate schedule, given the scientific evidence regarding marijuana’s safety and efficacy in some clinical conditions.”

The ACP took note of the historical fact that marijuana has been smoked for its medicinal properties for centuries. It cited extant scientific data and stated that preclinical, clinical, and anecdotal reports suggest numerous potential medical uses for marijuana. The ACP’s position paper recognized that while the indications for using marijuana to treat some conditions (e.g., HIV wasting and chemotherapy-induced nausea and vomiting) have been well documented, less information is available about other potential medical uses. The report reached several important conclusions. It stated that:

Additional research is needed to clarify marijuana’s therapeutic properties and determine standard and optimal doses and routes of delivery. Unfortunately, research expansion has been hindered by a complicated federal approval process, limited availability of research-grade marijuana, and the debate over legalization.

Marijuana’s categorization as a Schedule I controlled substance raises significant concerns for researchers, physicians, and patients. As such, the College’s policy positions on marijuana as medicine are as follows:

- ACP supports programs and funding for rigorous scientific evaluation of the potential therapeutic benefits of medical marijuana and the publication of such findings.
- ACP supports increased research for conditions where the efficacy of marijuana has been established to determine optimal dosage and route of delivery.
- Medical marijuana research should not only focus on determining drug efficacy and safety but also on determining efficacy in comparison with other available treatments.
- ACP encourages the use of nonsmoked forms of THC that have proven therapeutic value.
- ACP urges review of marijuana’s status as a schedule I controlled substance and its reclassification into a more appropriate schedule, given the scientific evidence regarding marijuana’s safety and efficacy in some clinical conditions.
- ACP strongly supports exemption from federal criminal prosecution; civil liability; or professional sanctioning, such as loss of licensure or credentialing, for physicians who prescribe or dispense medical marijuana in accordance with
state law. Similarly, ACP strongly urges protection from criminal or civil penalties for patients who use medical marijuana as permitted under state laws.52

MARIJUANA, SCHEDULING, AND POLITICS

The FD&C Act requires that a new drug be proven safe and effective for the specific condition for whose treatment approval is sought, not that it be proven superior to already approved medications. As discussed above, marijuana has documented beneficial properties for the treatment of a number of diseases and has minimal risks when used under a physician’s supervision. Yet, it remains a Schedule I controlled substance “without currently accepted medical use in treatment in the United States.”53 This decision was not made by scientific experts but by Congressional legislative fiat. What was the role of politics in Congress’ decision to circumvent, albeit legally, the review process that has governed approval decisions for almost all medications?54

In passing the CSA, Congress specifically designated marijuana as a Schedule I Controlled Substance, thereby pronouncing that it has no currently accepted medical use in treatment in the United States.55 This Congressional action was brought to the attention of the Supreme Court when the Oakland Cannabis Club challenged the federal government’s authority to enjoin its distribution of medical marijuana on the grounds that Congressional designation as a Schedule I controlled substance was invalid. The Court declared that Congressional scheduling was binding, and that it was of no legal consequence that the Schedule I designation had been based on Congressional action rather than scientific evidence. The Court stated:

The Cooperative points out, however, that the Attorney General [who would have acted on the scientific findings made by the FDA] did not place marijuana into schedule I. Congress put it there, and Congress was not required to find that a drug lacks an accepted medical use before including the drug in schedule I. We are not persuaded that this distinction has any significance to our inquiry . . . Nothing in the statute suggests that there are two tiers of schedule I narcotics, with drugs in one tier more readily available than drugs in the other. On the contrary, the statute consistently treats all schedule I drugs alike.57

Four years later, the high court again emphasized the significance of Congressional authority to issue a schedule I classification for marijuana:

In enacting the CSA, Congress classified marijuana as a Schedule I drug . . . Schedule I drugs are categorized as such because of their high potential for abuse, lack of any accepted medical use, and absence of any accepted safety for use in medically supervised treatment . . . By classifying marijuana as a Schedule I drug, as opposed to listing it on a lesser schedule, the manufacture, distribution, or possession of marijuana became a criminal offense, with the sole exception being use of the drug as part of a Food and Drug Administration pre-approved research study. The CSA provides for the periodic updating of schedules . . . Despite considerable efforts to reschedule marijuana, it remains a Schedule I drug.58

Thus, in the face of several well-controlled studies demonstrating marijuana’s safety and efficacy in relieving both pathologic and experimentally-induced pain as well as the often-incapacitating symptoms of nausea, vomiting, loss of appetite, and depression,59 the recommendations of several scientific groups (some with the support of the federal government) that research should be unrestrained by political considerations, and the finding by an administrative law judge as well as well-regarded scientific committees that its designation as a Schedule I controlled substance was unjustified60 marijuana remains a Schedule I medication and, as far as I know, there have been no realistic attempts to bring about a change in this situation.
Legislators rather than “experts qualified by scientific training and experience” have acted to deny marijuana admission to legitimate medical practice.

**THE CITIZENS OF CALIFORNIA DISAGREED WITH CONGRESS AND MAINTAINED THAT MARIJUANA HAD MEDICAL VALUE**

Why was the use of medical marijuana legitimized through legislation, ballot initiatives, and referenda in 13 states rather than by “experts qualified by scientific training and experience?” Although my response to this question will focus on California, it is likely that many of the factors that led to the adoption of California’s Proposition 215 also impelled the citizens of the other twelve states to take similar action.

The promulgation of Proposition 215 and its overwhelming acceptance by the people of California represented a popular sense that patients were being denied a medication that could alleviate suffering. It expressed a reaction to perceived federal intransigence and even arrogance, and the lack of interest in sponsoring research on this compound on the part of the pharmaceutical industry. The voters’ decision was, in effect, a repudiation of the proposition that scientific data should be dispositive in drug approval that was akin to the stance taken by the Congress. The voters’ view that powerful forces were preventing access to novel therapies manifested a recurring conflict between the desire for personal autonomy and what they perceived as paternalistic interference by the government.

This conflict is exemplified by the significant case brought by Angel Raich. Ms. Raich claimed that she had a fundamental right to use medical marijuana, an agent that she believed necessary to preserve her life. Although her use of medical marijuana was legal under California’s Proposition 215, it was illegal under federal law. Raich challenged the constitutionality of the CSA, asserting that her right to use marijuana was “deeply rooted in this nation’s history and traditions and implicit in the concept of ordered liberty.” The Court of Appeals for the Ninth Circuit denied her appeal. Her statements after this decision—“It’s not every day in this country that someone’s right to life is taken from them”—exemplified the thoughts and feelings of many advocates for medical marijuana. These individuals sincerely believed that they did not need outside scientific experts to approve what they were doing. Indeed, even the Ninth Circuit’s holding implied that if medical marijuana were to be eventually accepted and legalized, it would not necessarily require scientific evidence obtained through investigation but could be accomplished simply by judicial fiat or the will of the people.

**“GAMING THE SYSTEM”**

Will approval and legitimization of the cultivation, prescription, and dispensing of medical marijuana have unintended consequences? Recent events in California, 1 of 13 states that has approved the use of marijuana for medical purposes, suggest to some that legalization might increase the cultivation of and traffic in marijuana for purposes other than bona fide medical therapy. In the past year, the New York Times reported that marijuana farming is on the rise in California:

There is probably no marijuana-friendlier place in the country than here in Mendocino County, where plants can grow more than 15 feet high, medical marijuana clubs adopt stretches of highway, and the sticky, sweet aroma of cannabis fills this city’s streets during the autumn harvest.

Lately, however, residents of Mendocino County, like those in other parts of California, are wondering if the state’s embrace of marijuana for medicinal purposes has gone too far. . . .

In Arcata, home of Humboldt State University, town elders say roughly one in five homes are “indoor grows,” with rooms or even entire structures converted into marijuana greenhouses. . . .

In May, Arcata declared a moratorium on clubs to allow the city council time to address the problem. Los Angeles, which has more than 180 registered marijuana clubs, the most of any city, also declared a moratorium last year.

“There were a handful initially and then all the sudden, they started to sprout up all over,” said Dennis Zine, a member of
Legalization of marijuana for medical use, however, was not the cause of this problem. Rather, the ubiquitous Internet has ensured that the cultivation, distribution, and use of marijuana for non-medical purposes will not be confined to jurisdictions that have legalized its use. A recent “Google search” for “buy medical marijuana” resulted in 1,210,000 “hits” originating from throughout the world. Moreover, the phenomenon of permissive and illegal online purchasing is not confined to marijuana alone. Diversion and illegal use of FDA-approved controlled substances is a contemporary phenomenon, as evidenced by a telling report that the vast majority of “online pharmacies” do not require that customers provide a physician’s prescription in order to obtain controlled drugs. The National Center on Addiction and Substance Abuse (CASA) stated that only 2 out of 365 Web sites that sold prescription drugs online had been certified by the National Association of Boards of Pharmacy. Although only 42% of the Web sites surveyed explicitly stated that no prescription was required to obtain drugs, 85% actually sold their drugs without a prescription. CASA’s report stated that “even among the sites that require a prescription, half allow customers to fax their scrip in, which is an invitation to fraud.”

It was, perhaps, inevitable that similar abuses of marijuana would occur whether or not it were made legal for medical use. However, the illegal dispensing of approved controlled substances such as morphine and Valium has not resulted in banning the use of these medications when required for legitimate medical treatment. Similarly, blatantly inappropriate sales of marijuana masquerading as medical therapy would not justify the Federal government’s refusal to remove the current Schedule I classification for medical marijuana if scientific data suggested rescheduling were warranted.

Such illegal access to controlled substances (including marijuana were it to be approved) is not totally without remedy. While Internet crime may be extraordinarily difficult to combat, there is no reason to believe that either the civil or criminal justice systems are incapable of dealing effectively with illegal activities conducted outside the Web.

PART VI: WILL THE FUTURE USE OF MARIJUANA EXTRACTS MOOT THE QUESTION OF MEDICAL MARIJUANA?

As observed earlier, many of today’s useful medications are derived from plants. It should, therefore, not be surprising that pharmaceuticals derived from the plant Cannabis sativa are now, or soon will be, available. This section will examine two such compounds, dronabinol and Sativex, briefly discuss their pharmacologic properties, and address the question of whether their use as legal and approved agents in medical practice will render further consideration of smoked (or otherwise used) cannabis unnecessary.

DRONABINOL

Dronabinol (synthetic THC, Marinol) is a Schedule III oral medication approved by the FDA for the treatment of AIDS-related wasting and chemotherapy-induced nausea and vomiting. Although this approval for only two indications may appear fairly restrictive, once a drug has been approved by the FDA to treat a specific pathologic condition, it can usually be prescribed legally for any disease for which a physician deems such therapy appropriate (“off-label” prescription). Although physicians may prescribe the medication for uses not approved by the FDA, the manufacturer’s advertising and promotion for off-label therapy is regulated. Although pharmaceutical companies may not directly advertise their approved medications for off-label use, they may distribute scientific literature that supports such use. Some authorities, however, maintain that these proposed changes in federal oversight may not protect the public. Could dronabinol be substituted for marijuana itself for either an approved or an off-label use? The answer is not clear at this time. Dronabinol’s route of administration poses a significant problem, as the entire capsule must be taken orally and may neither be crushed nor chewed. This requirement may prove problematic in the face of nausea or vomiting. Moreover, although the delay in onset of action and the time to peak effect of dronabinol may pose no difficulties in the
treatment of chronic conditions such as AIDS wasting, it may represent a significant problem in treating acute nausea and vomiting. In contrast, smoked marijuana’s rapid onset and easy titration to the desired effect—antiemesis without unwanted psychogenic symptoms—suggest an advantage over dronabinol. Finally, the cost of dronabinol is greater than that of marijuana. For such reasons, many who advocate the medical use of marijuana maintain that dronabinol is not an entirely satisfactory substitute. It would therefore be both appropriate and essential in the future to undertake a scientific comparison of dronabinol’s utility and efficacy to that of smoked marijuana in order to assess whether, or under what conditions, dronabinol could replace marijuana as effective medical therapy.

SATIVEX

Sativex (GW Pharma), a cannabinoid-based oral-mucosal spray, was developed in response to the inherent problems posed by the oral medication dronabinol. Sativex contains equal amounts of Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD), which are found in Cannabis sativa, but is devoid of the other compounds found in the whole plant. The rapid absorption of Sativex allows easy titration, a property that may provide a major advantage over dronabinol.

In April 2005, GW Pharma received regulatory approval for Sativex in Canada for symptomatic relief of neuropathic pain in multiple sclerosis. In August 2007, Health Canada approved Sativex as an adjunctive analgesic treatment in patients with advanced cancer who experience moderate to severe pain during the highest tolerated dose of strong opioid therapy for persistent pain. The use of Sativex in treating multiple sclerosis is now allowed in the United Kingdom and the drug is currently undergoing late stage clinical testing in Europe and the United States. It is therefore likely that Sativex will eventually be approved by the FDA as a scientifically-based therapeutic agent.

Several published studies support the efficacy of Sativex in ameliorating the symptoms of neuropathic pain and spasticity. In a 5-week, randomized, double-blind, placebo-controlled study, the intensity of neuropathic pain of peripheral origin was significantly ameliorated by Sativex, as compared with placebo.

In another investigation, Iskedjian and coworkers summarized the safety and efficacy data derived from four studies evaluating the ability of Sativex to assuage the debilitating pain associated with multiple sclerosis. These randomized double-blinded studies compared Sativex and placebo and found Sativex to be superior to placebo. Multiple sclerosis-associated spasticity was significantly reduced by Sativex in another randomized, placebo-controlled study performed in three medical centers.

In view of the scientific data presented above, it is quite possible that Sativex will be approved by the FDA in the next few years. Because its rate of absorption is similar to that of smoked marijuana, it is reasonable to ask whether the FDA’s approval of Sativex will overcome any scientifically-based arguments favoring approval of medical marijuana as another Cannabis-derived medication. Because many might believe that the approval of Sativex will end the long debate over medical marijuana, it is scientifically appropriate (although not legally required) to determine whether Sativex is truly the equivalent of smoked marijuana in order to respond to this question. Because the Cannabis sativa plant contains many bioactive compounds besides THC and cannabidiol (see recommendations of the NIH Workshop, supra Part V), it cannot be stated a priori that Sativex will be an ideal replacement for marijuana in every medical situation.

COMPARING THE SAFETY AND EFFICACY OF DRONABINOL, SATIVEX, AND SMOKED MARIJUANA

Although it might appear counterintuitive that either Sativex or dronabinol could undergo a “blind” comparison with smoked marijuana, such an evaluation is not impossible. A frequently used approach is the “double-blind double-dummy” technique in which the blinded subjects randomly receive either (1) active drug (either Sativex or dronabinol) + placebo drug; or (2) placebo drug + active drug (Sativex or dronabinol). Although complete blinding may be difficult when dronabinol is being evaluated (because of its longer time to onset of action and
peak effect), the double dummy technique is appropriate and valuable when two rapidly effective compounds (smoked marijuana and Sativex) are being compared. Such testing is not only feasible but essential in order to demarcate the indications and contraindications of dronabinol, Sativex, and marijuana in the rational practice of medicine.

**PART VII: CONCLUSION**

At the beginning of this article, I posited a basic question: Should the approval or disapproval of medical marijuana as a legitimate therapeutic agent be governed by the same statute (and philosophy) that applies to all other new drugs or pharmaceutical agents, the Food, Drug, and Cosmetic Act, and should the drug be evaluated by the appropriate regulatory agency, the Food and Drug Administration, for its safety and efficacy as demonstrated by “evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience”? If not, should medical marijuana be exempt from scientific review and either be forbidden by the Congress or legitimized by a vote of the people?

What should have been a straightforward question has been complicated by politics, ideology, prejudice, and unwarranted fear. These have led to the repudiation of the concept that a new drug’s approval should be based on scientific evidence, rather than political and ideological considerations. Both the Congress, through unsubstantiated and inappropriate scheduling, and a majority of voters within 13 states, through approval by referendum or ballot initiatives, have cast aside the concept that a drug’s safety and efficacy should be assessed scientifically on the basis of its risks and benefits. Congress and the federal government have succumbed to a “reefer madness” philosophy and closed their eyes to the possibility that marijuana might be, on balance, an extremely beneficial addition to our medical armamentarium. At the same time—in part due to perceived governmental obstinacy—advocates of marijuana have rejected the role of scientific evidence and replaced it with political action. This has resulted in adoption of permissive medical marijuana statutes by 13 states. Both regimens are flawed. Scientific evidence should be dispositive in deciding whether the risk-benefit profile of marijuana justifies its approval by the FDA.

Public discourse leading to legislative action would be appropriate if the debate dealt with the legalization of recreational marijuana. However, this mode of decision making is flawed when applied to the question of whether marijuana should be grown, sold, given away, or “prescribed/recommended” as a drug by licensed health care professionals. The decision whether to legalize the medical use of marijuana should be based on a dispassionate scientific analysis; neither disapproval by the legislature nor approval by popular vote should be dispositive.

Medical marijuana is being advocated and recommended for use as a drug as defined by the FD&C Act. Although political considerations have made it difficult to pursue appropriate scientific studies, a number of such investigations have recently been published in the peer-reviewed literature. Data from these studies suggest that medical marijuana has demonstrated safety and efficacy in treating several devastating human pathologies. Some individuals may believe that this documentation now warrants marijuana’s approval for use as a legitimate therapeutic agent and that a Schedule I designation is no longer justified. Others may think that additional scientific scrutiny is necessary. In either case, it is no more appropriate for the Congress to legislate that marijuana has no “currently accepted medical use in treatment in the United States” than for a popular vote to reach the opposite conclusion and declare by referendum or ballot initiative that it is a legitimate pharmaceutical agent.

Instead, the FDA should be allowed to evaluate medical marijuana with the same methodology, standards, and diligence that the agency would apply to any other investigational drug. Although the FDA’s role in drug evaluation is not perfect deficiencies in its regulation and evaluation of pharmaceuticals should not be taken as an excuse to disregard the fundamental utility of the agency and to abandon the philosophy that science rather than politics should be dispositive with regard to acceptance or rejection of medications. If standards of safety and efficacy are met, the drug should be approved and then appropriately scheduled. Conversely, if medical marijuana’s analysis as a investigational new drug fails to satisfy these criteria, approval should be denied.

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Should marijuana be approved as a bona fide medication? I have not intended that this article provide an answer. Instead, I have strongly argued in favor of the concept that scientific data and methodology, rather than political and ideological considerations, can and should lead to a rational decision. Whether the data derived from current and future scientific investigations will justify the approval or disapproval of medical marijuana, or whether other purified Cannabis-derived medications will prove superior to the totality of ingredients found only in the whole plant—thereby mooting many of the questions this article has addressed—remains a challenging issue for the future.

REFERENCES AND NOTES

1. U. S. Pharmacopoeia, see http://www.usp.org/about USP (Last accessed August 29, 2008). The United States Pharmacopoeia (USP) is an official public standards-setting authority for all prescription and over-the-counter medicines and other health care products manufactured or sold in the United States. USP also sets widely recognized standards for food ingredients and dietary supplements. USP sets standards for the quality, purity, strength, and consistency of these products—critical to the public health. USP’s standards are recognized and used in more than 100 countries around the globe. These standards have helped to ensure public health throughout the world for close to 200 years. USP is a nongovernmental, not-for-profit public health organization whose independent, volunteer experts work under strict conflict-of-interest rules to set its scientific standards. USP’s contributions to public health are enriched by the participation and oversight of volunteers representing pharmacy, medicine, and other health care professions as well as academia, government, the pharmaceutical and food industries, health plans, and consumer organizations.


20. ARS Report for Congress, supra note 12 in the first Section of the paper.


22. Dronabinol (synthetic THC, MarinolTM) is an FDA-approved schedule III medication. SativexTM (an oromucosal spray containing equal amounts of Δ9-tetrahydrocannabinol and cannabidiol) is under investigation in the United States and Europe and has been approved in Canada.


24. The following four paragraphs are excerpted from Drugs, Addiction, and the Law, Chapter 15. 25. Drugs, Addiction, and the Law, Chapter 15. 26. Lisa M. Krieger, Study Targets Stalemate Over Medicinal Use of Marijuana, San Jose Mercury News, July 19, 1998 at 1A:

Five years ago, Abrams first tried to win permission to scientifically study the drug. He found a supplier of pot in the Netherlands, but the Drug Enforcement Administration (DEA) refused to let it be imported. Nor would the DEA donate pot confiscated in arrests.


According to international treaties, only an agency of the Federal government can produce and supply cannabis. Although NIDA has been the responsible Federal agency since 1974, any other Federal agency could assume both the costs and responsibilities of maintaining the farm and supplying cannabis. NIDA’s legal authority allows for the provision of cannabis only for drug abuse research purposes . . . In addition to providing cannabis for research activities, NIDA also provides cannabis to the seven patients still covered by the single patient INDs.


NIDA currently has a monopoly on the supply of marijuana available to researchers who have obtained FDA approval for their proposed protocols.

The cost to NIDA of its marijuana has been cited as a main justification for the need for extensive NIH peer-review of all new medical marijuana protocols. Just how expensive is NIDA marijuana? Dr. ElSohly, director of NIDA’s marijuana farm at the University of Mississippi, estimates that the production cost is $1,120 per kilogram. This is a relatively minor cost compared to NIDA’s estimated $487 million budget.

29. Lisa M. Krieger, Study Targets Stalemate Over Medicinal Use of Marijuana, San Jose Mercury News, July 19, 1998 at 1A:

The National Institutes of Drug Abuse would give him government-grown pot only if the National Institutes of Health approved the study. But his proposal was turned down by NIH, which . . . expressed concerns about the risks of smoking.


San Francisco AIDS specialist Dr. Donald Abrams has been trying to unravel marijuana’s mysteries since 1992, when he proposed a pilot trial to determine if marijuana helps to increase appetite in HIV-positive patients—give them the “munchies,” as it were—thereby warding off the debilitating weight loss associated with the AIDS wasting syndrome. “But our proposal was turned down time and again,” he says.

See also Drugs, Addiction, and the Law, Chapter 15.

30. Whether these events were actually a direct cause of or were simply associated in time with California’s action, on November 5, 1996, California voters passed the Compassionate Use Act (Proposition 215) by a wide margin (56% to 44%). This law permitted “seriously ill” patients and their primary caregivers to cultivate and
possess marijuana for the patients’ personal medical use if they had the “written or oral recommendation or approval of a physician.” Several diagnoses for which marijuana may have palliative benefit were listed in Proposition 215, but its use was not limited to these diagnoses, and there was no age limitation on those who used it. See infra note 183.


Inhaled marijuana is being used increasingly by people with HIV infection, especially for its purported benefit as an anti-emetic agent and an appetite stimulant in those with the AIDS wasting syndrome. Up to 2000 people infected with HIV are reported to be obtaining marijuana at a cannabis buyer’s club in our area . . . In an effort to determine whether inhaled marijuana is truly of any potential benefit and, more important, to evaluate its safety in people with AIDS, [we] designed a pilot study . . . of the overall feasibility of investigating inhaled marijuana use by such patients, before embarking on a full-scale trial of its efficacy. The pilot-drug-evaluation staff at the FDA provided valuable comments on the design of the protocol . . . The FDA and the institutional review board supported the study. Unfortunately, the DEA and the NIDA opposed it. Most disturbing was the absence of a response from either agency for an unacceptably long period, followed by the NIDA’s outright rejection of the proposal without any opportunity for dialogue or compromise. Such behavior is offensive not only to the investigators but to the patients for whom we seek to find safe and effective treatments.

32. Supra note 129. The availability of marijuana for scientific investigations also removed barriers to the studies that were detailed in Part IV (supra).

33. 68 FR 43755 (July 24, 2003):

Pursuant to Section 1301.33(a) of Title 21 of the Code of Federal Regulations (CFR), this is notice that on June 25, 2001, the University of Massachusetts, Lyle E. Craker, Professor, Department of Plant and Soil Science, Stockbridge Hall, Box 37245, Amherst, Massachusetts 01003, made application to the Drug Enforcement Administration (DEA) for registration as a bulk manufacturer of Marijuana (7360) and Tetrahydrocannabinols (7370), basic classes of Schedule I controlled substances. The University of Massachusetts-Amherst plans to bulk manufacture (cultivate) Marijuana and Tetrahydrocannabinols for distribution to approved researchers.

34. This is not the first time that an Administrative Law Judge’s ruling was overturned by the DEA. In 1998, Administrative Law Judge Francis L. Young granted a petition by the National Organization for the Reform of Marijuana Laws to have the DEA downgrade marijuana from a schedule I to a schedule II controlled substance. The administration rejected the decision.


37. Id.

38. This conference took place only a few months after California voters had passed Proposition 215.

39. Supra note 36.

40. Id.

41. Supra notes 15 and 41 in the first Section of the paper.

42. Supra note 36.

43. Id. (Emphasis added).


47. Id.

48. Id.

49. Supporting Research Into The Therapeutic Role Of Marijuana, A Position Paper Of The American College Of Physicians (2008). This paper, written by Tia Taylor, MPH, was developed for the Health and Public Policy Committee of the American College of Physicians: J. Fred Ralston, MD, FACP, Chair; Molly Cooke, MD, FACP, Vice Chair; Andrew A. Chang, MA, Charles Cutler, MD, FACP, MA; David A. Fleming, MD, FACP; Brian P. Freeman, MD, FACP; Robert Gluckman, MD, FACP; Mark Liebow, MD, FACP; Kenneth Musana, MB, ChB; Robert McLean, MD, FACP; Mark Purtle, MD, FACP; P. Preston Reynolds; and Kathleen Weaver, MD, FACP. It was approved by the Board of Regents in January 2008. (Last accessed on July 22, 2008, at http://www.acponline.org/advocacy/where_we_stand/other_issues/medmarijuana.pdf; http://www.acponline.org/acp_news/medmarinews.htm.)

50. See, e.g., the ACP’s recommendation that cannabis not be used to treat glaucoma: High intraocular pressure (IOP) is a known risk factor for glaucoma. Cannabinoids have been shown to have neuroprotective properties and to reduce IOP, pupil restriction, and
The Treasury Department collected and considered scientific and medical opinion prior to the Tax Act hearings, but the desire to present a solid front when the department appeared before the committees of Congress caused the officials to ignore anything that qualified or minimized the evils of marijuana. The political pressure to put “something on the books” . . . [made] the marijuana hearings a classic example of bureaucratic overkill.

Everyone from the Treasury Department who appeared for the Tax Act gave it full support while those who might have had more moderate views remained in the background. [Even] the most “liberal” spokesmen were among the most eager to protect the public by prohibiting cannabis.

Congressional action based on politics rather than scientific evidence has not been confined to marijuana. A far more recent example is the fate of an effective public health measure based on an inaccurate, but politically expedient belief, that needle exchange (supplying clean needles to drug users) would increase illegal drug use. Until 2008, Congress had repeatedly legislated against this proven means of preventing transmission of HIV and hepatitis. As a result, “The District of Columbia [was] the only city in the nation barred by federal law from investing its own locally raised tax dollars to support needle exchange programs.” See, e.g., Prevention Works: Needle Exchange in the Nation’s Capital (1998). (Last accessed August 23, 2008, at http://www.preventionworkscd.org/about.html.)

55. 21 U.S.C. §812(c).

56. Heroin, designated as a Schedule I controlled substance under 21 U.S.C. §812(a), is an accepted and legal therapeutic agent in many countries and there is no scientific justification for designating it as schedule I. Indeed, once heroin is administered to humans, it is converted to morphine (Schedule II) by the liver and, therefore, has properties not dissimilar to those of morphine. Its designation as schedule I exemplifies that the interaction of politics and science is not confined to medical marijuana. See, e.g., M Giovannelli, N Bedforth, Aitkenhead. Survey of intrathecal opioid usage in the UK. Eur J Anaesthesiol. 2008;25:118. (Opioids such as diamorphine were used in 136 (78.2%) of departments.) See also A Hallett, F O’Higgins, V Francis, TM Cook. Patient-controlled intranasal diamorphine for postoperative pain: an acceptability study. Anaesthesia 2000;55:532. (“We found patient-controlled [heroin] analgesia an effective technique, which was well tolerated by patients and . . . was without unpleasant side-effects.”) M Hewitt, A Goldman, GS Collins, M Childs, R Hain. Opioid use in palliative care of children and young people with cancer. J Pediatr. 2008;152:39. (The use of heroin was documented in 58% of pediatric patients undergoing palliative care for terminal cancer.) Jason M. Kendall, Barnaby C. Reeves, Victoria S. Latter. Multicentre randomised controlled trial of nasal diamorphine for analgesia in children and teenagers with cancer. BMJ. 2001;322:261. (“Nasal diamorphine [heroin] spray should be the preferred method of pain relief in children and teenagers presenting to emergency departments in acute pain with clinical fractures. The diamorphine spray should be used in place of intramuscular morphine.”) J Sawynok. The therapeutic use of heroin: a review of the pharmacological literature. Can J Physiol Pharmacol. 1986;64:1. (“Administered orally, heroin is approximately 1.5 times more potent than morphine in controlling chronic pain in terminal cancer patients . . . . Given parenterally for acute pain, heroin is 2–4 times more potent than morphine and faster in onset of action. When the potency difference is accounted for, the pharmacological effects of heroin do not differ appreciably from those of morphine.”)


58. Gonzales v. Raich, 545 U.S. 1, 14, 15 (2005) (emphasis added, citations omitted).

59. Note, however, that if medical marijuana were removed from schedule I and approved for relief of these conditions, it probably could then be used “off-label” for any purpose a physician deemed reasonable (further discussed in Part VI, infra). See United States v. Evers, 643 F.2d 1043 (5th Cir. 1981).
60. See, e.g., Gonzales v. Raich, 545 U.S. 1, n.23 (2005):

After some fleeting success in 1988 when an Administrative Law Judge (ALJ) declared that the DEA would be acting in an “unreasonable, arbitrary, and capricious” manner if it continued to deny marijuana access to seriously ill patients, and concluded that it should be reclassified as a Schedule III substance, Grinspoon v. DEA, 828 F. 2d 881, 883–884 (CA1 1987), the campaign has proved unsuccessful. The DEA Administrator did not endorse the ALJ’s findings, 54 Fed. Reg. 53767 (1989), and since that time has routinely denied petitions to reschedule the drug, most recently in 2001. 66 Fed. Reg. 20038 (2001).


In 1988, after two years of hearings, DEA administrative-law judge Francis Young recommended shifting marijuana to Schedule II on the grounds that it was safe and had a “currently accepted medical use in treatment.” Specifically, Judge Young found that “marijuana, in its natural form, is one of the safest therapeutically active substances known to man . . . .” At present, it is estimated that marijuana’s LD50 (median lethal dose) is around 1:20,000 or 1:40,000. In layman’s terms . . . a smoker would theoretically have to consume 20,000 to 40,000 times as much marijuana as is contained in one marijuana cigarette . . . nearly 1500 pounds of marijuana within about fifteen minutes to induce a lethal response.” As for medical use, the judge concluded, among other things, that marijuana “has a currently accepted medical use in treatment in the United States for nausea and vomiting resulting from chemotherapy treatment.” The administrator of the DEA rejected Young’s recommendation, on the basis that there was no scientific evidence showing that marijuana was better than other approved drugs [this is not required by the FDA statute—all that must be demonstrated is safety and efficacy]. Further attempts to get the courts to reclassify marijuana have been unsuccessful.

61. Supra note 21 in the first Section of the paper.
62. The Compassionate Use Act of 1996—SECTION 1. Section 11362.5 is added to the Health and Safety Code, to read: 11362.5.

(a) This section shall be known and may be cited as the Compassionate Use Act of 1996.

(b) (1) The people of the State of California hereby find and declare that the purposes of The Compassionate Use Act of 1996 are as follows:

(A) To ensure that seriously ill Californians have the right to obtain and use marijuana for medical purposes where that medical use is deemed appropriate and has been recommended by a physician who has determined that the person’s health would benefit from the use of marijuana in the treatment of cancer, anorexia, AIDS, chronic pain, spasticity, glaucoma, arthritis, migraine, or any other illness for which marijuana provides relief.

(B) To ensure that patients and their primary caregivers who obtain and use marijuana for medical purposes upon the recommendation of a physician are not subject to criminal prosecution or sanction.

(C) To encourage the federal and state governments to implement a plan to provide for the safe and affordable distribution of marijuana to all patients in medical need of marijuana.

(b) (2) Nothing in this section shall be construed to supersede legislation prohibiting persons from engaging in conduct that endangers others, nor to condone the diversion of marijuana for nonmedical purposes.

(c) Notwithstanding any other provision of law, no physician in this state shall be punished, or denied any right or privilege, for having recommended marijuana to a patient for medical purposes.

(d) Section 11357, relating to the possession of marijuana, and Section 11358, relating to the cultivation of marijuana, shall not apply to a patient, or to a patient’s primary caregiver, who possesses or cultivates marijuana for the personal medical purposes of the patient upon the written or oral recommendation or approval of a physician.

(e) For the purposes of this section, “primary caregiver” means the individual designated by the person exempted under this section who has consistently assumed responsibility for the housing, health, or safety of that person.

SECTION 2. If any provision of this measure or the application thereof to any person or circumstance is held invalid, that invalidity shall not affect other provisions or applications of the measure that can be given effect without the invalid provision or application, and to this end the provisions of this measure are severable.

63. Raich v. Gonzales, 500 F.3d 850, 855 (9th Cir. 2007):

Appellant Angel McClary Raich is a Californian who uses marijuana for medical treatment. Raich has been diagnosed with more than ten serious medical conditions, including an inoperable brain tumor, a seizure disorder, life-threatening weight loss, nausea, and several chronic pain disorders. Raich’s doctor . . . testified that he had explored virtually every legal treatment alternative, and that all were either ineffective or resulted in intolerable side effects [and] provided a list of
thirty-five medications that were unworkable because of their side effects.

64. Raich v. Gonzales, 500 F.3d 850, 863 (9th Cir. 2007).

65. See, e.g., Jesse McKinley, Dying Woman Loses Appeal On Marijuana As Medication, New York Times, March 15, 2007 at A18:

Angel McClary Raich says she uses marijuana [eating or smoking it every couple of hours] on doctors' recommendation to treat an inoperable brain tumor and a battery of other serious ailments [including scoliosis and chronic nausea]. Ms. Raich, 41, asserts that the drug effectively keeps her alive, by stimulating appetite and relieving pain, in a way that prescription drugs do not.

66. Bob Egelko, Jim Herron Zamora, Medical Pot User Loses Again in Federal Court, San Francisco Chronicle, March 15, 2007 at A11: “I don’t want that coffin, but from this point on I am walking dead,” she said. “I will continue to use cannabis. I will continue to smoke cannabis... This is real medicine and the federal government cannot tell us any differently.”

67. Raich v. Gonzales, 500 F.3d 850, 866 (9th Cir. 2007):

We agree with Raich that medical and conventional wisdom that recognizes the use of marijuana for medical purposes is gaining traction in the law as well. But that legal recognition has not yet reached the point where a conclusion can be drawn that the right to use medical marijuana is “fundamental” and “implicit in the concept of ordered liberty.” For the time being, this issue remains in the arena of public debate and legislative action. (Emphasis added.)


New guidelines from the California Attorney General’s office aim to clear up some of the confusion that has long plagued the state’s 1996 medical-marijuana law... The guidelines, issued by AG Jerry Brown this week, give legal sanction under state law to storefront medical-marijuana collectives, but also clarify the circumstances under which law enforcement can go after drug dealers using the law as a front for illicit marijuana sales. “It clarifies the rules and makes it easier for law enforcement to do their jobs... and the users and advocates are happy because it restated what is permitted by the initiative and the statute,” Brown said. “It did what law is supposed to do—it set the ground rules for action both by individuals and by the government.”

Dispensaries cannot be operated for profit, the guidelines say, and must maintain detailed records, including documents proving that customers are legitimate medical users. “The collective should not purchase marijuana from, or sell to, nonmembers; instead, it should only provide a means for facilitating or coordinating transactions between members,” the new guidelines state. “The cycle should be a closed circuit of marijuana cultivation and consumption with no purchases or sales to or from nonmembers. To help prevent diversion of medical marijuana to nonmedical markets, collectives and cooperatives should document each member’s contribution of labor, resources, or money to the enterprise. They also should track and record the source of their medical-marijuana dispensaries thought to be violating state and/or federal laws.


70. See, e.g., http://www.mainevocals.net/printable-medform.htm:

Medical Marijuana Provider Form (Maine)—

1. My name is: ___________________ (insert full name)
   My mailing address is: ________________ (insert full address)


3. In order to procure my marijuana, I need to either grow it or buy it from someone which is a problem and a danger to me. I am concerned that I won’t be able to grow enough or find enough marijuana to buy for my needs, and I need someone to help me to do this.

4. I hereby nominate, appoint, and constitute __________ as my medical marijuana provider for the sole purpose of assisting me with the growing of marijuana, and/or growing marijuana for my use, and/or supplying me with commercial marijuana which I require to treat my medical condition/disease.

Dated:
Signature:
Personally appeared the above-named. Before me on the date above-written and acknowledged his/her signature and the above stated facts as true to the best of his/her knowledge.
Notary Public/Attorney at Law ___________________
dronabinol for treating multiple sclerosis, spasticity, or depression. See, e.g., United States v. Evers, 643 F.2d 1043, 1048 (5th Cir. 1981):

Congress did not intend the Food and Drug Administration to interfere with medical practice... [or] regulate the practice of medicine as between the physician and the patient. Congress recognized a patient’s right to seek civil damages in the courts if there should be evidence of malpractice, and declined to provide any legislative restrictions upon the medical profession.


The U.S. Food and Drug Administration (FDA) today issued draft guidance on “Good Reprint Practices” for industry use in the distribution of medical or scientific journal articles and reference publications that involve unapproved uses of FDA-approved drugs and medical devices. Section 401 of the Food and Drug Administration Modernization Act set out guidelines that allowed the dissemination of information on unapproved uses of FDA-approved products. As long as the guidelines were met by the manufacturers, the dissemination of such materials was not viewed by the FDA as evidence of an intent to promote the product for an “off-label” use. However, Section 401 expired on Sept. 30, 2006. The FDA’s “Good Reprint Practices” draft guidance recommends principles manufacturers should follow when they distribute scientific or medical journal reprints, articles, or reference publications. Some of the principles include ensuring that the article or reference be published by an organization that has an editorial board. The organization also should fully disclose any conflicts of interest or biases for all authors, contributors or editors associated with the journal article. Articles should be peer-reviewed and published in accordance with specific procedures. In addition, the draft guidance recommends against distribution of special supplements or publications that have been funded by one or more of the manufacturers of the product in the article, and articles that are not supported by credible medical evidence are considered false and misleading and should not be distributed. The FDA retains legal authority to determine whether distribution of an article or publication constitutes promotion of an unapproved “new use,” or whether such activities cause a product to be considered misbranded or adulterated under The Federal Food, Drug and Cosmetic Act. (Emphasis added.)

74. Jerry Markon, Va. Pain Doctor’s Prison Term Is Cut to 57 Months; Originally Sentenced to 25 Years, Specialist Did More Good than Harm, Judge Says, Washington Post, July 14, 2007 at B1. (After Dr. William Hurwitz was convicted of illegal drug trafficking his 25-year prison term was voided (United States v. Hurwitz 459 F.3d 463 (4th Cir. 2006)). However, a second trial again convicted him of 16 counts of drug trafficking and he was sentenced to 57 months in jail.)


In this basis, physicians can legally prescribe dronabinol for treating multiple sclerosis, spasticity, or...
78. See, e.g., Mike Mitka. Critics say FDA’s off-label guidance allows marketing disguised as science. JAMA. 2008;299:1759; Aaron S. Kesselheim, Jerry Avorn. Pharmaceutical promotion to physicians and first amendment rights. New Engl J Med. 2008;358:1727, 1731. (“Courts should consider the complex nature of the evaluation of medications when applying the Central Hudson test in the pharmaceutical context and should permit appropriate and necessary constraints on commercial speech in the pharmaceutical industry.”); Bruce M. Psaty, Wayne Ray. FDA guidelines on off-label promotion and the state of the literature from sponsors. JAMA 2008;299:1949, 1051. (“Attempting to use peer-reviewed literature for a purpose [i.e., as a substitute for studies mandated and analyzed by the FDA] for which it is so ill suited is likely not only to fail to adequately regulate off-label use but also to degrade the quality of peer-reviewed literature.”).  


80. Note also that THC is not the only active and useful compound found in Cannabis sativa. For example, cannabidiol is another active constituent of the whole plant. (See infra, discussion of Sativex.)  


83. See, e.g., MS Society Welcomes Information on Sativex, UK, Medical News Today, December 14, 2007. (Last accessed August 29, 2008, at http://www.medicalnewstoday.com/articles/91814.php). Although currently unlicensed in the United Kingdom, it is legally available to people with multiple sclerosis and around 1,200 people have so far received the drug in the that country.  


86. Derick T Wade, Petra Makela, Philip Robson, Heather House, Cynthia Bateman. Do cannabis-based medicinal extracts have general or specific effects on symptoms in multiple sclerosis? A double-blind, randomized, placebo-controlled study on 160 patients. Mult. Scler. 2004;10:434. (“Spasticity [was] significantly reduced by Sativex in comparison with placebo. There were no significant adverse effects on cognition or mood . . . )”  

87. Although the FD&C Act does not require that a new drug be shown to be superior—or even equivalent—to already approved medications (supra note 41), the FDA’s approval of Sativex™ would very likely be used as a potent political argument in favor of denying approval to medical marijuana even if it were shown to be safe and effective.  

88. Justice Douglas, a jurist with impeccable liberal credentials, called attention to the phenomenon of overreaction, prejudice, and stigmatization: See, e.g., Robinson v. California, 370 U.S. 660, 672 (1962) (Douglas, J., concurring) (quoting N.Y.L.J., June 8, 1960, p. 4, col. 2): To be a confirmed drug addict is to be one of the walking dead . . . . The teeth have rotted out; the appetite is lost and the stomach and intestines don’t function properly. The gall bladder becomes inflamed; eyes and skin turn a bilious yellow. In some cases membranes of the nose turn a flaming red; the partition separating the nostrils is eaten away—breathing is difficult. Oxygen in the blood decreases; bronchitis and tuberculosis develop. Good traits of character disappear and bad ones emerge. Sex organs become affected. Veins collapse and livid purplish scars remain. Boils and abscesses plague the skin; gnawing pain racks the body. Nerves snap; vicious twitching develops. Imaginary and fantastic fears blight the mind and sometimes complete insanity results. Often times, too, death comes—much too early in life . . . . Such is the torment of being a drug addict; such is the plague of being one of the walking dead.  

Congress for a bill to establish a marijuana transfer tax. The bill became law, and until the Comprehensive Drug Abuse Act of 1970, marijuana was legally controlled through a transfer tax for which no stamps or licenses were available to private citizens.


Reefer Madness, a 1936 film was originally produced as a morality tale designed to convince parents of the dire events (including manslaughter, suicide, rape and automobile accidents) that would befall their children if they used marijuana. Since its original production, it took on new life as an “unintentional comedy among cannabis smokers,” inspired a off-Broadway musical satire in 2001, and has achieved the status of a “cult film.”

91. Although a “favorable” risk-benefit ratio is an ideal concept, the threshold required for a “favorable” cannot be expressed with mathematical precision. Instead, some may consider that the approach taken by regulatory bodies is akin to the standard for evaluating the presence or absence of “hard core pornography” proposed by Justice Stewart in Jacobellis v. Ohio, 378 U.S. 184, 197 (1964): “I know it when I see it.” There are several reasons for what I believe to be this inherent lack of precision. First of all, every individual determines his or her own standard for evaluating the balance of risks and benefits for any action, including approval of a new medication. Therefore, it would be difficult, indeed, for society to formulate a universally acceptable approach. Moreover, there are significant philosophical differences between basing the “proper” balance on the concept that nobody should be harmed, as opposed to the utilitarian approach that seeks to maximize the good while conceding that some may be adversely affected.


A technology has a societally acceptable level of risk if its benefits outweigh its risks for every member of society . . . There is no reason why these “benefits” should be restricted to economic consequences or even noneconomic ones for which putative economic equivalents exist. People could in principle, be compensated by peace of mind, feelings of satisfaction, or reduction of other risks. . . [In contrast,] one should look at the overall balance of consequences for society, while ignoring the balance actually experienced by individuals. Under this assumption, one would not care if a technology made society as a whole better off, at the price of making some of its members miserable. Nor would one care if a few people received very large net benefits, while many others had small net losses; or, if many people had small net benefits, while imposing large net losses on a few (e.g., those living near a landfill that accepts hazardous wastes from a large area).

Nonetheless, the drug approval process requires that decisionmakers within the FDA evaluate the risks and benefits of a proposed medication and determine whether the drug meets societally reasonable criteria for approval. While mathematical precision might be desirable as a basis for this decision, its absence should not be an insurmountable obstacle to the FDA’s legal mandate to make an appropriate decision.

92. See, e.g., Cohen and DSHEA at 211–213 (citations omitted):

Recent events have illuminated major deficiencies in the FDA’s ability to protect the public. Overly hasty and, in the views of some, far too permissive drug approval, real and perceived conflicts of interest and poor morale, lack of post-marketing surveillance, and the intrusive role of politics in the FDA’s decision making procedures have severely damaged the agency’s reputation. . . . The public’s response to at least some of these problems has resulted in significant changes in the way manufacturers report data and journals publish them.


Science, like any field of endeavor, relies on freedom of inquiry; and one of the hallmarks of that freedom is objectivity. Now, more than ever, on issues ranging from climate change to AIDS research to genetic engineering to food additives, government relies on the impartial perspective of science for guidance.