

MEDICAL MARIJUANA: THE CONFLICT BETWEEN SCIENTIFIC EVIDENCE AND POLITICAL IDEOLOGY

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Cannabis, more commonly referred to as marijuana, has a long history of medical use in this country and worldwide. Accounts dating back as far as 2700 B.C. describe the Chinese using marijuana for maladies ranging from rheumatism to constipation. There are similar reports of Indians, Africans, ancient Greeks and medieval Europeans using the substance to treat fevers, dysentery and malaria. In the United States, physicians documented the therapeutic properties of the drug as early as 1840, and the drug was included in the United States Pharmacopoeia, the official list of recognized medical drugs, from 1850 through 1942. During this period, lack of appetite was one of the indications for marijuana prescription.¹

The earliest available references to the cultivation of poppies and preparation of opium date back to about 5000 BC as seen in clay tablets left by the Sumerians . . . [and was] used in Egypt as far back as 2000 BC as a children's sedative and teething remedy. . . . Galen [who] was the leading most physician in Rome from about AD 169–192 . . . so enthusiastically lauded the virtues of opium that its popularity grew to new heights by the end of the second century. . . . Opium was also used extensively by Arab physicians, the most celebrated of whom was Avicenna (AD 980–1037). Avicenna recommended opium especially for diarrhoea and eye problems A form of opium known as “laudanum” (from the Latin word Laudare, meaning “to praise”) became very popular in the seventeenth century for treating dysentery. The British physician, Thomas Sydenham (1624–89), sometimes known as “the English Hippocrates,” virtually put an official stamp of approval by advocating its use in dysentery and other such conditions.²

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¹ Mathew W. Grey, Comment, *Medical Use of Marijuana: Legal and Ethical Conflicts in the Patient/Physician Relationship*, 30 U. RICH. L. REV. 249, 251–52 (1996) (footnotes omitted).

² ANIL AGRAWAL, NARCOTIC DRUGS 17–22 (1995).

TABLE OF CONTENTS

I. INTRODUCTION—MEDICAL MARIJUANA: FORBIDDEN FRUIT OR BOON FOR HUMANITY?	37
II. THE AUTHORITY OF THE FOOD, DRUG, AND COSMETIC ACT AND THE CONTROLLED SUBSTANCES ACT	42
A. <i>The FDA: New Drug Evaluation and Medical Marijuana</i>	42
1. <i>A Brief History of the FDA</i>	44
2. <i>How the FDA Evaluates New Drugs</i>	45
B. <i>The Controlled Substances Act: Scheduling and Medical Marijuana</i>	50
III. POTENTIAL RISKS OF USING MEDICAL MARIJUANA	52
A. <i>Marijuana and Death</i>	54
B. <i>Harmful Properties of Marijuana</i>	55
1. <i>Marijuana and Addiction Liability</i>	56
2. <i>Marijuana and Cognitive Impairment</i>	58
3. <i>Marijuana and Mental Illness</i>	62
4. <i>Marijuana Smoking and the Development of Pulmonary Cancer</i>	64
5. <i>Marijuana and the “Gateway” Hypothesis</i>	67
IV. POTENTIAL BENEFITS OF MEDICAL MARIJUANA.....	70
A. <i>Early History of Medical Marijuana</i>	71
B. <i>Scientific Evidence of the Benefits of Medical Marijuana</i>	72
C. <i>Marijuana, Scheduling, and Politics</i>	86
D. <i>“Gaming the System”</i>	92
VI. WILL THE FUTURE USE OF EXTRACTS OF MARIJUANA MOOT THE QUESTION OF MEDICAL MARIJUANA?	95
A. <i>Dronabinol</i>	95
B. <i>Sativex™</i>	97
C. <i>Comparing the Safety and Efficacy of Dronabinol, Sativex™, and Smoked Marijuana</i>	99
VII. CONCLUSION.....	100

I. INTRODUCTION—MEDICAL MARIJUANA: FORBIDDEN FRUIT OR BOON FOR HUMANITY?

Two plants—*Cannabis sativa* (marijuana) and *Papaver somniferum* (the opium poppy³)—which have been cultivated for millennia, have a remarkable ability to alleviate physical and mental pain. Yet both may also cause harm. Opioids have significant addiction liability, and even a small dose causes measurable respiratory depression while larger doses are capable of producing respiratory arrest and death.⁴ Even so, their undisputed capability to relieve pain⁵ is thought to far outweigh these risks. Consequently, opium and its derivatives are a legal mainstay in today's medical practice. In contrast, although marijuana⁶ is far less addictive than the opioids⁷ and there is no documented evidence of death

³ Morphine and some other opioids may be extracted from the opium poppy. See Jerome H. Jaffe & William R. Martin, *Opioid Analgesics and Antagonists*, in GOODMAN & GILMAN'S THE PHARMACOLOGICAL BASIS OF THERAPEUTICS, 494, 502 (Alfred Goodman Gilman et al., eds., 6th ed. 1980) Additional opioids possessing similar pharmacologic effects, but not found in the opium poppy, are the products of synthesis. See *id.*

⁴ *Id.* at 502 (“Morphine is a primary and continuous depressant of respiration The respiratory depression is discernible even with doses too small to disturb consciousness, and increases progressively as the dose is increased. In man, death from morphine poisoning is nearly always due to respiratory arrest.”).

⁵ See, e.g., *id.* at 499 (“In man, morphine [derived from opium] produces *analgesia*, *drowsiness*, *changes in mood*, and *mental clouding*. . . . When therapeutic doses of morphine are given to patients with pain, they report that the pain is less intense, less discomforting, or entirely gone. . . . In addition to relief of distress, some patients experience euphoria.”).

⁶ Although “marijuana” and “cannabis” refer to the same compound, I will refer to “marijuana” rather than “cannabis” unless “cannabis” was used in a quotation.

⁷ For example, one researcher compares the dependency rates of marijuana to those of alcohol and other drugs, including heroin, an opioid:

A new study by researchers at Johns Hopkins University (FA Wagner and JC Anthony, *From the First Drug Use to Drug Dependence: Developmental Periods of Risk for Dependence upon Marijuana, Cocaine, and Alcohol*, 26 NEUROPHARMACOLOGY 479 (2002)) gives us some [useful] numbers. Based upon data from the National Comorbidity Survey with 8,100 people (men and women ages 15 to 54) who were interviewed for when they first used drugs and for when they became dependent, it was found that 12 to 13 percent became dependent on alcohol in a 10-year period. About 15 to 16 percent of people who used cocaine became dependent in the 10-year period [5-6% during their first year of use], and about 8 percent of marijuana users became dependent during the same period. . . .

[These data] are very close to previously published incidence numbers for dependence: alcohol (10 percent of users); cocaine (17 to 18 percent of users); marijuana (4 percent of users) . . . nicotine (40 percent); heroin (40 percent).

resulting from its use, even in large doses,⁸ it is illegal under federal law to cultivate or distribute marijuana in order to treat patients or for a sick individual to use it on the advice of a physician.⁹ Indeed, in some jurisdictions, even a physician's recommendation¹⁰ to patients that marijuana might alleviate their symptoms is unlawful.¹¹ Nonetheless, medical marijuana has now been legalized by thirteen states either by legislation or direct statewide popular vote in referenda

Carlton K. Erickson, *Epidemiology of Dependence: Understanding the Population*, 1 ADDICTION PROFESSIONAL 6, 6–7 (2003); *see also* Sandra P. Welch & Billy R. Martin, *The Pharmacology of Marijuana*, in PRINCIPLES OF ADDICTION MEDICINE 249, 260 (Allan W. Graham et al., eds., 3d. ed. 2003) (“Clinical and epidemiologic evidence indicates that a cannabis dependence syndrome occurs in heavy chronic users, as exhibited by a lack of control over use and continued use of the drug despite adverse personal consequences. . . . The risk of becoming dependent on cannabis probably is more like the risk for alcohol than for nicotine or the opioids, with around 10% of those who ever use cannabis eventually meeting the criteria for dependence.”(citations omitted)).

⁸ STEVEN B. DUKE & ALBERT C. GROSS, AMERICA’S LONGEST WAR: RETHINKING OUR TRAGIC CRUSADE AGAINST DRUGS 51 (1993); *see also* J. Michael Walker & Susan M. Huang, *Cannabinoid Analgesia*, 95 PHARMACOLOGY & THERAPEUTICS 127, 133 (2002) (stating that “an overdose of [Δ^9 -THC] would almost certainly not be lethal”). Findings are similar for long-term use:

Millions . . . have used marijuana on a regular, almost daily basis for decades. Despite these massive numbers of long-term users, no reliable evidence has appeared that such use has *any* adverse effects on their physical health. . . . [I]n no less than nine official investigations of the problem, in both the United States and elsewhere, none have found any significant adverse effects on human health, even mental health.

DUKE & GROSS, *supra* at 8.

Other literature implies that marijuana’s effects on circulation and respiration are not lethal in nature:

The most consistent effects on the cardiovascular system are an increase in heart rate [and] an increase in systolic blood pressure The increase in heart rate is dose related, and its onset and duration correlate well with the concentration of Δ^9 -THC in blood. . . . There are no consistent changes in respiratory rate

Jaffe & Martin, *supra* note 3, at 561.

⁹ *See* Controlled Substances Act, 21 U.S.C. § 812 (2006) (classifying marijuana as a controlled substance with a high potential for abuse, no currently accepted medical value in the United States, and a lack of accepted safety for use under medical supervision); Dominica Minore Bassett, *Legislative Review Medical Use and Prescription of Schedule I Drugs in Arizona: Is the Battle Moot?*, 30 ARIZ. ST. L.J. 441, 453 (1998).

¹⁰ Physicians may *prescribe* only those drugs which have been approved by the Food and Drug Administration.

¹¹ *See Pearson v. McCaffrey*, 139 F. Supp. 2d 113, 120–21 (D.D.C. 2001).

or ballot initiative.¹² The federal government, however, has asserted that the Controlled Substances Act (CSA)¹³ preempts such actions by the individual states, a claim that has been upheld by the Supreme Court.¹⁴

This article examines the legal, political, policy, and ethical problems raised by the recognition of medical marijuana by almost one-quarter of our states in the face of federal opposition. It uses the term “medical marijuana” to refer to any form of *cannabis sativa* used (usually by smoking¹⁵) to treat a wide variety of pathologic states and diseases. Although draconian punishment can be imposed for

¹² See CONG. RESEARCH SERV., 109TH CONG.: REVIEW AND ANALYSIS OF FEDERAL AND STATE POLICIES 17–18 & n.59 (2005) (“Twelve states, [Alaska, California, Colorado, Hawaii, Maine, Montana, Nevada, New Mexico, Oregon, Rhode Island, Vermont, and Washington] covering about 22% of the U.S. population, have enacted laws to allow the use of cannabis for medical purposes.”), available at <http://digital.library.unt.edu/govdocs/crs/permalink/meta-crs-8244:1>. See also Dawson Bell, Proposal 1: Voters Support Letting Severely Ill Grow Own Pot, *Detroit Free Press*, November 5, 2008 at News 1. (“Michigan voters favored sanctioning the use of medical marijuana to treat debilitating illness . . . apparently rejecting arguments that doing so would increase crime and juvenile drug use. The marijuana measure, Proposal 1, led 63% to 37%, with half of all precincts tallied . . . When it goes into effect—10 days after the vote is certified later this month—patients suffering from cancer, glaucoma, HIV/AIDS and other conditions can be authorized to cultivate, possess and use marijuana without fear of prosecution under state law. Michigan becomes the 13th state to approve medical marijuana, meaning that one in four Americans will live in a place where the use of the herb for medical purposes will be legal, according to advocates for legalization.”).

¹³ 21 U.S.C. §§ 801–971.

¹⁴ See *Gonzales v. Raich*, 545 U.S. 1, 17 (2005). In *Gonzales*, the Court stated that

Our case law firmly establishes Congress’ power to regulate purely local activities that are part of an economic “class of activities” that have a substantial effect on interstate commerce. As we stated in *Wickard [v. Filburn]*, 317 U.S. 111, 125 (1942), “even if appellee’s activity be local and though it may not be regarded as commerce, it may still, whatever its nature, be reached by Congress if it exerts a substantial economic effect on interstate commerce.” We have never required Congress to legislate with scientific exactitude. When Congress decides that the “total incidence” of a practice poses a threat to a national market, it may regulate the entire class.

Id. (citations omitted).

¹⁵ Advocates of medical marijuana claim (with some pharmacologic justification) that smoking allows easy titration and rapid onset of its therapeutic effects, thereby allowing its users to inhale the minimal dose necessary to achieve the desired medical effects while avoiding the frequently undesired psychological attributes of marijuana. See J. Ryan Conboy, 55 FOOD & DRUG L.J. 601, 614 (2000) (discussing researcher’s acknowledgement of the benefits of inhaling marijuana compared to oral consumption due to the rapid onset and more consistent results achieved).

the “recreational” use of marijuana,¹⁶ this article will not address the contentious question of whether to legalize or decriminalize the use of marijuana solely for its psychotropic effects, a fascinating and important area of law and policy that is outside the scope of this paper.¹⁷ Instead, the specific focus of this article will be on

¹⁶ Weldon Angelos, a first-time offender, was convicted in federal court of selling marijuana in 2004 and received a mandatory minimum sentence of 55 years in prison. *United States v. Angelos*, 433 F.3d 738, 743 (10th Cir. 2006). While this harsh sentence was based on Weldon’s possession of a gun during the drug deals (although the weapon was never used), a sentence of six to eight years would have been required *even in the absence of a gun*. *United States v. Angelos*, 345 F. Supp. 2d 1227, 1232 (D. Utah 2004). On December 4, 2005, the Supreme Court refused to hear Angelos’ appeal. *Angelos v. United States*, 549 U.S. 1077 (2006). While this may be an extreme example, the imposition of significant incarceration is by no means an isolated phenomenon. Conviction of possession of more than one kilogram of marijuana in Rhode Island carries a mandatory minimum sentence of 10 years. *See* Elizabeth Gudrais, *State May Revise Guidelines for Drug Sentences*, PROVIDENCE J. June 14, 2007, at A1. Possession of larger amounts may result in a maximum sentence of life in prison while the highest mandatory minimum sentences imposed by Connecticut and Massachusetts are five years. *Id.* However, even a *short* period of incarceration can have an extraordinary impact. Jonathan Magbie received a sentence of 10 days in prison for marijuana possession despite being a quadriplegic and first-time offender. Henri E. Cauvin, *D.C. Jail Stay Ends in Death For Quadriplegic Md. Man; Care Provided by Hospital, Corrections Dept. in Question*, WASH. POST, Oct. 1, 2004, at B1. Unfortunately, failure of the prison to provide essential medical care resulted in his death during his incarceration. *Id.*

¹⁷ Recreational marijuana has not always been a drug subject to opprobrium.

Unlike opiates and cocaine, marijuana was introduced during a period of drug intolerance. Consequently, it was not until the 1960s, 40 years after marijuana cigarettes had arrived in America, that it was widely used. The practice of smoking cannabis leaves came to the U.S. with Mexican immigrants, who had come North during the 1920s to work in agriculture, and it soon extended to white and black musicians.

As the Great Depression of the 1930s settled over America, the immigrants became an unwelcome minority linked with violence and with growing and smoking marijuana. Western states pressured the federal government to control marijuana use. The first official response was to urge adoption of a uniform state Narcotics law. Then a new approach became feasible in 1937, when the Supreme Court upheld the National Firearms Act. This act prohibited the transfer of machine guns between private citizens without purchase of a transfer tax stamp—and the government would not issue the necessary stamp. Prohibition was implemented through the taxing power of the federal government.

Within a month of the Supreme Court’s decision, the Treasury Department testified before 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.

the conflict between the development of policies based on evidence obtained through the use of scientific methods¹⁸ and those grounded on ideological and political considerations that have repeatedly entered the longstanding debate regarding the legal status of medical marijuana.¹⁹ The article addresses a basic question: should the approval of medical marijuana be governed by the same statute that applies to all other drugs or pharmaceutical agents, the Food, Drug, and Cosmetic Act (FD&C Act),²⁰ after the appropriate regulatory agency, the Food and Drug Administration (FDA), has evaluated its safety and efficacy?²¹ If not, should medical marijuana be exempted from scientific review and, instead, be evaluated by the Congress, state legislatures, or popular vote? This article argues that advocacy is a poor substitute for dispassionate analysis, and that popular votes should not be allowed to trump scientific evidence in deciding whether or not marijuana is an appropriate pharmaceutical agent to use in modern medical practice.

Part II will examine the authority of the Food, Drug, and Cosmetic Act and the Controlled Substances Act, focusing on their application to the approval of medical marijuana. The article proposes that since those advocating for medical marijuana are proposing its use as a drug, it should be evaluated as a drug according to the statutory requirements of the Food, Drug, and Cosmetic Act.

Part III will address the known risks of medical marijuana as documented in the peer-reviewed scientific literature. When possible, I will distinguish between

David F. Musto, *Opium, Cocaine and Marijuana in American History*, 265 SCIENTIFIC AMERICAN 40, 45–46 (1991).

¹⁸ Ismail Serageldin, *Science in Muslim Countries*, 321 SCIENCE 745, 745 (2008) (“[T]he scientific method should operate through observation, measurement, experiment, and conclusion, the purpose being to ‘search for truth, not support of opinions’” (quoting *Ibn Al-Haytham*, (965–c.1040))).

¹⁹ Note, however, that the “recreational” use of marijuana far exceeds its legal (under state law) incorporation into the practice of medicine, the focus of the remainder of this article. For example, while 11.1 million individuals (80% of those reporting any illicit drug use) used marijuana within one month prior to the survey, in 1997, OFFICE OF NAT’L DRUG CONTROL POLICY, THE NATIONAL DRUG CONTROL STRATEGY: 1999 at 13 (1999), a 2005 report estimated that only 115,000 people had made use of medical marijuana in the ten states in which the cultivation, possession, and use of marijuana for medical purposes was legal at the time. Susan Okie, *Medical Marijuana and the Supreme Court*, 353 NEW ENGL. J. MED. 648, 649 (2005). Although this number probably increased as legalization was extended to a total of thirteen states by 2007, see *supra* note 12, it is clear that the number of people using marijuana for therapeutic purposes will continue to be miniscule in comparison to its recreational use.

²⁰ 21 U.S.C. §§ 301–399 (2006).

²¹ Safety and efficacy must be demonstrated by “evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience.” 21 U.S.C. § 355(d)(7).

the adverse effects of recreational and medical use of marijuana since its pathology may not be identical in both settings.

Part IV will summarize the known benefits of medical marijuana as demonstrated in the peer-reviewed scientific literature.

Part V will examine the battle between investigators who have attempted to obtain scientifically valid data to use as a basis for formulating public policy and those who, apparently for ideological and political reasons, have erected barriers to such studies. I will propose that both disapproval by the Congress and approval by state referenda are equally inappropriate since each bypasses the normal FDA regulatory and evaluation procedure.

Part VI will examine the potential impact of two approved medications that contain at least one active ingredient of marijuana and analyze why their legitimate use does not moot the question of whether medical marijuana should also be accepted.

Part VII will conclude that activists on both sides are responsible for the current state of affairs and that scientific evidence devoid of political considerations should be allowed to guide future decisions regarding the status of *Cannabis sativa* when used for medical purposes.

II. THE AUTHORITY OF THE FOOD, DRUG, AND COSMETIC ACT AND THE CONTROLLED SUBSTANCES ACT

A. *The FDA: New Drug Evaluation and Medical Marijuana*

Marijuana is not just a natural remedy, an “herbal cure,” or a “holy and gracious” herb.²² Marijuana, whether smoked or taken orally as a therapeutic—not recreational—agent, is a *drug* as defined by the FD&C Act.²³ “The term ‘drug’ means . . . articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and . . . articles (other than food) intended to affect the structure or any function of the body of man or any other animals.”²⁴ New drugs (pharmaceuticals) are subject to stringent premarket approval. The FD&C Act requires that all new drugs be scientifically evaluated before they may be allowed to enter the stream of

²² Famous Quotes about Cannabis, Apr. 19, 2007, <http://www.woyano.com/view/2073/Famous-Quotes-About-Cannabis> (“To forbid or even seriously restrict the use of so holy and gracious a herb would cause widespread suffering and annoyance, and to large bands of worshipped ascetics, deep-seated anger. It would rob the people of a solace in discomfort, of a cure in sickness, of a guardian whose precious protection saves them from the attacks of evil influences” (quoting J. M. Campbell, NOTE ON THE RELIGION OF HEMP BRITISH INDIAN DRUGS COMMISSION REPORT 1839–1894)).

²³ 21 U.S.C. § 321(g)(1).

²⁴ *Id.*

interstate commerce.²⁵ As a result, drugs may not be advertised and sold in the absence of “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.”²⁶

The Food and Drug Administration is charged with ensuring the safety and efficacy of drugs marketed within the United States.²⁷ Its authority is based on the government’s responsibility to provide for public safety, a power that may at times be used in ways that abrogate individual rights.²⁸ The tension between the state’s police power and personal autonomy was set forth exquisitely by the Supreme Court over a century ago in a case pitting an individual’s assertion of the right to refuse vaccination during a smallpox epidemic in Boston against the Commonwealth of Massachusetts which invoked its police power to enforce this necessary public health measure:

The liberty secured by the Constitution of the United States to every person within its jurisdiction does not import an absolute right in each person to be, at all times and in all circumstances, wholly freed from restraint. There are manifold restraints to which every person is necessarily subject for the common good. On any other basis organized society could not exist with safety to its members. . . . Even liberty itself, the greatest of all rights, is not unrestricted license to act according to one’s own will [but is] liberty regulated by law.²⁹

The authority and justification for governmental regulation of pharmaceutical agents in order to ensure public safety was reiterated in 1979.³⁰ In a case involving patients who claimed that an unapproved drug, Laetrile, represented their last hope for survival, the Supreme Court held that public safety must prevail over the rights of both terminally ill patients seeking a cure and “inventive minds” who manufacture and sell unproven panaceas:

To accept the proposition that the safety and efficacy standards of the Act have no relevance for terminal patients is to deny the Commissioner’s authority over all drugs, however toxic or ineffectual, for such individuals. If history is to be any guide, this new market would not be long overlooked. Since the turn of the century, resourceful

²⁵ 21 U.S.C. § 355(a) (“No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application . . . is effective with respect to such drug.”).

²⁶ 21 U.S.C. § 355(d).

²⁷ See 21 U.S.C. § 393 (b).

²⁸ See, e.g., *Jacobson v. Massachusetts*, 197 U.S. 11, 26 (1905) (holding vaccination law is an allowable restraint on each person for the “common good” of society).

²⁹ *Id.*

³⁰ See *United States v. Rutherford*, 442 U.S. 544, 558–559 (1979).

entrepreneurs have advertised a wide variety of purportedly simple and painless cures for cancer, including liniments of turpentine, mustard, oil, eggs, and ammonia; peat moss; arrangements of colored floodlamps; pastes made from glycerine and limburger cheese. . . . In citing these examples, we do not, of course, intend to deprecate the sincerity of Laetrile's current proponents, or to imply any opinion on whether that drug may ultimately prove safe and effective for cancer treatment. But this historical experience does suggest why Congress could reasonably have determined to protect the terminally ill, no less than other patients, from the vast range of self-styled panaceas that inventive minds can devise.³¹

1. A Brief History of the FDA

Today's FDA was born in response to investigative journalism and developed out of disasters rather than foresight.³² Much of the impetus behind its origin in 1906 came from the public's reaction to the revelation of abuses within the food industry.³³ The need for government regulation became grossly apparent through shocking disclosures of unsanitary conditions in food processing plants, none more significant than those revealed in Upton Sinclair's chilling novel *The Jungle*, which vividly described the fraud and abuse occurring in the meat packing industry in the early 1900s.³⁴ The novel's powerful role in precipitating the passage of the first Food and Drug Act is displayed in the following excerpt:

There would be meat that had tumbled out on the floor, in the dirt and saw-dust, where the workers had tramped and spit uncounted billions of consumption germs. There would be meat stored in great piles in rooms; and the water from leaky roofs would drip over it, and thousands of rats would race about on it. It was too dark in these storage places to see well, but a man could run his hand over these piles of meat and sweep off handfuls of the dried dung of rats. These rats were nuisances, and the packers would put poisoned bread out for them; they would die, and then rats, bread, and meat would go into the hoppers together. This is no fairy-story, and no joke; the meat would be shoveled into carts, and the man who did the shoveling would not trouble to lift out a rat even when he saw one³⁵

³¹ *Id.* at 557–58.

³² See, e.g., Peter J. Cohen, *Science, Politics, and the Regulation of Dietary Supplements: It's Time to Repeal DSHEA*, 31 AM. J.L. & MED. 175, 178 (2005).

³³ See *id.*

³⁴ UPTON SINCLAIR, *THE LOST FIRST EDITION OF UPTON SINCLAIR'S THE JUNGLE* (Gene DeGruson ed., Peachtree Publishers 1988) (1906).

³⁵ *Id.* at 121–22.

Congress reacted to these disclosures by passing the original Federal Foods and Drug Act in 1906.³⁶ This Act, the progenitor of today's FD&C Act, prohibited interstate commerce of misbranded and adulterated food, drinks, and drugs and required accurate listing of contents (including narcotics and marijuana) on labels of patent medicines shipped in interstate commerce.³⁷ The subsequent evolution of food and drug legislation clearly illustrates what I term "government by crisis." It took the elixir of sulfanilamide tragedy,³⁸ in which a mislabeled and adulterated medication killed over one hundred people in fifteen states, as far east as Virginia and as far west as California, to bring about passage of the Food, Drug, and Cosmetic Act of 1938.³⁹ This act required not only that drugs be correctly labeled but that they meet safety standards prior to marketing.⁴⁰ It was not until 1962, after the use of thalidomide by pregnant women had resulted in the birth of thousands of newborns with major physical disabilities, that the Kefauver-Harris Amendment mandated that drugs be demonstrated *effective* as well as safe before they could enter interstate commerce.⁴¹ These and other changes in the scope of the FD&C Act were made out of the conviction that only strong governmental action could protect individuals from harm that they had no way of combating on their own.⁴²

2. *How the FDA Evaluates New Drugs*

Before a drug is permitted to enter the stream of interstate commerce,⁴³ the FD&C Act⁴⁴ requires that the FDA evaluate its safety and efficacy as demonstrated

³⁶ See PETER BARTON HUTT & RICHARD A. MERRILL, *FOOD AND DRUG LAW: CASES AND MATERIALS* 8 (2d. ed. 1991) (1980).

³⁷ James Harvey Young, *The Long Struggle for the 1906 Law*, FDA CONSUMER, June 1981, at 16, available at <http://www.foodsafety.gov/~lrd/history2.html>.

³⁸ Carol Ballentine, *Taste of Raspberries, Taste of Death: The 1937 Elixir Sulfanilamide Incident*, FDA CONSUMER, June 1981, at 18, available at <http://www.fda.gov/oc/history/elixir.html>.

³⁹ Arthur H. Hayes, Jr., *Food and Drug Regulations After 75 Years*, 246 J. AM. MED. ASS'N, 1223, 1224 (1981).

⁴⁰ 21 U.S.C. § 355(b)(1) (2006).

⁴¹ Kefauver-Harris Amendment of 1962, Pub. L. No. 87-781, 76 Stat. 780 (codified in scattered sections of 21 U.S.C. §§ 301-399); see also C. Frederick Beckner III, *The FDA's War on Drugs*, 82 GEO. L.J. 529, 529-30 (1993) (explaining the effect of the Kefauver-Harris Amendment).

⁴² Beckner, *supra* note 41, at 530 (describing how information asymmetries in the pharmaceutical industry create market failures that demonstrate the need for consumer protection).

⁴³ The *Commerce Clause* encompasses virtually all aspects of drug marketing and advertising, as they are "part of an economic 'class of activities' that have a substantial effect on interstate commerce." *Gonzales v. Raich*, 545 U.S.1, 2, 17 (2005).

⁴⁴ Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 321 et. seq.

by “evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience.”⁴⁵ The Act does not require that the new drug be proven superior to already approved drugs,⁴⁶ only that the sponsor of the drug provide “substantial evidence that the drug will have the effect it purports”⁴⁷

That marijuana is a botanical should not, in itself, preclude scientific investigation of the drug and, if warranted, its approval as a legitimate therapeutic agent. Botanicals are the source of the active ingredients in many drugs commonly used in today’s medical practice. Digitalis leaf, derived from *Digitalis purpurea* (the foxglove plant), is the source of drugs commonly used to treat congestive heart failure.⁴⁸ *Papaver somniferum* (the opium poppy) provides opium⁴⁹ from which morphine used to treat pain is derived.⁵⁰ Donnatal™, a medication used to treat irritable bowel syndrome, contains belladonna alkaloids—originally found in *Atropa belladonna*, the deadly nightshade plant—as one of its active ingredients.⁵¹ Ephedrine (derived from the plant *Ephedra sinica*) is used to treat hypotension⁵² and aspirin (found in the bark of *Salix alba*, the White Willow tree,⁵³ is a

⁴⁵ 21 U.S.C. § 321.

⁴⁶ See, e.g., Robert Temple, Susan S. Ellenberg, Placebo-Controlled Trials and Active-Control Trials in the Evaluation of New Treatments, 133 ANN INTERN MED 455, 460 (2000) (“[U]nder law, a drug need not be superior to or even as good as [another drug] to be approved.”); see also HUTT & MERRILL, *supra* note 36, at 527 (“The history of the 1962 Amendments clearly reveals Congress’ intention that FDA not refuse to approve a drug on the ground of ‘relative efficacy,’ *i.e.*, that a more effective drug is available.”).

⁴⁷ 21 U.S.C.A. § 355(d).

⁴⁸ See Paul J. Hauptman & Ralph A. Kelley, *Digitalis*, 1999 CIRCULATION 1265, 1265 (explaining the use of *digitalis purpurea* to treat congestive heart failure), available at <http://circ.ahajournals.org/cgi/content/full/99/9/1265>.

⁴⁹ See Jaffe & Martin, *supra* note 3, at 494, 509 (“Powdered opium . . . is a light brown powder. The official morphine content of opium is 10.0 to 10.5% by weight. . . . Paregoric, U.S.P. (*camphorated opium tincture*) is a hydroalcoholic preparation in which there is also benzoic acid, camphor, and anise oil. The usual adult dose is 5 to 10 ml, which corresponds to 2 to 4 mg of morphine.”).

⁵⁰ See Paul L. Schiff, Jr., *Opium and Its Alkaloids*, 66 AM. J. OF PHARMACEUTICAL EDUC. 186, 189 (2002), available at <http://www.ajpe.org/legacy/pdfs/aj660217.pdf>; William H. Wehmacher, *Digitalis Treatment Decreases Mortality and Morbidity in Heart Failure Patients*, 108 CARDIOLOGY, 157, 157–58 (2007).

⁵¹ See E.A. Mayer, K. Tillisch & S. Bradesi, *Review Article: Modulation of the Brain-gut Axis As a Therapeutic Approach in Gastrointestinal Disease*, 24 ALIMENTARY PHARMACOLOGY & THERAPEUTICS 919, 921 (2006); Donnatal Facts and Comparisons at Drugs.com, <http://www.drugs.com/cdi/donnatal.html> (last visited Mar. 28, 2009).

⁵² See Marcel P. Vercauteren et al., *Prevention of Hypotension by a Single 5-mg Dose of Ephedrine During Small-Dose Spinal Anesthesia in Prehydrated Cesarean Delivery Patients*, 90 ANESTHESIA & ANALGESIA 324, 327 (2000).

⁵³ S. Chrubasik et al., *Treatment of Low Back Pain Exacerbations with Willow Bark Extract: A Randomized Double-Blind Study*, 109 AM. J. MED. 9, 9 (2000).

ubiquitous over-the-counter remedy.⁵⁴ Taxol™, a potent therapy for breast cancer,⁵⁵ is derived from *Taxus brevifolia* (Pacific Yew Tree).⁵⁶ All of these agents are legal and FDA-approved when employed for legitimate therapeutic use.⁵⁷

With this background, this article now briefly outlines the statutory procedure for conducting adequate testing for safety and efficacy in appropriate animals and then humans.⁵⁸ After the initial studies of the pharmacological and physiological effects have been completed in animals, the manufacturer must apply to the FDA for an investigational new drug (IND) exemption which, if approved, allows the drug to be transported across state lines for extensive testing of safety and efficacy in humans.⁵⁹ The IND application must provide the FDA with information

⁵⁴ *Id.*

⁵⁵ See M. Hezari et al., *Purification and Characterization of Taxa-4(5),11(12)-diene Synthase from Pacific Yew (Taxus Brevifolia) that Catalyzes the First Committed Step of Taxol Biosynthesis*, 322 ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS 437, 437 (1995).

⁵⁶ See Frankie Ann Holmes et al., *Phase II Trial of Taxol, an Active Drug in the Treatment of Metastatic Breast Cancer*, Abstract 83 J. NAT'L CANCER INST. 1797, 1797 (1991), available at <http://inci.oxfordjournals.org/cgi/content/abstract/abstract/83/24/1797-a>.

⁵⁷ See Tyler M. Simpson, *Balking at Responsibility: Baseball's Performance-Enhancing Drug Problem in Latin America*, 14 L. & BUS. REV. AM. 369, 376 (2008); U.S. Food & Drug Administration, "Taxol" <http://www.accessdata.fda.gov/Scripts/cder/DrugsatFDA/>; see also Taxol Information from Drugs.com, <http://www.drugs.com/taxol.html> (last visited Mar. 11, 2009) (noting common therapeutic uses of Taxol); Access Medicine—Hyoscyamine, Atropine, Scopolamine & Phenobarbital (Donnatal, others), <http://www.accessmedicine.com/content.aspx?aID=2697089> (last visited Mar. 11, 2009) (noting common therapeutic uses of Donnatal). The multi-billion dollar "dietary supplement" industry depends on the use of a wide variety of botanical agents that are exempt from the strict FDA pre-market review demanded for pharmaceutical agents. Dietary Supplement Health and Education Act of 1994, Pub. L. No. 103-417, 108 Stat. 4325 (codified as amended in scattered sections of 21 U.S.C. §§ 301–399 (2000)); see, e.g., David M. Eisenberg et al., *Trends in Alternative Medicine Use in the United States, 1990–1997: Results of a Follow-up National Study*, 280 J. AM. MED. ASS'N 1569, 1569 (1998) ("Use of at least 1 of 16 alternative therapies during the previous year increased from 33.8% [of those surveyed] in 1990 to 42.1% in 1997 (P≤.001). The therapies increasing the most included herbal medicines . . . [and] megavitamins . . . [A]lternative therapies were used most frequently for chronic conditions, including back problems, anxiety, depression, and headaches.").

I have previously proposed that the majority of these dietary supplements should be subject to premarket review identical to that required for new pharmaceutical agents. See *supra* Cohen, note 32. In this article, I suggest that a similar approach to the evaluation of medical marijuana would be both good science and rational policy.

⁵⁸ In setting forth the FDA's review process, I have made use of an excellent discussion of the review process: see James L. Zelenay, Jr., *The Prescription Drug User Fee Act: Is a Faster Food and Drug Administration Always a Better Food and Drug Administration?*, 60 FOOD & DRUG L.J. 261, 266–88 (2005).

⁵⁹ Investigational New Drug Application, 21 C.F.R. § 321.1(a) (2008).

regarding proposed clinical investigations; the chemistry, formula, and manufacturing details of the investigational drug; and any pharmacological or physiological data from prior studies.⁶⁰ The FDA has thirty days to respond to the IND application, after which the manufacturer may begin clinical testing if it has not heard from the FDA.⁶¹ Of course, the FDA can halt clinical testing at any time if the agency feels that new information indicates the investigational new drug no longer meets safety and efficacy standards.⁶²

Clinical testing is not carried out by the FDA itself but is the responsibility of the drug's manufacturer (sponsor). The necessary investigations, conducted by academic institutions or by private contractors, involve three discrete phases designed to document safety and efficacy through "evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience."⁶³ In Phase I, the drug's toxicity and human tolerance to it are examined usually in fewer than one hundred subjects with the primary purpose of evaluating potential toxicity rather than efficacy (although gaining knowledge of effectiveness is not precluded).⁶⁴ In Phase II, which begins after dose-response and toxicity data are deemed sufficient to continue the process of clinical investigation, detailed studies are carried out in several hundred humans.⁶⁵ This phase, involving "controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication . . . in patients with the disease or condition under study,"⁶⁶ is designed to verify the drug's effectiveness, major side effects, and appropriate dose.⁶⁷ In Phase III, which is commenced once the drug under consideration has been deemed sufficiently safe and effective for further testing and evaluation, large-scale studies—involving as many as several thousand patient volunteers—are conducted to determine complications of low incidence as well as efficacy in a large cohort of the general population with the disease.⁶⁸

Once these three phases of drug evaluation have been completed, the manufacturer of the drug files a New Drug Application (NDA) with the FDA.⁶⁹ This document must provide the results of all preclinical and clinical investigations and include the names of all of the clinical investigators; describe all components of the drug; document manufacturing, processing, and packaging methods; and

⁶⁰ Zelaney, *supra* note 58, at 267 n.48.

⁶¹ *Id.* at 267 n.49.

⁶² *Id.*

⁶³ See 21 U.S.C. § 355(d) (2006) (defining "substantial evidence").

⁶⁴ See 21 C.F.R. § 312.21(a) (2008) (describing Phase I of the investigation process).

⁶⁵ See *id.* § 312.21(b) (describing Phase II of the investigation process).

⁶⁶ *Id.*

⁶⁷ *Id.*

⁶⁸ See *id.* § 312.21(c) (describing Phase III of the investigation process).

⁶⁹ Zelaney, *supra* note 58, at 268.

furnish samples of the proposed labeling.⁷⁰ If the FDA deems the benefits of using the drug for the purposes proposed in the NDA outweigh its risks, it will grant approval and the drug may then enter the stream of interstate commerce.⁷¹

The FDA's approval of an NDA does not require that the investigational new drug be superior to, or even as effective as, an already approved medication.⁷² The data need only demonstrate that it is safe and effective.⁷³ Therefore, for medical marijuana, as with any other investigational new drug, only its safety and efficacy need be demonstrated—*not its superiority*.

An important part of regulatory oversight involves the labeling and advertising of approved drugs. A manufacturer can explicitly advertise or otherwise promote medications *only* for indications approved by the FDA.⁷⁴ Furthermore, all advertising must be based on data that were approved by the FDA for inclusion in the labeling of the drug.⁷⁵ A drug may be deemed to be misbranded “because the labeling or advertising is misleading.”⁷⁶ Thus, the Act requires both proven safety and efficacy *and* accurate labeling and advertising of a drug.⁷⁷ As a condition of approval, the FDA may require postmarket surveillance studies (“Phase IV studies”) to gain the additional knowledge that is possible only with observation of even larger numbers of patients.⁷⁸ Even after the FDA's final approval has been gained, the FDA can suspend or revoke the manufacturer's

⁷⁰ See 21 U.S.C. § 355(b)(1) (2006) (listing the required content of the NDA application).

⁷¹ See Zelaney, *supra* note 58, at 268–69 (describing the FDA's review process).

⁷² See 21 U.S.C. § 355(d) (listing the possible grounds for denying the NDA application).

⁷³ See *id.*

⁷⁴ See 21 U.S.C. § 352 (describing drug advertising and labeling requirements).

⁷⁵ See *id.* § 352(n) (listing advertising requirements); 21 C.F.R. § 202.1 (listing advertising requirements).

⁷⁶ 21 U.S.C. § 321(n).

⁷⁷ See *supra* notes 72–73, 76 and accompanying text.

⁷⁸ See, e.g., Peter J. Cohen, ‘Off-Label’ Use of Prescription Drugs: Legal, Clinical and Policy Considerations, 14 EUR. J. ANAESTHESIOLOGY 231, 233 (1997).

[A]cquisition of information concerning drug action does not stop at the time of FDA approval. Invaluable information, not available during the limited phase of clinical investigation, is gleaned only through post-market surveillance. Newly approved drugs are administered to patients with a variety of diseases, and who may be taking a panoply of other medications. Adverse effects occurring with extremely low frequency, unlikely to have been noted during the phase of clinical investigation, may only become manifest after approval. Often, clinical studies designed to gather data to support the NDA do not include members of every group who will eventually receive the medication.

Id.

license based on new evidence that calls into question the drug's safety or efficacy.⁷⁹

Recent events have illuminated major deficiencies in the FDA's ability to protect the public, including overly hasty and, in the views of some, far too permissive drug approval; real and perceived conflicts of interest; and lack of appropriate postmarketing surveillance.⁸⁰ In addition, what some consider to be an intrusion by politics into the FDA's decision-making procedures has severely damaged the agency's reputation.⁸¹ Finally, the Administration and some members of the Congress have proposed changes that some believe will undermine the FDA's authority to regulate the advertising of off-label use⁸² and thereby threaten the agency's ability to protect the public.⁸³ Even so, these deficiencies in the FDA's regulation of pharmaceuticals do not provide a rationale for disregarding its major role in protecting the public. Indeed, the FDA, in its "watchdog" function, has successfully served the public far more often than not.⁸⁴ Therefore, this analysis considers the FDA in light of its successes and promises rather than these deficiencies.

B. The Controlled Substances Act: Scheduling and Medical Marijuana

If the FDA finds that a drug's addiction liability requires additional regulation under authority granted by the Controlled Substances Act (CSA),⁸⁵ it petitions the Drug Enforcement Agency (DEA) to place the drug on the list of controlled substances.⁸⁶ The scheduling process⁸⁷ begins with a scientific review performed by two divisions of the Department of Health and Human Services (DHHS)—the FDA and the National Institute on Drug Abuse (NIDA), the latter of which is an institute of the National Institutes of Health (NIH).⁸⁸ Once their analysis is

⁷⁹ See 21 U.S.C. § 355(e) (listing the grounds for withdrawal of approval of an application).

⁸⁰ See *Cohen*, *supra* note 32, at 211–13 (discussing the major deficiencies in the FDA's ability to protect the public).

⁸¹ *Id.* at 212.

⁸² Off-label use, the prescription of drugs for purposes that were not part of the approved NDA, is further discussed in Part VI.

⁸³ See *infra* notes 311–313 and accompanying text.

⁸⁴ See, e.g., *Cohen*, *supra* note 32, at 179. The FDA's oversight was responsible for averting a major disaster by prohibiting the use of thalidomide in the United States after its widespread distribution in Europe had led to the catastrophe of malformed infants born after maternal use of the compound. See *id.*

⁸⁵ 21 U.S.C. §§ 801–971.

⁸⁶ John H. King, *Federal Regulations for the Prescription of Controlled Substances*, in *MARIHUANA AND MEDICINE* 745, 747 (Gabriel G. Nahas et al., eds., 1999) Petitions may also be filed by any other interested parties such as the pharmaceutical sponsor, public interest group, or concerned physicians. *Id.*

⁸⁷ See *id.* at 745–50 (describing the scheduling process).

⁸⁸ *Id.* at 747.

complete, DHHS makes a preliminary binding⁸⁹ recommendation that is printed in the Federal Register for public comment.⁹⁰ Thereafter, if the scientific experts of the FDA recommend that scientific evidence supports placing the drug on the list of scheduled controlled substances, the actual level of scheduling—as determined by specific factors detailed in the CSA⁹¹—is assigned by the DEA.⁹² In assigning

⁸⁹ Once the FDA recommends that the drug be scheduled, the DEA is responsible for assigning the level of scheduling. *Id.* at 748. In doing so, however, the scientific findings presented by the FDA and NIDA are *binding* on the DEA. *Id.*

⁹⁰ *Id.*

⁹¹ Controlled Substances Act 21 U.S.C. §§ 801–904 (2006). The specific factors for scheduling are set forth in the CSA as follows:

Title 21, § 812. Schedules of controlled substances

(a) Establishment

There are established five schedules of controlled substances, to be known as schedules I, II, III, IV, and V. Such schedules shall initially consist of the substances listed in this section. The schedules established by this section shall be updated and republished on a semiannual basis during the two-year period beginning one year after October 27, 1970, and shall be updated and republished on an annual basis thereafter.

(b) Placement on schedules; findings required

Except where control is required by United States obligations under an international treaty, convention, or protocol, in effect on October 27, 1970, and except in the case of an immediate precursor, a drug or other substance may not be placed in any schedule unless the findings required for such schedule are made with respect to such drug or other substance. The findings required for each of the schedules are as follows:

(1) Schedule I.—

(A) The drug or other substance has a high potential for abuse.

(B) The drug or other substance has no currently accepted medical use in treatment in the United States.

(C) There is a lack of accepted safety for use of the drug or other substance under medical supervision.

(2) Schedule II.—

(A) The drug or other substance has a high potential for abuse.

(B) The drug or other substance has a currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions.

(C) Abuse of the drug or other substances may lead to severe psychological or physical dependence.

(3) Schedule III.—

(A) The drug or other substance has a potential for abuse less than the drugs or other substances in schedules I and II.

(B) The drug or other substance has a currently accepted medical use in treatment in the United States.

the appropriate schedule, the DEA must ensure that the determination is based on objective and verifiable scientific findings.⁹³ The level of scheduling is based on the following questions: (1) Does the drug have a “currently accepted medical use” in the United States?⁹⁴ (2) What is the drug’s safety under medical supervision? Will it be a hazard to those using it or to others? (3) What is its addiction liability? (4) Is there a potential for (or history of) significant diversion for illegal use? (5) Are individuals using it on their own initiative or only on physician’s prescription? (6) Is the drug similar in its pharmacology to other controlled drugs?⁹⁵

The Controlled Substances Act also provides that the Congress may take any action it wishes regarding scheduling on its own *without regard to available scientific evidence*.⁹⁶ The significance of this authority will be discussed further in Part V.

III. POTENTIAL RISKS OF USING MEDICAL MARIJUANA

The decision of whether or not to grant approval of any new drug requires a careful balancing of its potential risks and benefits. All approved medications used in the legitimate practice of medicine are associated with adverse effects; there is

(C) Abuse of the drug or other substance may lead to moderate or low physical dependence or high psychological dependence.

(4) Schedule IV.—

(A) The drug or other substance has a low potential for abuse relative to the drugs or other substances in schedule III.

(B) The drug or other substance has a currently accepted medical use in treatment in the United States.

(C) Abuse of the drug or other substance may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in schedule III.

(5) Schedule V.—

(A) The drug or other substance has a low potential for abuse relative to the drugs or other substances in schedule IV.

(B) The drug or other substance has a currently accepted medical use in treatment in the United States.

(C) Abuse of the drug or other substance may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in schedule IV.

21 U.S.C. § 812.

⁹² See KING, *supra* note 86, at 745 (“The DEA must determine whether a substance meets the criteria for any of the schedules.”).

⁹³ *Id.* at 746.

⁹⁴ *Id.* (citing 21 U.S.C. § 812(b)(1)(B)).

⁹⁵ *Id.*

⁹⁶ See, e.g., Gonzales v. Raich, 545 U.S. 1, 14 (2005) (“In enacting the CSA, Congress classified marijuana as a Schedule I drug.”) (*emphasis added*).

no *a priori* reason why marijuana should be different. Before assessing the potential pathology of marijuana, it is necessary to distinguish between its recreational and medical use.

When used recreationally, marijuana might be taken in large doses over long periods of time for its psychotropic effects. In contrast, when used as medical therapy, marijuana is administered only in doses sufficient to produce the desired clinical effect and only for as long as is medically necessary. The effects of any pharmaceutical agent, whether beneficial or pathologic, depend on the route of administration (e.g., oral, intravenous, intramuscular, or smoked), the dose administered, the pharmacologically active fraction of the administered dose that reaches the desired site of action, the rate at which the drug is metabolically inactivated, and the frequency and duration of use. Thus, it may be misleading to assume that marijuana's properties as manifested in individuals who have used it frequently, often in large quantities, and over a long period of time, can predict the effects of marijuana in patients who use it only as often as necessary under the advice of a medical professional and who carefully titrate the drug to achieve a desired clinical effect.

Another factor to consider is the significant biologic differences between the developing brains of children and adolescents⁹⁷ and the more mature brains of

⁹⁷ See JUVENILE JUSTICE CENTER, AMERICAN BAR ASSOCIATION, CRUEL AND UNUSUAL PUNISHMENT: THE JUVENILE DEATH PENALTY, ADOLESCENCE, BRAIN DEVELOPMENT AND LEGAL CULPABILITY 1 (2004), available at <http://www.abanet.org/crimjust/juvjus/Adolescence.pdf>.

Scientists are now utilizing advances in magnetic resonance imaging (MRI) to create and study three-dimensional images of the brain without the use of radiation (as in an x-ray). This breakthrough allows scientists to safely scan children over many years, tracking the development of their brains.

Researchers at Harvard Medical School, the National Institute of Mental Health, UCLA, and others, are collaborating to “map” the development of the brain from childhood to adulthood and examine its implications.

.....
This discovery gives us a new understanding into juvenile delinquency. The frontal lobe is “involved in behavioral facets germane to many aspects of criminal culpability,” explains Dr. Ruben C. Gur, neuropsychologist and Director of the Brain Behavior Laboratory at the University of Pennsylvania. “Perhaps most relevant is the involvement of these brain regions in the control of aggression and other impulses. . . . If the neural substrates of these behaviors have not reached maturity before adulthood, it is unreasonable to expect the behaviors themselves to reflect mature thought processes.

The evidence now is strong that the brain does not cease to mature until the early 20s in those relevant parts that govern impulsivity, judgment, planning for the future, foresight of consequences, and other characteristics that make people morally culpable. . . . Indeed, age 21 or 22 would be closer to the ‘biological’ age of maturity.

adults.⁹⁸ These differences in brain structure and function suggest that marijuana's long-term pathology may be age dependent and that a "universal" policy applying to all age groups is therefore probably unwarranted.

At the present time, only limited data regarding adverse effects of medical marijuana are available. This contrasts sharply with our extensive knowledge of the pathology of both recreational marijuana and cocaine, morphine, and other "hard" drugs.

A. *Marijuana and Death*

Many legal drugs subject to the CSA are both indispensable to modern medical practice and potentially lethal (e.g., morphine, Fentanyl™, Demerol™, and Phenobarbital). Indeed, an appreciation of the possibility that such medications can cause death when used inappropriately is essential to medical training. For instance, the mechanism by which drugs such as morphine can cause death is set forth in a major textbook of pharmacology: "Morphine is a primary and continuous depressant of respiration . . . The respiratory depression is discernible even with

Id. at 1–2 (footnotes omitted). One court cited the significant biological differences between the developing brains of children and adolescents as follows:

Three general differences between juveniles under 18 and adults [are recognized under our laws]. First, as any parent knows and as the scientific and sociological studies respondent and his *amici* cite tend to confirm, "[a] lack of maturity and an underdeveloped sense of responsibility are found in youth more often than in adults and are more understandable among the young. These qualities often result in impetuous and ill-considered actions and decisions." It has been noted that "adolescents are overrepresented statistically in virtually every category of reckless behavior." In recognition of the comparative immaturity and irresponsibility of juveniles, almost every State prohibits those under 18 years of age from voting, serving on juries, or marrying without parental consent.

The second area of difference is that juveniles are more vulnerable or susceptible to negative influences and outside pressures, including peer pressure. This is explained in part by the prevailing circumstance that juveniles have less control, or less experience with control, over their own environment. ("[A]s legal minors, [juveniles] lack the freedom that adults have to extricate themselves from a criminogenic setting").

The third broad difference is that the character of a juvenile is not as well formed as that of an adult. The personality traits of juveniles are more transitory, less fixed.

Roper v. Simmons, 543 U.S. 551, 569–70 (2005) (citations omitted).

⁹⁸ Adults are more likely candidates for medical marijuana than patients in the pediatric age group.

doses too small to disturb consciousness, and increases progressively as the dose is increased. In humans, death from morphine poisoning is nearly always due to respiratory arrest.”⁹⁹ In contrast, there is no evidence that the recreational use of marijuana is associated with death. The absence of lethal action (whether marijuana is used recreationally or medically) is documented in the American Society of Addiction Medicine’s *Principles of Addiction Medicine*: “In healthy young users, [marijuana’s] cardiovascular effects are unlikely to be of clinical significance. Documented evidence of death resulting from recreational use, even in large doses, is lacking.”¹⁰⁰

The possibility that marijuana might cause death is not mentioned in a discussion of its pathology in a standard textbook of pharmacology.¹⁰¹ The author only calls attention to a reversible effect of marijuana on heart rate and blood pressure suggesting an absence of a relationship between use of marijuana and death:

The most consistent effects on the cardiovascular system are an increase in heart rate [and], an increase in systolic blood pressure The increase in heart rate is dose related, and its onset and duration correlate well with concentrations of Δ^9 - THC in blood There are no consistent changes in respiratory rate. . . .¹⁰²

Obviously, marijuana can be a factor in causing death when it accompanies the use of other potent drugs such as alcohol or heroin, or is smoked during potentially hazardous activities such as driving.

B. Harmful Properties of Marijuana

It is not an exaggeration to state that all approved pharmaceuticals are associated with some degree of pathology; although these effects are not necessarily life threatening. Marijuana is not an exception. However, risk alone is a poor determinant of whether marijuana should be approved as a legitimate therapeutic agent. Far more important to the analysis of marijuana and, indeed, all investigational new drugs, is the relationship of their inherent risks to their proposed benefits.¹⁰³ In this section, I will analyze the available evidence concerning the addiction liability of marijuana, its possible association with

⁹⁹ Jaffe & Martin, *supra* note 3, at 494, 502.

¹⁰⁰ Welch & Martin, *supra* note 7, at 261–63.

¹⁰¹ See, e.g., Jerome H. Jaffe, *Drug Addiction and Drug Abuse*, in GOODMAN AND GILMAN’S: THE PHARMACOLOGICAL BASIS OF THERAPEUTICS 535, 561–62 (Alfred Goodman Gilman et al., eds., 6th ed. 1980).

¹⁰² *Id.* at 561.

¹⁰³ THOMAS M. GARRETT, HAROLD W. BAILLIE & ROSELEEN M. GARRETT, HEALTH CARE ETHICS 54–55 (2d ed. 1993) (“Unless there is a sufficient reason not to, one has an obligation do those acts that are likely to do more good than harm.”).

cognitive impairment, whether its use is either associated with or causes mental illness, the question of marijuana smoking and pulmonary carcinoma (lung cancer), and marijuana's role as a "gateway drug."

1. *Marijuana and Addiction Liability*

Although there is little doubt that recreational marijuana is associated with addiction liability, its ability to produce dependence is less significant than that associated with either alcohol or pharmaceutical agents such as morphine, Phenobarbital, and Valium™, which are all used in the legitimate practice of medicine.¹⁰⁴

Clinical and epidemiologic evidence indicates that a cannabis dependence syndrome occurs in heavy chronic users, as exhibited by a lack of control over use and continued use of the drug despite adverse personal consequences [However, t]he risk of becoming dependent on cannabis probably is more like the risk for alcohol than for . . . the opioids, with around 10% of those who ever use cannabis eventually meeting the criteria for dependence.¹⁰⁵

Epidemiological data from a national study indicate that about 10 percent of regular marijuana users become addicted to it.¹⁰⁶ This incidence is more like that of alcohol use (15 percent becoming addicted) than either nicotine (32 percent) or the opioids (23 percent).¹⁰⁷ These data did not escape public attention. An Op-Ed piece published in the Washington Post emphasized that marijuana's addiction liability was less than that of either alcohol or nicotine, both of which are legal drugs: "Fewer than one in 10 marijuana smokers become regular users of the drug, and most voluntarily cease their use after 34 years of age. By comparison, 15 percent of alcohol consumers and 32 percent of tobacco smokers exhibit symptoms of drug dependence."¹⁰⁸

Although the use of recreational marijuana may result in addiction, the relevant question to consider is the possibility of becoming addicted when marijuana is used for medical purposes as directed by a licensed health care professional. However, marijuana has not been used in a medical context for a sufficiently long period to allow the collection of scientific observations and data

¹⁰⁴ See J.C. Anthony, L.A. Warner & R.C. Kessler, *Comparative Epidemiology of Dependence on Tobacco, Alcohol, Controlled Substances and Inhalants: Basic Findings from the National Comorbidity Survey*, 2 EXPERIMENTAL AND CLINICAL PSYCHOPHARMACOLOGY 244, 251 (1994).

¹⁰⁵ Welch & Martin, *supra* note 7, at 260 (citations omitted).

¹⁰⁶ *Id.*

¹⁰⁷ Anthony et al., *supra* note 104, at 254–55.

¹⁰⁸ Keith Stroup & Paul Armentano, *The Problem is Pot Prohibition*, WASH. POST, May 4, 2002, at A19.

analysis necessary for a definite answer. Nonetheless, valid information concerning the likelihood that patients will become addicted to marijuana when using it medically may be extrapolated from the medical use of other controlled substances whose ability to produce addiction has been well documented. As Denise Kandel has observed:

There are, unfortunately, no empirical data to guide policy. However, inferences can be made from appropriate medical use of morphine, which does not lead to addiction. This is a curious phenomenon that points out the complexity of drug behavior and the role of psychological and social conditions in shaping its development.¹⁰⁹

The use of opioids is a significant component of pain therapy; when using these drugs, treating physicians must be aware of the possibility of addiction.¹¹⁰ Nonetheless, when the benefits and risks of opioid therapy are balanced, these drugs are generally considered to be a legitimate component of treatment.¹¹¹ A discussion of pain management by Barry Stimmel, a specialist in pain management, typifies this view:

Existing evidence suggests that iatrogenic [physician-induced] drug dependence is a real phenomenon but one that occurs infrequently when dependence-producing drugs are prescribed in an appropriate manner. Consistent narcotic use in chronic pain of known etiology that is unable to be relieved by other means, while associated with physical dependence [in contrast to true *addition*¹¹²], may nonetheless allow an individual to function in a productive manner.¹¹³

¹⁰⁹ Denise B. Kandel, *Does Marijuana Use Cause the Use of Other Drugs?* 289 J. AM. MED. ASS'N 482, 483 (2003).

¹¹⁰ See Barry Stimmel, *Constraints on Prescribing and the Relief of Pain*, in PRINCIPLES OF ADDICTION MEDICINE 1479, 1479–80 (Allan W. Graham et al., eds., 3rd ed. 2003) (“Fear of producing addiction to narcotics is foremost in the minds of most physicians when asked to provide medication for pain relief. This fear often interferes with their ability to provide adequate analgesia.”).

¹¹¹ See *id.*

¹¹² Physical dependence and tolerance, a normal consequence of opioid administration, differs significantly from addiction. See, e.g., Charles P. O’Brien, *A 50-Year-Old Woman Addicted to Heroin: Review of Treatment for Heroin Addiction*, 300 J. AM. MED. ASS'N 314, 315 (2008) (“[I]t is essential to distinguish between addiction, which involves a [pathologic] compulsion to take drugs, and simple tolerance with physical dependence, which is a normal phenomenon seen in everyone treated with opiates over the long term. In fact, tolerance begins with the first dose of opiates . . .”).

¹¹³ Stimmel, *supra* note 110, at 1480.

Experience with other approved controlled substances used appropriately in the practice of medicine suggests that while the possibility of addiction (in contrast to physical dependence or tolerance) cannot be ruled out, it should be balanced with the potential benefits of the drug.¹¹⁴ The basic principle of balancing risk and benefit when deciding whether to approve a drug for medical treatment is equally applicable when evaluating the acceptability of marijuana as a safe and effective medication.

2. *Marijuana and Cognitive Impairment*

(a) *Recreational Marijuana Use and Cognitive Impairment*

Can the recreational use of marijuana cause cognitive impairment? The most obvious answer is “yes”—after all, this is the basic reason for its recreational use. The consensus of workers in the field is that chronic recreational use of marijuana may be associated with cognitive dysfunction and, indeed, that this significant pathology is related to structural changes in the brain.¹¹⁵ “Marijuana has an adverse effect on cognitive functions and tests, but the *sine qua non* of use appears to be impairment of the ability to learn. . . . Marijuana intoxication interferes with the formation of new memories. . . . Depersonalization and other behavioral effects also have been associated with marijuana use.”¹¹⁶

A recent study demonstrated that smoking four joints or more per week resulted in a decrement in mental test performance; subjects who had smoked regularly for a decade or more did the worst.¹¹⁷ The investigators found that long-term marijuana users were impaired 70 percent of the time on a decision-making test, compared to 55 percent for short-term users and 8 percent for nonusers.¹¹⁸

More significant than the acute effects of marijuana is that cognitive dysfunction may persist after its use has ceased. This phenomenon was described by Pope and Yurgelon-Todd who measured cognitive function after sufficient abstinence to ensure that the subjects were not acutely intoxicated by the drug:

Heavy marijuana use [daily for at least one month,]¹¹⁹ is associated with residual neuropsychological effects even after a day of supervised

¹¹⁴ See *infra* Part IV.

¹¹⁵ See, e.g., Mark S. Gold, *The Pharmacology of Marijuana*, in PRINCIPLES OF ADDICTION MEDICINE 163, 164–66 (Allan W. Graham & Terry K. Schultz, eds., 2nd ed. 1998).

¹¹⁶ *Id.* at 165.

¹¹⁷ Lambros Messinis, Anthoula Kyprianidou, Sonia Malefaki & Panagiotis Papathanasopoulos, *Neuropsychological Deficits in Long-term Frequent Cannabis Users*, 66 NEUROLOGY 737, 737–39 (2006).

¹¹⁸ *Id.*

¹¹⁹ Harrison G. Pope, Jr. & Deborah Yurgelon-Todd, *The Residual Cognitive Effects of Heavy Marijuana Use in College Students*, 275 J. AM. MED. ASS’N 521, 521 (1996).

abstinence from the drug. However, the question remains open as to whether this impairment is due to a residue of drug in the brain, a withdrawal effect from the drug, or a frank neurotoxic effect of the drug.¹²⁰

Block and coworkers tested subjects' memory as demonstrated by memorizing words. Although marijuana users refrained for at least twenty-six hours prior to testing (in order to obviate any residual acute cognitive effects of marijuana), they required approximately three times the number of word presentations to demonstrate the same degree of recall evidenced by nonusing controls.¹²¹ The authors therefore suggested that marijuana use altered memory-related brain function, an effect that persisted beyond the expected period of acute marijuana-induced pathology.¹²² These changes in brain function appeared to be related to or associated with anatomic and metabolic alterations in the brain (it is also possible that a longer period of abstinence might have resulted in different findings):

Using positron emission tomography (PET), memory-related regional cerebral blood flow was compared in frequent marijuana users and nonusing control subjects after 26+ h[ours] of monitored abstinence. Memory-related blood flow in marijuana users, relative to control subjects, showed decreases in prefrontal cortex, increases in memory-relevant regions of cerebellum, and altered lateralization in hippocampus. Marijuana users differed most in brain activity related to episodic memory encoding.¹²³

However, other investigators have been unable to demonstrate that the hippocampus, an area of the brain that plays a significant role in memory, is involved in marijuana's possible effects on memory.¹²⁴ For example, Tzilos and colleagues state:

¹²⁰ *Id.*

¹²¹ See Robert I. Block et al., *Effects of Frequent Marijuana Use on Memory-Related Regional Cerebral Blood Flow*, 72 PHARMACOLOGY BIOCHEMICAL BEHAVIOR, 237, 241, 246 (2002). See also Nadia Solowij, Robert S. Stephens, Roger A. Roffman, Thomas Babor, Ronald Kadden, Michael Miller, Kenneth Christiansen, Bonnie McRee, Janice Vendetti, *Cognitive Functioning of Long-term Heavy Cannabis Users Seeking Treatment* 287 J. Amer. Med. Ass. 1123 (2002) (Long-term heavy cannabis users showed impairments in memory and attention that endured beyond the period of intoxication).

¹²² See Block, *supra* note 121, at 245–49.

¹²³ *Id.* at 237.

¹²⁴ See Golfo K. Tzilos et al., *Lack of Hippocampal Volume Change in Long-Term Heavy Cannabis Users*, 14 AM. J. ADDICTION, 64–65 (2005).

We used magnetic resonance imaging to investigate these effects in a group of 22 older, long-term cannabis users (reporting a mean [SD] of 20,100 [13,900] lifetime episodes of smoking) and 26 comparison subjects with no history of cannabis abuse or dependence. When compared to control subjects, smokers displayed no significant adjusted differences in volumes of gray matter, white matter, cerebrospinal fluid, or left and right hippocampus. Moreover, hippocampal volume in cannabis users was not associated with age of onset of use nor total lifetime episodes of use. These findings are consistent with recent literature suggesting that cannabis use is not associated with structural changes within the brain as a whole or the hippocampus in particular.¹²⁵

This study did not dispute that marijuana could produce long-term cognitive effects. Rather, it suggested that marijuana's action on brain sites other than the hippocampus might be responsible for these mental changes.¹²⁶

In view of these studies indicating that the use of recreational marijuana impairs mental ability, it should not be surprising that its use may also be associated with a significant decrement in driving ability. A recent study of fatal automobile accidents conducted in France demonstrated the presence of marijuana in 8.8 percent of drivers found to be at fault compared with only 2.8 percent of those involved in fatal accidents but deemed to be without fault.¹²⁷ Parenthetically, alcohol was associated with a far greater number of such accidents.¹²⁸

The pathological effects of chronic recreational marijuana use by a judge (Superior Court Judge Philip Marquardt) who was presiding at a capital murder case have been substantiated in case law.¹²⁹ In what may be one of the most dramatic illustrations of marijuana's effect on mental function documented in the legal (as opposed to medical) literature, the Court of Appeals for the Ninth Circuit stated: It is the raw material from which legal fiction is forged:

A vicious murder, an anonymous psychic tip, a romantic encounter that jeopardized a plea agreement, an allegedly incompetent defense, and a death sentence imposed by a purportedly drug-addled judge. But, as Mark Twain observed, "truth is often stranger than fiction because fiction has to make sense."

.....
Judge Marquardt advised the parties that he would deliberate over the weekend and announce his decision on Monday. Unbeknownst to

¹²⁵ *Id.* at 64 (emphasis omitted).

¹²⁶ *See id.* at 64–65, 69–70.

¹²⁷ Bernard Laumon et al., *Cannabis Intoxication and Fatal Road Crashes in France: Population Based Case-Control Study*, 331 BRIT. MED. J. 1371, 1374 (2005).

¹²⁸ *Id.* (While 2.5% of fatal crashes were attributed to the use of marijuana, at least 28.6% were caused by the use of alcohol.).

Summerlin [the defendant], Judge Marquardt was a heavy user of marijuana at the time, a fact that the State conceded in the federal habeas proceedings before the district court in this case.

The amount of marijuana that Judge Marquardt may have used during the trial or deliberations is unknown because the district court did not allow discovery on this issue, although there is record support for Summerlin's claim that Judge Marquardt was either having difficulty concentrating or experiencing short-term memory loss.¹³⁰

There are instances during pretrial hearings and at trial when Judge Marquardt exhibited confusion over facts that had just been presented to him. He also made some quite perplexing, if not unintelligible, statements at various times during the trial.¹³¹

It is important to note that while marijuana's acute detrimental effects on cognition have been well-documented by some investigators, there is no consensus regarding the long-term sequelae of its chronic use. In a study of 1,318 subjects during a twelve-year period, Lyketsos and coworkers demonstrated that although the "Mini-Mental State Examination" had demonstrated a decline in cognitive function of marijuana users during this period, the changes were similar in heavy users, light users, and nonusers of marijuana.¹³² The authors, therefore, concluded that "over long time periods, in persons under age 65 years, . . . [cognitive decline] is closely associated with aging and educational level but does not appear to be associated with cannabis use."¹³³

Other data support the hypothesis that chronic marijuana use does not produce changes in cognitive function that are irreversible:

U.S. government-sponsored population studies conducted in Jamaica, Greece and Costa Rica found no significant cognitive differences between long-term marijuana smokers and nonsmokers. Similarly, a 1999 study of 1,300 volunteers published in the *American Journal of Epidemiology* reported "no significant differences in cognitive decline between heavy users, light users, and nonusers of cannabis" over a 15-year period. Most recently, a meta-analysis of neuropsychological studies of long-term marijuana smokers by the U.S. National Institute on Drug Abuse reaffirmed this conclusion.¹³⁴

¹²⁹ Summerlin v. Stewart, 341 F.3d 1082, 1084 (9th Cir. 2003).

¹³⁰ *Id.* at 1084, 1089–90.

¹³¹ *Id.* at 1090 n.2.

¹³² Constantine G. Lyketsos et al., *Cannabis Use and Cognitive Decline in Persons Under 65 Years of Age*, 149 AMER. J. EPIDEMIOL. 794, 794 (1999).

¹³³ *Id.*

¹³⁴ Stroup & Armentano, *supra* note 108, at A19.

(b) *Medical Marijuana and Long-Term Cognitive Impairment*

In contrast to the effects of its recreational use, what are the cognitive effects of controlled exposure to marijuana administered to treat symptomatic pathology as recommended by a physician? The basic answer is that at this point in time there is no definite answer. Nonetheless, there are a few relevant considerations to keep in mind.

Most important is that medical marijuana is recommended to patients as a *bona fide* medical treatment to relieve the pathologic symptoms of their disease, not to enable patients to get “high.”¹³⁵ This is analogous to the prescription of opioids, e.g., morphine, for legitimate medical treatment of both acute and chronic pain, not for their psychotropic effects. Morphine, like marijuana, even when used under a physician’s direction, can cause cognitive changes; indeed, this is a reason why some patients reject its use for long-term therapy and seek other modes of alleviating their distress.¹³⁶ In most cases, however, this adverse effect is dose-related and therefore can often be controlled by decreasing the dose of either drug.¹³⁷

Finally, physicians are often confronted with the problem of making not the *best* choice but the *least worst* choice. In balancing the burdens and potential benefits of marijuana,¹³⁸ it is a truism for the practicing physician that many of the conditions for which marijuana has been recommended—pain, spasticity, nausea, lack of appetite, weight loss, and depression—can also produce cognitive impairment.

3. *Marijuana and Mental Illness*

Perhaps of even greater concern than the effects of marijuana on cognition is its possible association with manifestations of serious psychiatric illness. Available scientific data suggest that there may be a strong association between some forms of psychiatric abnormalities and the recreational use of marijuana.¹³⁹ Jaffe has documented the effect of recreational marijuana:

¹³⁵ See, e.g., Mark Wallace et al., *Dose-dependent Effects of Smoked Cannabis on Capsaicin-Induced Pain and Hyperalgesia in Healthy Volunteers*, 107 ANESTHESIOLOGY 785, 795 (2007). Smoked marijuana in appropriate doses relieved pain in healthy volunteers but did not appear to produce significant decrements in mental performance. See discussion *infra* Part IV.

¹³⁶ See Jaffe & Martin, *supra* note 3, at 508.

¹³⁷ *Id.* at 509–09.

¹³⁸ See *infra* Part IV.

¹³⁹ See Cécile Henquet et al., *Prospective Cohort Study of Cannabis Use, Predisposition for Psychosis, and Psychotic Symptoms in Young People*, 330 BRIT. MED. J. 11, 11 (2005).

Higher doses of Δ^9 -THC can induce frank hallucinations, delusions, and paranoid feelings. Thinking becomes confused and disorganized; depersonalization and altered time sense are accentuated. Anxiety reaching panic proportions may replace euphoria, often as a result of the feeling that the drug-induced state will never end. With high enough doses, the clinical picture is that of a toxic psychosis with hallucinations, depersonalization, and loss of insight; this can occur acutely or only after months of use.¹⁴⁰

A confounding factor is that preexisting psychiatric illness may play a significant role in the development of mental illness in individuals using marijuana.¹⁴¹ For example, Henquet and colleagues evaluated and compared 2,437 individuals fourteen to twenty-four years of age with and without a history of preexisting psychosis; psychiatric symptoms were evaluated at the initial interview and during a follow up four years later.¹⁴²

After adjustment for age, sex, socioeconomic status, urbanicity, childhood trauma, predisposition for psychosis at baseline, and use of other drugs, tobacco, and alcohol, cannabis use at baseline increased the cumulative incidence of psychotic symptoms at follow up The effect of cannabis use was much stronger in those with any predisposition for psychosis at baseline There was a dose-response relation with increasing frequency of cannabis use.¹⁴³

The authors concluded that cannabis use moderately increases the risk of psychotic symptoms in young people but has a much stronger effect in those with evidence of predisposition for psychosis.¹⁴⁴

Three additional studies have suggested that frequent use of marijuana may lead to (or be associated with) depression and other mental illness.¹⁴⁵ The first study, by doctors in Australia, tracked 1,600 teenage students for seven years.¹⁴⁶ The research showed that young women who used marijuana every day were five times more likely to suffer from depression and anxiety than nonusers.¹⁴⁷ Teenage girls who used the drug at least once every week were twice as likely to develop

¹⁴⁰ Jaffe, *supra* note 101, at 561 (citation omitted).

¹⁴¹ *See id.*

¹⁴² Henquet, *supra* note 139, at 11.

¹⁴³ *Id.*

¹⁴⁴ *Id.*

¹⁴⁵ *See generally* BBC News, Cannabis Link to Depression, Friday, 22 November, 2002, 00:00 GMT, available at <http://news.bbc.co.uk/2/hi/health/2498493.stm>.

¹⁴⁶ George C. Patton et al., *Cannabis Use and Mental Health in Young People: Cohort Study*, 325 BRIT. MED. J. 1195, 1195 (2002).

¹⁴⁷ *Id.* at 1197.

depression compared to those who did not use the drug.¹⁴⁸ A study by Swedish researchers provided evidence that marijuana use can significantly increase the risk of schizophrenia.¹⁴⁹ The study found that 0.71 percent of roughly 50,000 Swedish military conscripts who smoked marijuana in the late 1960s developed schizophrenia.¹⁵⁰ A third investigation by British researchers found that schizophrenia is more likely in people who start using the drug as teenagers.¹⁵¹ In a study of a thousand people in their early twenties, one in ten who used marijuana as a teenager had since been diagnosed with schizophrenia.¹⁵²

Whether marijuana *caused* these phenomena directly or whether it was only *associated* with them is a significant question that likely could be completely answered only by subjecting randomly selected subjects (without a preexisting history of psychiatric illness) to long-term exposure to the drug and comparing them with a similar and also randomly selected nonexposed cohort. Although such a study might provide a definitive answer to the question, it would clearly be unethical. Moreover, whether controlled medical use will lead to psychiatric illness is another important question to which we do not yet have the answer. Therefore, future studies of medical marijuana should include evaluating possible long-term effects on mental health.

4. *Marijuana Smoking and the Development of Pulmonary Cancer*

Can smoking marijuana cause lung cancer as does the smoking of tobacco? This is an area of considerable controversy. Several respected researchers have supported the hypothesis that smoking marijuana and lung cancer are causally related.¹⁵³ Gold has called attention to the ability of some ingredients found both in marijuana and tobacco smoke to cause pulmonary symptoms:

Marijuana and tobacco smoke are very similar, and the effects of marijuana smoking are similar to the effects of tobacco smoking. Marijuana smoke contains many of the same carcinogenic components identified in tobacco smoke Chronic marijuana smoking (at least four days a week for six to eight weeks) results in mild airway obstruction, which may not be readily reversible with abstinence. Marijuana smoking

¹⁴⁸ *Id.*

¹⁴⁹ Stanley Zammit et al., *Self Reported Cannabis Use as a Risk Factor for Schizophrenia in Swedish Conscripts of 1969: Historical Cohort Study*, 325 BRIT. MED. J. 1199, 1202 (2002).

¹⁵⁰ *Id.* at 1200.

¹⁵¹ Louise Arseneault et al., *Cannabis Use in Adolescence and Risk for Adult Psychosis: Longitudinal Prospective Study*, 325 BRIT. MED. J. 1212, 1212–13 (2002).

¹⁵² *Id.*

¹⁵³ See Mark S. Gold, *The Pharmacology of Marijuana*, in PRINCIPLES OF ADDICTION MEDICINE 163, 164 (Allan W. Graham & Terry K. Schultz eds., 2d ed. 1998).

also causes decreased exercise tolerance, chronic cough, bronchitis and decreased pulmonary function.¹⁵⁴

Similarly, Mehra and colleagues advise caution without presenting specific epidemiologic data. “Given the prevalence of marijuana smoking and studies predominantly supporting biological plausibility of an association of marijuana smoking with lung cancer on the basis of molecular, cellular, and histopathologic findings, physicians should advise patients regarding potential adverse health outcomes until further rigorous studies are performed that permit definitive conclusions.”¹⁵⁵

Moir and coworkers measured the concentrations of known carcinogens in tobacco and marijuana smoke and found them to be similar thereby suggesting that marijuana and tobacco had the same potential to cause lung cancer.¹⁵⁶ However, their data did not examine the actual incidence of lung cancer in marijuana smokers:

The chemical composition of tobacco smoke has been extensively examined, and the presence of known and suspected carcinogens in such smoke has contributed to the link between tobacco smoking and adverse health effects. . . . [Although] there have been only limited examinations of marijuana smoke . . . [a]mmonia was found in mainstream marijuana smoke at levels up to 20-fold greater than that found in tobacco. Hydrogen cyanide, NO, NOx [toxic oxides of nitrogen], and some aromatic amines were found in marijuana smoke at concentrations 3–5 times those found in tobacco smoke.¹⁵⁷

The authors concluded that the presence “of known carcinogens and other chemicals implicated in respiratory diseases is important information for public health and communication of the risk related to exposure to such materials.”¹⁵⁸

On the basis of such data, Aldington and coworkers declared that “smoking a single marijuana joint is equivalent to smoking 2.5 to 5 cigarettes in terms of damage to the lungs.”¹⁵⁹ However, they also stressed the importance of the mode of using the particular cigarette: “The deep drags taken by marijuana users, along with their penchant for holding smoke in before exhaling, can cause problems like

¹⁵⁴ *Id.* (citations omitted).

¹⁵⁵ Reena Mehra et al., *The Association Between Marijuana Smoking and Lung Cancer: A Systematic Review*, 166 ARCHIVES INTERNAL MED. 1359, 1359 (2006).

¹⁵⁶ David Moir et al., *A Comparison of Mainstream and Sidestream Marijuana and Tobacco Cigarette Smoke Produced Under Two Machine Smoking Conditions*, 21 CHEMICAL RES. TOXICOLOGY 494, 496–500 (2007).

¹⁵⁷ *Id.*

¹⁵⁸ *Id.*

¹⁵⁹ Sarah Aldington et al., *The Effects of Cannabis on Pulmonary Structure, Function and Symptoms*, 62 THORAX 1058, 1062 (2007).

obstructed airways and hyperinflation of the lungs. The lack of filters on marijuana joints also contributes to lung problems. All of the smokers reported coughing and wheezing as acute manifestations of marijuana smoking.”¹⁶⁰

Although only tobacco smokers demonstrated signs of emphysema, a chronic pulmonary disease, the authors concluded that the equivalence “between cannabis joints and tobacco cigarettes in causing airflow obstruction is of major public health significance.”¹⁶¹

Nevertheless, strong epidemiological data argue against the hypothesis that cigarette and marijuana smoke are similar in their ability to cause lung cancer. For example, Hashibe and coworkers studied 2,252 volunteers including 1,212 with signs of cancer, of whom 39 percent had evidence of pulmonary cancer, to determine whether or not there was an association between marijuana use and the risk of developing lung and upper digestive tract cancer.¹⁶² Those with cancer and an approximately equal number of cancer-free controls were matched with respect to age, gender, and the neighborhoods in which they lived.¹⁶³ The subjects were interviewed with a standardized questionnaire.¹⁶⁴ On the basis of their data, the authors concluded that “the association of these cancers with marijuana, even long-term or heavy use, is not strong and may be below practically detectable limits,”¹⁶⁵ and thereby argued that smoking marijuana (in contrast to tobacco) is not positively associated with lung cancer.¹⁶⁶ It is noteworthy that the considerable media publicity¹⁶⁷ that this study received after its publication typified the often bitter conflict between scientific evidence and ideological advocacy that continues to pervade the discussion of medical marijuana. Finally, a recent study provided further evidence that the pathology of smoked tobacco and smoked marijuana are

¹⁶⁰ *See id.* at 1060–61.

¹⁶¹ *Id.* at 1063.

¹⁶² *See* Mia Hashibe et al., *Marijuana Use and the Risk of Lung and Upper Aerodigestive Tract Cancers: Results of a Population-Based Case-Control Study*, 15 *CANCER EPIDEMIOLOGY BIOMARKERS PREVENTION* 1829, 1829–30 (2006).

¹⁶³ *Id.*

¹⁶⁴ *Id.* at 1830.

¹⁶⁵ *Id.* at 1829.

¹⁶⁶ *See id.* at 1831–33.

¹⁶⁷ *See, e.g.*, Marc Kaufman, *Study Finds no Cancer-Marijuana Connection*, WASH. POST, May 26, 2006, at A3 (“The largest study of its kind has unexpectedly concluded that smoking marijuana, even regularly and heavily, does not lead to lung cancer. The new findings ‘were against our expectations,’ said Donald Tashkin [the senior author] of the University of California at Los Angeles, a pulmonologist who has studied marijuana for 30 years. ‘We hypothesized that there would be a positive association between marijuana use and lung cancer, and that the association would be more positive with heavier use,’ he said. ‘What we found instead was no association at all, and even a suggestion of some protective effect.’ . . . While no association between marijuana smoking and cancer was found, the study findings, presented to the American Thoracic Society International Conference this week, did find a 20-fold increase in lung cancer among people who smoked two or more packs of cigarettes a day.”).

not necessarily identical. The investigators demonstrated that while smoking both tobacco and marijuana “synergistically increased the risk of respiratory symptoms and COPD [chronic obstructive pulmonary disease],” this pulmonary abnormality did *not* develop when only marijuana was smoked.¹⁶⁸

In summary, the question of whether medically recommended smoked marijuana can cause pulmonary carcinoma is currently unanswered and awaits further epidemiologic studies.

5. *Marijuana and the “Gateway” Hypothesis*

One of the most controversial claims about the effects of marijuana use is that while marijuana itself may not cause significant harm, it can serve as a “gateway” or “trigger” that predisposes the user to experiment with and become dependent on more harmful drugs. Supporters of the gateway hypothesis acknowledge that many possible mechanisms might contribute to this phenomenon. It is theorized that marijuana may “‘trigger’ a biochemical craving for other psychoactive substances.”¹⁶⁹ It is also proposed that the “permissive atmosphere associated with its use” is an equally plausible explanation of why marijuana users escalate their use to other drugs.¹⁷⁰ That one’s peers are also using marijuana is yet another possible explanation of marijuana’s capacity to function as a gateway to other drugs.¹⁷¹

Well-founded arguments have been raised against the gateway hypothesis. For example, although a large proportion of our population has used marijuana at some point in time, the majority has eventually stopped, or markedly diminished its use, and has not progressed to using other illegal substances.¹⁷² In addition, and relevant to the thrust of this article, data presented in a recent report provide strong support for the view that medical use of a controlled substance will not inevitably progress to dependence on either the same drug or on other drugs with addiction liability.¹⁷³ Mannuzza and coworkers concluded that initiation of methylphenidate (Ritalin) treatment in children with attention deficit hyperactivity disorder (ADHD)

¹⁶⁸ Wan C. Tan, Christine Lo, Aimee Jong, Li Xing, Mark J. FitzGerald, William M. Vollmer, Sonia A. Buist, Don D. Sin, *Marijuana and Chronic Obstructive Lung Disease: A Population-Based Study*, 180 CAN. MED. ASS. J. 814 (2009).

¹⁶⁹ PETER J. COHEN, DRUGS, ADDICTION, AND THE LAW: POLICY, POLITICS, AND PUBLIC HEALTH 30 (2004).

¹⁷⁰ *Id.*

¹⁷¹ *Id.* at 30–32.

¹⁷² *See, e.g.*, OFFICE OF NAT’L DRUG CONTROL POLICY, NATIONAL DRUG CONTROL STRATEGY 26–28 (1999) (reporting that in a one month period during 1997, approximately 11.1 million individuals self-reported having used marijuana; however, during the same period of time, only 1.5 million (13.5%) reported using either powdered or crack cocaine).

¹⁷³ Salvatore Mannuzza et al., *Age of Methylphenidate Treatment Initiation in Children With ADHD and Later Substance Abuse: Prospective Follow-Up Into Adulthood*, 165 AM. J. PSYCHIATRY, 604, 608 (2008).

at an early age (six to twelve years) did not increase the risk of later substance abuse disorders and, indeed, had beneficial long-term effects on ameliorating the symptoms of their ADHD.¹⁷⁴

Moreover, the observations and data supporting the gateway hypothesis do not permit a distinction between marijuana as a *direct cause* of later drug use and a simple *association* of marijuana's use with later behavior. For example, Lynskey and colleagues sought to determine whether there was an association between early marijuana use and subsequent progression to use of and addiction to other drugs by examining genetic and shared environmental influences.¹⁷⁵ They surveyed an Australian national volunteer sample of 311 young adult identical and dizygotic (nonidentical) same-sex twin pairs who varied in their early (prior to age seventeen) marijuana use.¹⁷⁶ Those who had used marijuana by age seventeen had a 2.1 to 5.2 times greater incidence of other drug and alcohol abuse or dependence than did their co-twin who had not used marijuana before age seventeen.¹⁷⁷ However, while early marijuana use and later addiction to other drugs appeared to be related, the association did not differ significantly between identical and fraternal (nonidentical) twins.¹⁷⁸ The authors therefore concluded that while genetic factors were unlikely to be a significant factor in marijuana's acting as a "gateway" to later drug use, the available data did not allow them to distinguish between *cause* and *association*:

The association [between early marijuana use and later drug use and abuse or dependence] may arise from the effects of the peer and social context within which cannabis is used and obtained. In particular, early access to and use of cannabis may reduce perceived barriers against the use of other illegal drugs and provide access to these drugs.¹⁷⁹

Kandel's perceptive editorial accompanying Lynskey's article reiterated the problem of differentiating between cause and association in humans:

Whether or not a true *causal link* exists between the use of marijuana and other drugs, the association between the 2 has been well established.

. . . .

¹⁷⁴ *Id.* at 605, 608.

¹⁷⁵ Michael T. Lynskey et al., *Escalation of Drug Use in Early-Onset Cannabis Users vs. Co-twin Controls*, 289 J. AM. MED. ASS'N 427, 427–28 (2003).

¹⁷⁶ *Id.*

¹⁷⁷ *Id.* at 430.

¹⁷⁸ *Id.* at 427, 431. If both identical and fraternal twins have the same environmental background and identical twins share the same genetic makeup why did only *one* of the twins voluntarily begin to use marijuana? Does this suggest that an individual's behavior does not depend solely upon genetic and environmental influences?

¹⁷⁹ *Id.* at 427.

[T]he central question remains: does marijuana use cause the use of other illicit drugs? The search for causes in the absence of direct experimental manipulation may be elusive. Nonetheless, the search for mechanisms is necessary if only to explain the association between the use of different drug classes. . . . [Only in human beings] can one explore the many other social, psychological, and contextual factors that are also important in drug use behavior.¹⁸⁰

In summary, while the gateway drug hypothesis may be attractive to some, it has not been scientifically validated. Moreover, even if this hypothesis were substantiated, marijuana would not be a unique “gateway” to other drugs. For example, although there is an association between tobacco smoking and alcohol use,¹⁸¹ both remain legal activities unconstrained by the possibility that each might function as a “gateway” to the other. Finally, as with alcohol and tobacco, even if recreational marijuana were a gateway drug, this would not necessarily provide a rationale for public policy barring the use of marijuana for medical therapy.¹⁸²

While the debate regarding marijuana as a gateway drug has focused mainly on its recreational use, its medical use may have a significantly different spectrum of effects. While the medical use of other controlled drugs does not lead to experimentation with other drugs, we simply do not know whether the use of marijuana for medical purposes will have this undesired effect. As Kandel concluded: “There are, unfortunately, no empirical data to guide policy. However, inferences can be made from appropriate medical use of morphine, which does not lead to addiction.”¹⁸³

¹⁸⁰ Kandel, *supra* note 109, at 483 (2003) (emphasis added).

¹⁸¹ See, e.g., Christi A. Patten et al., *Can Psychiatric and Chemical Dependency Treatment Units be Smoke Free?*, 13 J. SUBSTANCE ABUSE TREATMENT 107, 107–08 (1996) (describing the potential difficulties of prohibiting smoking in alcohol dependency programs); Allan C. Collins & Michael J. Marks, *Animal Models of Alcohol-Nicotine Interactions*, in ALCOHOL AND TOBACCO: FROM BASIC SCIENCE TO CLINICAL PRACTICE 129, 129 (Joanne Fertig & John P. Allen eds., 1995) (“[Approximately] 70 percent of alcoholics are heavy smokers (i.e., smoke more than [one pack of] cigarettes per day), compared with 10 percent of the general population.”).

I should also note that my work with drug-dependent physicians suggests that alcohol use often precedes the abuse of, and addiction to, illegal drugs.

¹⁸² See Keith Stroup & Paul Armentano, Editorial, *The Problem is Pot Prohibition*, WASH. POST, May 4, 2002, at A19 (“[It is reasonable to suggest] that marijuana, like other drugs, is not for kids. We permit adults to do many activities that we forbid children to do, such as motorcycle riding, skydiving, signing contracts, getting married, drinking alcohol and smoking tobacco. But we do not condone arresting adults who responsibly engage in these activities in order to dissuade our children from doing so. Nor can we justify arresting adult marijuana smokers at the pace of some 734,000 per year on the grounds of sending a message to children.”).

¹⁸³ Kandel, *supra* note 109, at 483.

Finally, the risks and benefits of the medical use of marijuana cannot be considered as though they are unique to this drug. Rather, they must be evaluated in light of the knowledge of the risks of all approved, legal, and potentially addicting controlled prescription drugs. Morphine, meperidine, Fentanyl™, barbiturates, and tranquilizers such as diazepam (Valium™) are among the many FDA-approved and DEA-scheduled controlled substances that play a significant role in legitimate medical practice. Their addicting liability alone has not automatically been allowed to contraindicate their use. It would be contrary to the basic principles of medical ethics to forgo the use of these medications to treat the physical and emotional effects of chronic pain due to metastatic cancer because of fear that they might cause addiction or function as gateway drugs. It would be unfortunate, indeed, if opioid-induced pain relief were denied during or after surgery because of concern about its possible risks, while ignoring its known benefits.¹⁸⁴ The linchpin for medical decision making is not *risk*—for no treatment is without risk—but the *balancing of risks and benefits*. Both must be carefully and scientifically evaluated; available scientific evidence should be dispositive.

IV. POTENTIAL BENEFITS OF MEDICAL MARIJUANA

The medical use of marijuana, once officially recognized by the United States Pharmacopoeia¹⁸⁵ (based on anecdotal rather than scientific evidence), was eventually made illegal by Congressional legislation.¹⁸⁶ This section will provide a

¹⁸⁴ See, e.g., Peter J. Cohen, *Medical Marijuana, Compassionate Use, and Public Policy: Expert Opinion or Vox Populi?*, 36 HASTINGS CENTER REP. 19, 20 (2006) (“As an anesthesiologist, I have legally administered more narcotics (in the course of providing medical care) than many low-level illegal drug dealers.”).

¹⁸⁵ The United States Pharmacopeia (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 130 countries around the globe. These standards have helped to ensure public health throughout the world for close to 200 years.

USP is a non-governmental, 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.

About USP-An Overview, <http://www.usp.org/aboutUSP/> (last visited Mar. 11, 2009).

¹⁸⁶ 21 U.S.C. § 801 (2006).

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.

A. *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.¹⁸⁷ In the same year, another government-recognized publication declared (supported more by anecdotal input than scientific data): “The complaints in which it [cannabis] has been specially recommended are neuralgia, gout, rheumatism, tetanus, hydrophobia, epidemic cholera, convulsions, chorea, hysteria, mental depression, insanity, and uterine hemorrhage.”¹⁸⁸ 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.¹⁸⁹

More recently, in 1974, an herbal medical text proposed (again apparently without supporting scientific evidence):

The principal use of Hemp in medicine is for easing pain and inducing sleep, and for a soothing influence 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 all painful urinary affections. An infusion of the seed is useful in after pains and prolapsus

¹⁸⁷ THE PHARMACOPOEIA OF THE U.S., EXTRACTUM CANNABIS (3d ed. 1851) (“*Extract of hemp*. An alcoholic extract of the dried tops of *Cannabis sativa* . . . variety *Indica*.”).

¹⁸⁸ GEORGE B. WOOD & FRANKLIN BACHE, THE DISPENSATORY OF THE UNITED STATES OF AMERICA 354 (9th ed. 1851); Ian William Goddard *Cannabis: Medical Reality versus Authoritarian Brutality*, available at <http://www.ukcia.org/research/MedicalRealityVsAuthoritarianBrutality.html> (quoting GEORGE B. WOOD & FRANKLIN BACHE, THE DISPENSATORY OF THE UNITED STATES OF AMERICA 354 (9th ed.1851)).

¹⁸⁹ THE PHARMACOPOEIA OF THE U.S., EXTRACTUM CANNABIS PURIFICATUM (4th ed. 1864).

uteri. The resin may be combined with ointments [to remedy] . . . inflammatory and neuralgic complaints.¹⁹⁰

Anecdotal reports¹⁹¹ 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.¹⁹²

B. 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, while 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 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.”¹⁹³ 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 HIV-AIDS. While anecdotal reports from the AIDS community have proclaimed the efficacy of smoked marijuana, it was not until 2007¹⁹⁴ that these claims were clearly verified when the efficacy of smoked marijuana in treating

¹⁹⁰ M. GRIEVE, *A MODERN HERBAL* 397 (C. F. Leyel ed., Hafner Press 1974) (1931).

¹⁹¹ Such anecdotal reports are not confined to marijuana, but have anteceded scientific documentation of the efficacy of many of today's commonly used therapeutic agents. Thomas Sydenham (1624–1689) said, “Among the remedies which it has pleased Almighty God to give to man to relieve his sufferings, none is so universal and so efficacious as opium.” Thomas Sydenham—The Hippocrates of English Medicine, <http://opioids.com/opium/thomas-sydenham.html> (last visited Mar. 11, 2009).

¹⁹² George J. Annas, *Reefer Madness—the Federal Response to California's Medical-Marijuana Law*, 337 *NEW ENG. J. MED.* 435, 436 (1997) (citation omitted).

¹⁹³ Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 321 (2006).

¹⁹⁴ See discussion *infra* Part V.

such pain was reported in a scientific, peer-reviewed publication by Donald Abrams and coworkers.¹⁹⁵ 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% Δ 9-tetrahydrocannabinol) or identical placebo cigarettes¹⁹⁶ three times daily for five days.¹⁹⁷ The investigators evaluated both the individual subjects' quantitative description of chronic pain intensity and the percentage of subjects who reported more than a 30 percent reduction in pain intensity.¹⁹⁸ They found that smoked marijuana reduced daily pain by an average of 34 percent.¹⁹⁹ Over twice as many of the subjects who smoked marijuana reported a significant reduction in pain compared with the placebo group.²⁰⁰ Pain relief was rapid; the first marijuana cigarette reduced chronic pain by 72 percent while only 15 percent of the placebo group reported immediate relief.²⁰¹ No serious adverse events occurred during the study.²⁰² The authors concluded that "smoked cannabis was well tolerated and effectively relieved chronic neuropathic pain from HIV-associated sensory neuropathy."²⁰³

Abrams's study involved volunteers with symptoms of pathological (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 fifteen healthy volunteers.²⁰⁴ Three doses of marijuana were administered: low (2 percent), medium (4 percent), and high (8 percent Δ 9-tetrahydrocannabinol by weight). While the low dose had no analgesic effect, there was a significant decrease in capsaicin-induced pain within forty-five minutes after the medium dose was smoked.²⁰⁵ However, as with some other analgesic agents, the highest dose actually produced an increase in subjective pain perception.²⁰⁶ An important observation was that there was no significant impairment of performance among volunteers in the study as evaluated by neuropsychological testing.²⁰⁷

¹⁹⁵ D. I. Abrams et al., *Cannabis in Painful HIV-Associated Sensory Neuropathy: A Randomized Placebo-Controlled Trial*, 68 *NEUROLOGY* 515 (2007).

¹⁹⁶ From which the cannabinoids had been extracted.

¹⁹⁷ See Abrams et al., *supra* note 195, at 516.

¹⁹⁸ *Id.* at 517.

¹⁹⁹ *Id.*

²⁰⁰ *Id.*

²⁰¹ *Id.* at 518.

²⁰² *Id.*

²⁰³ *Id.* at 515.

²⁰⁴ Wallace et al., *supra* note 135, at 785.

²⁰⁵ *Id.*

²⁰⁶ *Id.* at 791.

²⁰⁷ *Id.* at 790–91.

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 colleagues²⁰⁸ 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.²⁰⁹ Thirty-eight patients with central and peripheral neuropathic pain smoked a high dose (7 percent), low-dose (3.5 percent), or placebo marijuana.²¹⁰ Smoked marijuana produced a dose-related analgesic response.²¹¹ Minimal and well-tolerated psychoactive effects were observed with the lower dose.²¹² However, higher doses were associated with some acute cognitive effects, particularly with regard to memory.²¹³ The authors concluded that while 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.²¹⁴

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 (1–8 percent THC) to alleviate HIV-

²⁰⁸ Barth Wilsey et al., *A Randomized, Placebo-Controlled, Crossover Trial of Cannabis Cigarettes in Neuropathic Pain*, 9 J. PAIN 506 (2008).

²⁰⁹ *Id.* at 507–08.

²¹⁰ *Id.* at 508–09.

²¹¹ *Id.* at 511–12.

²¹² *Id.* at 513–14.

²¹³ *Id.* at 515–16. The ability of some drugs to affect memory is certainly not confined to marijuana. Dealing with undesirable mental effects of approved medications is an essential component of pain management. Moreover, memory loss is not always an undesirable pharmacologic effect; legal anti-anxiety and amnesia-inducing drugs (falling within the ambit of the CSA) may be prescribed specifically for their ability to modify memory. *See, e.g.*, David V. Heisterkamp & Peter J. Cohen, *The Effect of Intravenous Premedication with Lorazepam (Ativan), Pentobarbitone or Diazepam on Recall*, 47 BRIT. J. ANAESTHESIA 79, 81 (1975) (“Lorazepam 3 and 5 mg was found to affect anterograde recall significantly Patient acceptance of lorazepam was very good [and two patients] requested the drug for a second operation.”).

²¹⁴ Wilsey et al., *supra* note 208, at 506.

associated neuropathic pain with that of a placebo.²¹⁵ Active and placebo cigarettes were administered four times daily for five consecutive days followed by a two week “washout” period.²¹⁶ Another five-day period was then reinstated with the control and active group reversed.²¹⁷ Subjects and investigators were blinded regarding whether they had received the placebo or active drug.²¹⁸ Active marijuana produced a statistically significant decrement in the subjects’ pain score while their mood and daily functioning improved.²¹⁹ Side effects were mild and self-limited; however, two of the thirty-four subjects dropped out of the investigation because of unpleasant symptoms.²²⁰ The authors concluded that “smoked cannabis was generally well tolerated and effective [in treating] patients with medically refractory pain due to HIV.”²²¹

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.²²² While 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.²²³ Sylvestre and colleagues found that smoked marijuana significantly ameliorated these symptoms, thereby enabling significantly more patients to complete therapy than those who did not use marijuana.²²⁴ 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 HCV treatment by helping them maintain adherence to the challenging medication regimen.”²²⁵ 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

²¹⁵ See Ronald J. Ellis et al., *Smoked Medicinal Cannabis for Neuropathic Pain in HIV: A Randomized, Crossover Clinical Trial*, NEUROPSYCHOPHARMACOLOGY 2009:34:672.

²¹⁶ *Id.* at 1–2.

²¹⁷ *Id.* at 2.

²¹⁸ *Id.* at 6–7.

²¹⁹ *Id.*

²²⁰ *Id.* at 1, 5.

²²¹ *Id.* at 1.

²²² See Diana L. Sylvestre et al., *Cannabis Use Improves Retention and Virological Outcomes in Patients Treated for Hepatitis C*, 18 EUR. J. GASTROENTEROLGY & HEPATOLOGY 1057, 1057 (2006) (citing that cannabis use relieves “side-effects associated with HCV treatment, including nausea, anorexia, weight loss, musculoskeletal pain, insomnia, anxiety, and mood instability”).

²²³ *Id.*

²²⁴ *Id.* at 1060.

²²⁵ *Id.* at 1057, 1062.

cannabis use for HCV treatment needs to be explored in larger study populations, we advocate that in the interim existing barriers to cannabis use are removed for drug users undergoing HCV treatment until the conclusive empirical basis for evidence-based guidance is available.²²⁶

These scientific data strongly suggest that marijuana has medical utility. Therefore, its designation as a Schedule I controlled substance²²⁷ 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 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.

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. It considers why it took so long for peer-reviewed studies evaluating the medical use of marijuana to appear in the scientific literature. The article will then ask why, in face of the documented safety and efficacy of medical marijuana, Congress continues to designate it as a Schedule I controlled substance and therefore illegal for medical use. It continues by exploring the question of why the medical use of marijuana was legitimized by popular vote in California and twelve other states²²⁸ rather than by “experts qualified by scientific training and experience.”²²⁹ Finally, this article queries 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”?

A. 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?

²²⁶ Benedikt Fischer et al., *Treatment for Hepatitis C Virus and Cannabis Use in Illicit Drug User Patients: Implications and Questions*, 18 EUR. J. GASTROENTEROLOGY & HEPATOLOGY 1039, 1039 (2006).

²²⁷ See 21 U.S.C. § 812(c)(10) (2006).

²²⁸ CRS Report for Congress, *supra* note 12, at 12–16.

²²⁹ See 21 U.S.C. § 321(p)(1) (defining the term “new drug” as used in the Federal Food, Drug, and Cosmetic Act).

Some might prefer a simple answer: since marijuana is a naturally occurring botanical, it cannot be patented,²³⁰ thus removing any incentive for investing the considerable amount of corporate funds required when seeking FDA approval. This consideration does not apply to the purified derivatives or extracts of marijuana²³¹ which have either been approved or are currently undergoing clinical evaluation.²³²

This article argues that this is far too facile an explanation for the inordinate delay in bringing information of the medical efficacy of marijuana into the scientific literature. This article will demonstrate how one scientist, attempting to conduct “science, not ideology,”²³³ 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.²³⁴

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 and produce objective gains in body weight.”²³⁵ 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.²³⁶ However, Dr. Abrams was

²³⁰ See, e.g., *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980) (stating “[t]he laws of nature, physical phenomena, and abstract ideas have been held not patentable”); see also Jessie A. Leak, *Herbal Medicines: What Do We Need to Know*, ASA NEWSLETTER, Feb. 2000, at 6, available at http://www.asahq.org/Newsletters/2000/02_00/herbal0200.html (recognizing “[p]lants and parts of plants are not patent-eligible”); Christopher Mitchell & Mehdi Ganjeizadeh, *Claiming Pitfalls in Bioinformatics Patent Applications*, 4 THE SCITECH LAW 5 (2008) (noting that for a patent claim to contain eligible subject matter, it must recite a “new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof” (quoting 35 U.S.C. § 101)).

²³¹ Dronabinol (synthetic THC, Marinol™) is an FDA-approved schedule III medication. See 21 C.F.R. § 1208.13(g) (2008). Sativex™ (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. See Ethan B. Russo, *Cannabinoids in the Management of Difficult to Treat Pain*, 4 THERAPEUTICS & CLINICAL RISK MGMT. 245, 251 (2008).

²³² See *infra* Part VI.

²³³ THE NATIONAL INSTITUTES OF HEALTH, NATIONAL INSTITUTE ON DRUG ABUSE: A RESOURCE GUIDE 38 (2005), <http://www.aamc.org/research/adhocgp/pdfs/nida.pdf>.

²³⁴ See COHEN, *supra* note 169, at 292.

²³⁵ *Id.*

²³⁶ *Id.*

denied permission to import marijuana from the Netherlands as he had originally planned or to use illegal marijuana that had been seized by the DEA.²³⁷

Since the National Institute on Drug Abuse (NIDA) grows marijuana and is the only domestic source for scientific investigators,²³⁸ Dr. Abrams requested their assistance, a request that would have involved only a minimal expense to NIDA.²³⁹ However, it was then the policy of the NIH to restrict its provision of marijuana only to investigators who had received a peer-reviewed NIH grant to conduct a study.²⁴⁰ Because Abrams's funding had originated at his university, and not the National Institutes of Health (NIH) of which NIDA is a part, he was refused access to NIH's marijuana.²⁴¹

²³⁷ Lisa M. Krieger, *Study Targets Stalemate Over Medicinal Use of Marijuana*, SAN JOSE MERCURY NEWS, July 19, 1998, at 1A (explaining that “[f]ive 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”).

²³⁸ NATIONAL ADVISORY COUNCIL ON DRUG ABUSE, PROVISION OF MARIJUANA AND OTHER COMPOUNDS FOR SCIENTIFIC RESEARCH: RECOMMENDATIONS OF THE NATIONAL INSTITUTE ON DRUG ABUSE NATIONAL ADVISORY COUNCIL (1998), <http://www.nida.nih.gov/about/organization/nacda/marijuanastatement.html> (“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. . . . [i]n addition to providing cannabis for research activities, NIDA also provides cannabis to the seven patients still covered by the single patient INDs.”).

²³⁹ See MULTIDISCIPLINARY ASSN. FOR PSYCHEDELIC STUDIES, REPORT TO NIDA’S EXPERT PANEL ON MEDICAL MARIJUANA RESEARCH, (1997), *available at* <http://www.maps.org/mmj/022597mmj.shtml> (“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.”).

²⁴⁰ See COHEN, *supra* note 169, at 292.

²⁴¹ Krieger, *supra* note 237 (“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.”); *see also* *Waiting to Inhale: Hemp for Health?*, MSNBC, Nov. 1997, http://www.erowid.org/plants/cannabis/cannabis_medical_media6.shtml (“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

In May of 1996, hoping that the NIH had changed its policies, Dr. Abrams resubmitted his study proposal to the NIH.²⁴² 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.²⁴³ In October 1996, four years after he had first initiated requests to obtain marijuana legally, he was again informed that the NIH would not supply it.²⁴⁴

In 1998, after six years of frustrating attempts to obtain marijuana²⁴⁵ either in the United States or abroad, the NIH finally approved Dr. Abrams's request and he

turned down time and again,' he says."); *see also* COHEN, *supra* note 169, at 292 (describing Dr. Abrams' struggles to get research materials).

²⁴² COHEN, *supra* note 169, at 292.

²⁴³ *Id.*

²⁴⁴ 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.

COHEN, *supra* note 169, at 293.

²⁴⁵ For Abrams' personal response to NIDA's intransigence, see Donald I. Abrams et al., 333 *NEW ENGL. J. MED.* 670, 671 (1995), in which he states:

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.

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.²⁴⁶

This was not the only instance in which the federal government appeared to place significant roadblocks in the way of university-sponsored research directed toward 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 2003²⁴⁷ 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.²⁴⁸ 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

²⁴⁶ See Abrams et al., *supra* note 195, at 515. The availability of marijuana for scientific investigations also removed barriers to the studies that were detailed in Part IV. See *supra* Part IV.

²⁴⁷ See Manufacturer of Controlled Substance, 68 Fed. Reg. 43,755 (Drug Enforcement Admin. July 24, 2003) (notice of application). The notice states that:

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.

Id.

²⁴⁸ See *id.* ("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.").

it.²⁴⁹ She stated in that opinion that the federal government's system for evaluating requests for marijuana for clinical study had hindered investigation of the drug's safety and effectiveness.²⁵⁰ As of mid-2008, the case is still pending.²⁵¹ 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 "[t]he government maintains that no sound scientific studies exist to support marijuana's medical value."²⁵²

The federal government's stance regarding scientific investigation of medical marijuana has, however, been far from monolithic. While those individuals within the NIH who acted on Dr. Abrams's 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,"²⁵³ 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" in February 1997.²⁵⁴

At this forum,²⁵⁵ 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.²⁵⁶ The participants suggested that although $\Delta 9$ -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.²⁵⁷ They noted the plant may also contain other compounds with important therapeutic properties.²⁵⁸ Moreover, "the bioavailability

²⁴⁹ Amy Lynn Sorrel, *DEA Judge's Ruling Could Help Medical Marijuana Research*, AMER. MED. NEWS, Mar. 19, 2007, <http://www.ama-assn.org/amednews/2007/03/19/gvsb0319.htm>.

²⁵⁰ See *id.* 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." *Id.*

²⁵¹ Mark Kaufman, *Researchers Press DEA to Let Them Grow Marijuana*, WASH. POST, May 24, 2007, at A03.

²⁵² Sorrel, *supra* note 250.

²⁵³ NATIONAL INSTITUTES OF HEALTH, WORKSHOP ON THE MEDICAL USE OF MARIJUANA (1997) [hereinafter NATIONAL INSTITUTES OF HEALTH], <http://www.nih.gov/news/medmarijuana/MedicalMarijuana.htm>. I did not participate in this workshop.

²⁵⁴ *Id.*

²⁵⁵ This conference took place only a few months after California voters had passed Proposition 215. *Id.*

²⁵⁶ *Id.*

²⁵⁷ See *id.* ("The availability of THC in capsule form does not fully satisfy the need to evaluate the potential medical utility of marijuana.")

²⁵⁸ *Id.*

and pharmacokinetics of THC from smoked marijuana are substantially different than those of the oral dosage form.”²⁵⁹

The expert group proposed that the possibly beneficial (or even superior²⁶⁰) role of smoked marijuana cannot be delineated without proper investigation.²⁶¹ 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.²⁶² 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
- Glaucoma²⁶³

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.*²⁶⁴

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 to discuss the medical use of marijuana (*Workshop on Prospects for Cannabinoid Drug Development*,

²⁵⁹ *Id.*

²⁶⁰ See *supra* note 15 (explaining that smoking marijuana allows greater drug effectiveness and thus requires a lower dosage).

²⁶¹ See NATIONAL INSTITUTES OF HEALTH, *supra* note 253.

²⁶² *Id.*

²⁶³ *Id.*

²⁶⁴ *Id.* (emphasis added).

National Academies of Sciences–Institute of Medicine) was held in February 1998; the proceedings were published in 1999.²⁶⁵ Discussion at this meeting centered on both the adverse effects and potential benefits of smoked marijuana.²⁶⁶ 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.²⁶⁷ Some participants stressed—as had those at the NIH conference held the preceding year—that since the whole marijuana plant contains many possibly active cannabinoids besides THC, its possible efficacy may not be replicated by medications containing only THC.²⁶⁸

Nonetheless, the suggestion by an impartial conference of experts that marijuana might have some medical utility that should be discussed 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.²⁶⁹

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 inserts the health agency into yet another fierce political fight

. . . . [It] directly contradicts a 1999 review by the Institute of Medicine [IOM], a part of the National Academy of Sciences, the

²⁶⁵ See generally INSTITUTE OF MEDICINE, MARIJUANA AND MEDICINE: ASSESSING THE SCIENCE BASE, (Janet E. Joy et al., eds., 1999).

²⁶⁶ See *id.* at 15–16 (describing the discussions that took place at the National Academy of Sciences–Institution of Medicine workshops).

²⁶⁷ See *id.* at 20–24 (discussing the range of participants and their utilization of medical marijuana).

²⁶⁸ *Id.* at 3, 150. See *infra* Part VI (discussing dronabinol, a cannabinoid).

²⁶⁹ Press Release, U.S. Food and Drug Administration, Inter-Agency Advisory Regarding Claims that Smoked Marijuana Is a Medicine (Apr. 20, 2006), www.fda.gov/bbs/topics/NEWS/2006/NEW01362.html.

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."²⁷⁰

Dr. John Benson, cochairman 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."²⁷¹ 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."²⁷²

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.²⁷³ The ACP paper stressed that this agent was neither devoid of potentially harmful effects nor universally effective.²⁷⁴

²⁷⁰ Gardiner Harris, *F.D.A. Dismisses Medical Benefit from Marijuana*, N.Y. TIMES, Apr. 21, 2006, at A1.

²⁷¹ *Id.*

²⁷² *Id.*

²⁷³ TIA TAYLOR, AM. COLL. OF PHYSICIANS, SUPPORTING RESEARCH INTO THE THERAPEUTIC ROLE OF MARIJUANA 1 (2008), available at http://www.acponline.org/advocacy/where_we_stand/other_issues/medmarijuana.pdf.

²⁷⁴ See, e.g., *id.* at 3. The ACP recommends that cannabis not be used to treat glaucoma, stating that:

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 conjunctival hyperemia. Smoked or eaten marijuana and oral THC can reduce IOP by approximately 25% in people with normal IOP who have visual field changes, with similar results exhibited in healthy adults and glaucoma patients. However, the effects of cannabinoids on IOP are short-lived, and high doses are required to produce any effects at all. There is concern that long-term use of marijuana could reduce blood flow to the optic nerve because of its systemic hypotensive effects and its potential for interaction with other antiglaucoma drugs. In addition, the cardiovascular and psychoactive effects of smoked marijuana contraindicate its use in glaucoma patients, many of whom are elderly and have comorbidities. This led to the development and testing of a topical THC, but its effect on IOP was insignificant. As a result, the IOM and American Academy of Ophthalmology concluded that no scientific evidence has demonstrated increased benefits or diminished risks of marijuana use to treat glaucoma compared with the wide variety of pharmaceutical agents currently available.

Id. (citations omitted).

Nonetheless, it strongly recommended that marijuana should not be summarily rejected as a bona fide therapeutic agent and urged “an evidence-based review of marijuana’s status as a Schedule I controlled substance to determine whether it should be reclassified to a different schedule.”²⁷⁵ The ACP paper stated that the review “should consider the scientific findings regarding marijuana’s safety and efficacy in some clinical conditions as well as evidence on the health risks associated with marijuana consumption, particularly in its crude smoked form.”²⁷⁶

The ACP took note of the historical fact that marijuana has been smoked for its medicinal properties for centuries.²⁷⁷ It cited extant scientific data and stated that “[p]reclinical, clinical, and anecdotal reports suggest numerous potential medical uses for marijuana.”²⁷⁸ 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.”²⁷⁹ 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.

²⁷⁵ *Id.* at 8.

²⁷⁶ *Id.* at 8.

²⁷⁷ *Id.* at 1.

²⁷⁸ *Id.*

²⁷⁹ *Id.* at 1.

- 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.²⁸⁰

C. 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.”²⁸¹ This decision was not made by scientific experts but by Congressional legislative fiat. What was the role of politics in Congress’s decision to circumvent, albeit legally, the review process that has governed approval decisions for almost all medications?²⁸²

²⁸⁰ *Id.*

²⁸¹ 21 U.S.C. § 812(b)(1) (2006) (“The drug . . . has a high potential for abuse . . . [and] has no currently accepted medical use in treatment in the United States.”).

²⁸² The marijuana-related conflict between political ideology and scientific evidence is not a recent phenomenon, but was seen over 70 years ago during Congressional hearings to discuss the Marijuana Tax Act. *See, e.g.*, DAVID F. MUSTO, *THE AMERICAN DISEASE: ORIGINS OF NARCOTIC CONTROL* 225, 228 (Oxford University Press Expanded ed. 1999) (1973).

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.

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. The statute²⁸³ designates the following compounds as Schedule I controlled substances:

- Marihuana
- Tetrahydrocannabinols
- Peyote
- Lysergic acid diethylamide
- Heroin²⁸⁴

Id.

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. *See, e.g.*, Prevention Works!—Harm Reduction in the Nation’s Capital, <http://www.preventionworksdc.org/about.html> (last visited Mar. 27, 2008). 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.” *Id.*

²⁸³ 21 U.S.C. § 812(c).

²⁸⁴ Heroin, designated as a schedule I controlled substance under 21 U.S.C. § 812(b)(10), is an accepted and legal therapeutic agent in many countries therefore there is no scientific justification for designating it as schedule I. *See, e.g.*, M. Giovannelli, N. Bedforth, A. Aitkenhead, *Survey of Intrathecal Opioid Usage in the UK*, 25 EUR. J. ANAESTHESIOLOGY 118, 118 (2008) (finding that opioids such as diamorphine were used in 136 (78.2%) of departments); *see also* A Hallett et al., *Patient-Controlled Intranasal Diamorphine for Postoperative Pain: An Acceptability Study*, 55 ANAESTHESIA 532, 538 (2000) (“We conclude that patient-controlled intranasal [heroin] is an effective form of postoperative pain relief which was well tolerated by patients and nurses with acceptably few side-effects.”); M. Hewitt et al., *Opioid Use in Palliative Care of Children and Young People with Cancer*, 152 J. PEDIATRICS 39, 39 (2008) (stating that the use of heroin was documented in 58% of pediatric patients undergoing palliative care for terminal cancer); Jason M. Kendall et al., *Multicentre Randomised Controlled Trial of Nasal Diamorphine for Analgesia in Children and Teenagers with Clinical Fractures*, 322 BRIT. MED. J. 261, 261 (2001) (“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*, 64 CAN. J. PHYSIOLOGY AND PHARMACOLOGY 1, (1986) (“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.”). Indeed, once heroin is administered to humans, it is converted to morphine

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.²⁸⁵ 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.²⁸⁶ 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.²⁸⁷

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.²⁸⁸

(schedule II) by the liver and, therefore, has properties not dissimilar to those of morphine. Rania Habal, *Toxicity: Heroin*, EMEDICINE, Aug. 12, 2008, <http://www.emedicine.com/med/TOPIC1003.HTM> (“Heroin is rapidly converted to 6-monoacetylmorphine (6-MAM) by the liver, brain, heart, and kidney and may not be detected in the blood at the time of blood draw. 6-MAM is then converted to morphine.”). Its designation as schedule I exemplifies that the interaction of politics and science is not confined to medical marijuana.

²⁸⁵ See *United States v. Oakland Cannabis Buyers' Cooperative*, 532 U.S. 483, 491 (2001).

²⁸⁶ *Id.* at 492–93.

²⁸⁷ *Id.* (emphasis added) (citations omitted).

²⁸⁸ *Gonzales v. Raich*, 545 U.S. 1, 13 (2005) (emphasis added) (citations omitted).

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,²⁸⁹ 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 unjustified,²⁹⁰ marijuana remains a Schedule I medication and there have been no realistic attempts to bring about a change in this situation. Legislators rather than "experts qualified by scientific training and experience"²⁹¹ have acted to deny marijuana admission to legitimate medical practice.

²⁸⁹ 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. See *United States v. Evers*, 643 F.2d 1043, 1048 (5th Cir. 1981) (discussing "off-labeling" of prescription drugs and holding that "[o]nce (an approved) new drug is in a local pharmacy after interstate shipment, the physician may, as part of the practice of medicine, lawfully prescribe a different dosage for his patient, or may otherwise vary the conditions of use from those approved in the package insert, without informing or obtaining the approval of the Food and Drug Administration"). For further discussion, see *infra* Part VI.

²⁹⁰ See, e.g., *Gonzales*, 545 U.S. at 15 n.23 ("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)."); see also George J. Annas, *Reefer Madness—the Federal Response to California's Medical-Marijuana Law*, 337 NEW ENGL. J. MED. 435, 438 (1997) ("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 LD-50 (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.").

²⁹¹ See 21 U.S.C. § 321(p)(1) (2006).

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 thirteen states rather than by “experts qualified by scientific training and experience?” While this article’s 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 215²⁹² and its overwhelming acceptance by the people of California

²⁹² Compassionate Use Act of 1996, CAL. HEALTH & SAFETY CODE § 11362.5 (West 2001). The Act states:

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.

(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

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 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.²⁹³ Ms. Raich claimed that she had a fundamental right to use medical marijuana, an agent that she believed necessary to preserve her life.²⁹⁴ Although her use of medical marijuana was legal under California's Proposition 215, it was illegal under federal law.²⁹⁵ 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."²⁹⁶ The Court of Appeals for the Ninth Circuit denied her appeal.²⁹⁷ Her statements after this decision—"It's not every day in this country that someone's right to life is taken from them"²⁹⁸ and "[t]oday you are looking at someone who really is walking dead"²⁹⁹—exemplified

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.

²⁹³ Raich v. Gonzales, 500 F.3d 850, 855 (9th Cir. 2007).

²⁹⁴ *Id.* ("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. [Additionally, he] provided a list of thirty-five medications that were unworkable because of their side effects.").

²⁹⁵ *Id.* at 854–55.

²⁹⁶ *Id.* at 863.

²⁹⁷ *Id.* at 869.

²⁹⁸ *See, e.g.,* Jesse McKinley, *Dying Woman Loses Appeal On Marijuana As Medication*, N.Y. TIMES, Mar. 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.").

²⁹⁹ *Id.*; *see also* Bob Egelko & Jim Herron Zamora, *Medical Pot User Loses Again in Federal Court*, S.F. CHRON., Mar. 15, 2007, at A11 (quoting Angel Raich as saying, "I don't want that coffin, but from this point on I am walking dead. . . . 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").

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.³⁰⁰

D. "Gaming the System"

Will approval and legitimization of the cultivation, prescription, and dispensing of medical marijuana have unintended consequences? Recent events in California, one of thirteen 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.³⁰¹ In the

³⁰⁰ *Raich*, 500 F.3d at 866 ("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) (citation omitted)).

³⁰¹ This problem has not escaped the notice of California's Attorney General. *See, e.g., California Issues New Medical-Marijuana Guidelines*, JOIN TOGETHER, Sep. 2, 2008, <http://www.jointogether.org/news/headlines/inthenews/2008/california-issues-new.html>. Indeed, the following article notes the following:

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

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. . . .

[I]n 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 the Los Angeles City Council. "We had marijuana facilities next to high schools and there were high school kids going over there and there was a lot of abuse taking place."³⁰²

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 nonmedical 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.³⁰³

document each member's contribution of labor, resources, or money to the enterprise. They also should track and record the source of their marijuana."

...
Brown's office and federal law enforcement continue to conduct raids on medical-marijuana dispensaries thought to be violating state and/or federal laws.

Id.

³⁰² Jesse McKinley, *Marijuana Hotbed Retreats on Medicinal Use*, N.Y. TIMES, June 9, 2008, at A1.

³⁰³ See, e.g., Head Shop Supply: Medical, Medicinal Marijuana Seeds, <http://www.headshopsupply.com/medical.php> (last visited Mar. 16, 2008) ("[G]rowing medical marijuana is now legal in many states in the United States such as California, Nevada, Alaska and Oregon If you are wondering how to become licensed for medical marijuana as a grower or a user you can seek out and ask questions at your local compassion club. If you are licensed to grow a certain number of plants for personal

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.³⁰⁴ The National Center on Addiction and Substance Abuse (CASA) stated that only two out of 365 websites that sold prescription drugs online had been certified by the National Association of Boards of Pharmacy.³⁰⁵ Although only 42 percent of the websites surveyed explicitly stated that no prescription was required to obtain drugs, 85 percent actually sold their drugs without a prescription.³⁰⁶ 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.”³⁰⁷

It was, perhaps, inevitable that similar abuses of marijuana would occur whether or not it was 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 civil³⁰⁸ or the criminal justice systems³⁰⁹ are incapable of dealing effectively with illegal activities conducted outside the web.

medical marijuana use and you need medical marijuana seeds we have many available at a discount price for medical marijuana growing.”); Mary Jane’s Garden: Marijuana Seeds & Supplies, <http://www.maryjanesgarden.com> (last visited Mar. 16, 2008) (“Amsterdam Marijuana Seeds now has on [*sic*] for sale where you can get 10 free when you buy indoor or outdoor pot seeds for a limited time only.”); Medical Marijuana Provider Form, <http://www.mainevocals.net/printablemedform.htm> (last visited Mar. 16, 2008); *see also* Welcome to SIMM, <http://www.medicalmarijuana.org> (last visited Mar. 16, 2008) (“Our purpose—to produce and supply patients with high quality medical cannabis, at the lowest possible price.”).

³⁰⁴ *85 Percent of Online Pharmacies Don’t Require Prescription, CASA Study Finds*, July 10, 2008, <http://www.jointogether.org/news/research/summaries/2008/85-percent-of-online.html>.

³⁰⁵ *Id.*

³⁰⁶ *Id.*

³⁰⁷ *Id.*

³⁰⁸ *See Hurwitz v. Bd. of Medicine*, No. 96-676, 1998 WL 972259, at *2 (Va. Cir. Ct. June 30, 1998) (holding that “the board of medicine exercised its summary suspension power, concluding that the doctor’s unprofessional conduct, coupled with an apparent unquestioning compliance with patients’ requests for prescriptions and refills, all justified board intervention to prevent danger to his patients. ‘It [was] not just a “clerical error” [for

VI. WILL THE FUTURE USE OF EXTRACTS OF MARIJUANA 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.

A. Dronabinol

Dronabinol (also known as “synthetic THC” or “Marinol”) is a Schedule III oral medication approved by the FDA for the treatment of AIDS-related wasting and chemotherapy-induced nausea and vomiting.³¹⁰ Although this approval for only two indications may appear 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).³¹¹ While physicians may prescribe the medication for uses not approved by the FDA, the manufacturer's advertising and promotion for off-label

the doctor] to fail to record the justification for refilling prescriptions, but it [was] an absence of certifying the medical necessity for the excess dosage in the patient's medical records as required by Va. Code Ann. § 54.1-2971.01”).

³⁰⁹ See 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*, WASH. POST, July 14, 2007, at B1. (noting that after Dr. William Hurwitz was convicted of illegal drug trafficking his 25-year prison term was voided. See *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).

³¹⁰ See, e.g., *Marinol—the Legal Medical Use for the Marijuana Plant*, <http://www.justice.gov/dea/ongoing/marinol.html> (last visited Mar. 16, 2009); *Marinol Product Information*, <http://www.solvaypharmaceuticalsus.com/products/marinolproductinformation/0,998,12413-2-0,00.htm> (Last visited Mar. 28, 2009).

³¹¹ See, e.g., *United States v. Evers*, 643 F.2d 1043, 1048 (5th Cir. 1981) (holding that “a physician has a right to prescribe any lawful drug for any purpose 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”). On this basis, physicians can legally prescribe Dronabinol for treating multiple sclerosis, spasticity, or depression.

therapy is regulated.³¹² Pharmaceutical companies may not directly advertise their approved medications for off-label use, but they may distribute scientific literature that supports such use.³¹³ Some authorities, however, maintain that these proposed changes in federal oversight may not protect the public.³¹⁴

³¹² See Press Release, U.S. Food and Drug Administration, FDA Proposes Guidance for Dissemination of Information on Unapproved Uses of Medical Products (February 15, 2008), available at <http://www.fda.gov/bbs/topics/NEWS/2008/NEW01798.html>.

³¹³ *Id.*

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.

Id. (emphasis added).

³¹⁴ See, e.g., Mike Mitka, *Critics Say FDA’s Off-Label Guidance Allows Marketing Disguised as Science*, 299 J. AM. MED. ASS’N 1759, 1759 (2008) (“Critics say the proposed guidance, as currently written, will allow companies to selectively use as a marketing tool peer-reviewed journal articles that support off-label use of their product. They also argue the guidelines could possibly harm public health by allowing manufacturers a back door for putting products into health care setting for unapproved uses without having to conduct rigorous clinical studies to gain FDA approval.”); Aaron S. Kesselheim & Jerry Avorn, *Pharmaceutical Promotion to Physicians and First Amendment Rights*, 358 NEW ENGL. J.

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.³¹⁵ This requirement may prove problematic in the face of nausea or vomiting. Moreover, while 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.³¹⁶ 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.

B. *Sativex*TM

*Sativex*TM (produced by GW Pharma), a cannabinoid-based oral-mucosal spray, was developed in response to the inherent problems posed by the oral medication Dronabinol.³¹⁷ *Sativex*TM contains equal amounts of Δ -9-tetrahydrocannabinol (THC) and cannabidiol (CBD) which are found in *Cannabis sativa*, but is devoid of the other compounds found in the whole plant.³¹⁸ The rapid absorption of *Sativex*TM allows easy titration, a property that may provide a major advantage over Dronabinol.³¹⁹

MED. 1727, 1731 (2008) (“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*, 299 J. AM. MED. ASS'N 1949, 1951 (2008) (“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.”).

³¹⁵ See, *Marinol Prescribing and Safety Information*, http://www.solvaypharmaceuticals-us.com/static/wma/pdf/1/3/2/5/0/004InsertText500012_RevMar2008.pdf (Last visited Mar. 16, 2009).

³¹⁶ 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 GW Pharmaceutical: FAQs, <http://www.gwpharm.com/faqs.asp> (last visited Mar. 16, 2009) (addressing frequently asked questions about *Sativex*).

³¹⁷ *Id.*

³¹⁸ See *id.*

³¹⁹ See *id.*

In April 2005, GW Pharma received regulatory approval for Sativex™ in Canada for symptomatic relief of neuropathic pain in multiple sclerosis.³²⁰ 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.³²¹ The use of Sativex™ in treating multiple sclerosis is now allowed in the United Kingdom³²² and the drug is currently undergoing late-stage clinical testing in Europe and the United States.³²³ 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 five-week, randomized, double-blind, placebo-controlled study, the intensity of neuropathic pain of peripheral origin was significantly ameliorated by Sativex™, as compared with placebo.³²⁴

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.³²⁵ These randomized, double-blinded studies compared Sativex™ and placebo and found Sativex™ to be superior to placebo.³²⁶ Multiple sclerosis-associated spasticity was significantly reduced by Sativex™ in another randomized, placebo-controlled study performed in three medical centers.³²⁷

³²⁰ *Multiple Sclerosis—Canada Approves Cannabis Derived Pharmaceutical Treatment, Sativex™(reg)*, MEDICAL NEWS TODAY, Apr. 22, 2005, <http://www.medicalnewstoday.com/articles/23299.php>.

³²¹ Press Release, GW Pharmaceuticals, Innovative Treatment Option for Cancer Pain Now Available in Canada (Jul. 8, 2007), available at <http://production.investis.com/gwp/pressreleases/currentpress/2007-08-07>.

³²² See, e.g., *MS Society Welcomes Information on Sativex™, UK*, MEDICAL NEWS TODAY, Dec. 14, 2007, <http://www.medicalnewstoday.com/articles/91814.php> (stating that 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).

³²³ See GW Pharmaceutical: Research & Development / Product Pipeline, http://www.gwpharm.com/research_pipeline.asp (last visited Mar. 16, 2009).

³²⁴ Turo J. Nurmikko et al., *Sativex™ Successfully Treats Neuropathic Pain Characterised by Allodynia: A Randomised, Double-blind, Placebo-controlled Clinical Trial*, 133 PAIN 210, 217–19 (2007).

³²⁵ Michael Iskedjia et al., *Meta-analysis of Cannabis Based Treatments for Neuropathic and Multiple Sclerosis-related Pain*, 23 CURR. MED RES. & OPIN. 17, 17 (2007).

³²⁶ *Id.* (“[T]he cannabidiol/THC buccal spray [was] effective in treating neuropathic pain in MS.”).

³²⁷ Derick T. Wade et al., *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*, 10 MULTIPLE SCLEROSIS 434, 434 (2004)

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. Since 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.³²⁸ Since 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. Since the *Cannabis sativa* plant contains many bioactive compounds besides THC and cannabidiol,³²⁹ it cannot be stated a priori that Sativex™ will be an ideal replacement for marijuana in every medical situation.

*C. Comparing the Safety and Efficacy of Dronabinol, Sativex™,
and Smoked Marijuana*

While 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 #1 (e.g., active Sativex™ spray) + placebo drug #2 (smoked inactive marijuana); or (2) placebo drug #1 (inactive Sativex™ spray) + active drug #2 (e.g., smoked active marijuana).³³⁰ While 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.

(noting that spasticity was significantly reduced by Sativex™ in comparison with placebo and that “[t]here were no significant adverse effects on cognition or mood”).

³²⁸ Although the FD&C Act does not require that a new drug be shown to be superior—or even equivalent—to already approved medications, 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. See 21 U.S.C. § 355(b)(1) (2006).

³²⁹ See *supra* Part V (discussing recommendations of the NIH Workshop).

³³⁰ See Steven R. Salbu, *Regulation of Drug Treatments for HIV and AIDS: A Contractarian Model of Access*, 11 YALE J. ON REG. 401, 435–36 (1994) (explaining how double-blind experiments are particularly useful in testing effects of medication).

VII. CONCLUSION

At the beginning of this article, a basic question was posited: 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”³³¹ 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,³³² and unwarranted fear.³³³ These have led to the

³³¹ Federal Food, Drug, and Cosmetic Act 21 U.S.C. 355(e) (2006).

³³² A justice 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).

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.

Id.

³³³ *See, e.g.,* David F. Musto, *Opium, Cocaine and Marijuana in American History*, 265 *SCI. AM.* 40, 45–46 (1991). Musto explains that

The practice of smoking cannabis leaves came to the U.S. with Mexican immigrants, who had come North during the 1920s to work in agriculture, and it soon extended to white and black jazz musicians.

As the Great Depression of the 1930s settled over America, the immigrants became an unwelcome minority linked with violence and with growing and smoking marijuana. Western states pressured the federal government to control marijuana use. The first official response was to urge adoption of a uniform state antinarcotics law. Then a new approach became feasible in 1937, when the Supreme Court upheld the National Firearms Act. This act prohibited the

repudiation of the concept that a new drug's approval should be based on scientific evidence, rather than political and ideological considerations. Both Congress, through unsubstantiated and inappropriate scheduling, and a majority of voters within thirteen states, through approval by referenda 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"³³⁴ 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 thirteen 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.³³⁵

transfer of machine guns between private citizens without purchase of a transfer tax stamp—and the government would not issue the necessary stamp. Prohibition was implemented through the taxing power of the federal government.

Within a month of the Supreme Court's decision, the Treasury Department testified before 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.

Id.

³³⁴ See, e.g., *Reefer Madness* (aka *Tell Your Children*) (George A. Hirliman Productions 1936) (a 1936 film that 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 an off-Broadway musical satire in 2001, and has achieved the status of a "cult film").

³³⁵ Although a "favorable" risk-benefit ratio is an ideal concept, the threshold required for "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.

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. While 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 Congress to legislate that marijuana has

Baruch Fischhoff, Professor of Social and Decision Sciences and of Engineering and Public Policy at Carnegie Mellon University, discussed the risk-benefit equation in terms of technological innovations:

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).

Baruch Fischhoff, *Acceptable Risk: A Conceptual Proposal*, <http://www.fplc.edu/risk/vol15/winter/fischhof.htm> (last visited Mar. 16, 2008) (emphasis added).

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.

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. While the FDA’s role in drug evaluation is not perfect,³³⁶ 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 an investigational new drug fails to satisfy these criteria, approval should be denied.³³⁷

Should marijuana be approved as a bona fide medication? This article was not intended to provide an answer. Instead, it has 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 mooted many of the questions this article has addressed—remains a challenging issue for the future.

³³⁶ See, e.g., Cohen, *supra* note 32, at 211–13 (“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.” (citations omitted)).

³³⁷ Restoring Scientific Integrity in Policy Making: Scientists Sign-on Statement, http://www.ucfusa.org/scientific_integrity/abuses_of_science/scientists-sign-on-statement.html (last visited Mar. 16, 2009) (quoting statement made by President George H.W. Bush in an address to the National Academy of Science made on April 23, 1990: “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”).

Addendum: Since the paper was submitted, the United States Attorney General has adopted a new policy: there will be no federal prosecutions of the use of marijuana for medical purposes provided that it is done in compliance with state law.³³⁸

³³⁸ Solomon Moore, Dispensers of Marijuana Find Relief in Policy Shift, *The New York Times*, March 20, 2009 at A15:

Attorney General Eric H. Holder Jr. [has stated] that the federal authorities would no longer take action against medical marijuana dispensaries if they were in compliance with state and local laws.

While 13 states, including California, have laws allowing medical use of marijuana, they had not been recognized by the federal government. . . .

Mr. Holder's statement that he would not authorize raids on medical marijuana dispensaries appeared to shift Justice Department policy, at least rhetorically, away from the Bush administration's stated policy of zero tolerance for marijuana, regardless of state laws. Advocates of medical marijuana welcomed the change. . . .

A spokesman for the drug enforcement agency, Garrison Courtney, pointed out that the attorney general's statement indicated that the federal authorities would continue to go after marijuana dispensaries that broke state and federal laws by selling to minors, selling excessive amounts or selling marijuana from unsanctioned growers.