The 1995 Cannabis Rescheduling Petition

By Jon Gettman

Contents:

Statutory Cover Letter

Exhibit A. The proposed rules for repeal, in the form proposed by the petitioner

Exhibit B. A statement of the grounds which the petitioner relies for the repeal of the rules.

Exhibit C. A summary of any relevant medical or scientific evidence known to the petitioner

Section 1) Actual or Real Potential for Abuse

Section 2. Pharmacology.

Section 3) Scientific knowledge on marijuana's mechanism of action.

Section 4) History and current pattern of abuse.

Section 5. Scope, Duration, and Significance of Use.

Section 6. Public Health

Section 7) Psychic or physiological dependence liability.

Section 8) Related or Precursor Chemicals
July 10, 1995

ADMINISTRATOR, DRUG ENFORCEMENT ADMINISTRATION
Department of Justice
Washington, D.C.  20537

DEAR SIR:  The undersigned Jon Gettman hereby petitions the Administrator to initiate proceedings for the repeal of a rule or regulation pursuant to section 201 of the Controlled Substances Act.

   Attached hereto and constituting a part of this petition are the following:
   (A) The proposed rules in the form proposed by the petitioner.
   (B) A statement of the grounds which the petitioner relies for the repeal of the rules, and,
   (C) a summary of any relevant medical or scientific evidence known to the petitioner.

   All notices to be sent regarding this petition should be addressed to:
       Jon Gettman
       [withheld]
       Lovettsville, VA, 22080

Respectfully yours,

[signed]
Jon Gettman
Exhibit A.

The proposed rules for repeal, in the form proposed by the petitioner:

The rules placing marihuana in schedule I [21 CFR 1308.11(d)(17)],
tetrahydrocannabinols in schedule I [21 CFR 1308.11(d)(25)], Dronabinol in schedule II
[21 CFR 1308.12(f)(1)] and Nabilone in schedule II [21 CFR 1308.12(f)(2)] are repealed
because there is no scientific evidence that they have sufficient abuse potential to warrant
schedule I or II status under the Controlled Substances Act.

Petitioner's Note:

This is not necessarily a petition for the removal of the listed drugs and substances
from scheduling under the CSA, but a petition to have them removed from schedules I
and II.

Should the Department of Health and Human Services confirm the scientific and
medical basis for this petition, a consideration of the appropriate scheduling of marijuana
should be made at that time, on the basis of the HHS evaluation and in accordance with
existing law.
Exhibit B

A statement of the grounds which the petitioner relies for the repeal of the rules.

This exhibit consists of 8 abstracts, each followed by a list of sources cited in the corresponding sections of Exhibit C which summarize the evidence supporting these assertions and additional evidence in support of the repeal of the rules in question.

Section 1) Actual or Real Potential for Abuse

The assertion that any use of a presently illegal drug constitutes drug abuse is far too broad, lacks scientific validity, and does not allow for a distinction between truly dangerous and non-dangerous drugs.

The accepted contemporary legal convention for evaluating the abuse potential of a drug or substance is the relative degree of self-administration the drug induces in animal subjects.

Marijuana does not induce self-administration in animal subjects. Therefore, the dependence liability of marijuana is, at least, significantly lower than well-known drugs of abuse which do induce self-administration in animals, such as heroin, cocaine, and amphetamines.
References Cited in Section 1.


Iwamoto, E. & Martin, W. "A Critique of Drug Self-Administration as a Method for Predicting Abuse


Section 2) Pharmacology.

Contrary to prior assertions by the DEA, the chemistry, toxicology, and pharmacology of marijuana has been subjected to extensive study and peer review, and have been well-characterized in scientific literature.

The effects of marijuana smoke on the lungs have been extensively studied. While marijuana smoke has more tar and carbon monoxide than tobacco smoke, in several other areas marijuana smoke is demonstrably less harmful than tobacco smoke, as in effect on small airway function, effect on bronchoalveolar lavage (BAL) macrophages, effect on phagocytic behavior or the respiratory burst of human pulmonary alveolar macrophages, and oxidant release of pulmonary alveolar macrophages. The tar in marijuana smoke can be reduced by filtration (such as with a waterpipe), and many gas-phase cytotoxins in the smoke are water soluble. The carbon monoxide levels produced by marijuana smoke are influenced by breathholding, which provides a diminishing return in contributions to plasma levels of the drug's active ingredient and thus can be reduced by changes in smoking techniques. Efforts to promote safer marijuana use through the use of waterpipes and changes in smoking habits are impossible under existing, schedule 1 based, policy.

The absorption of THC from marijuana smoke is well characterized, and variables such as dosage stability, route of administration, bioavailability, puff volume, THC content, and breathholding time have all been investigated for their effect on absorption.

The pharmacology, toxicology, and chemistry of marijuana and its constituent chemicals have been published in scientific journals, and structure activity relationships for the cannabinoids have been established and correlated with animal tests. A stable
pharmacological profile of the substance's effects is available, as is epidemiological data on the incidence and prevalence of minor side effects. The substance has a well-established and extremely low toxicity. There are no cases of overdose on record.

This knowledge allows scientists to make valid assertions about marijuana on the basis of research on its separate constituent parts.

Prior hypotheses that marijuana's mechanism of action involved cell membrane perturbation have been abandoned by the scientific community on two grounds, 1) extremely serious problems with method affect the validity of findings supporting the hypotheses, and 2) a receptor-based mechanism of action has been determined, localized, and characterized over the last seven years.

References Cited in Section 2.


Tashkin, D. P., "Pulmonary Complications of Smoked Substance Abuse." Western Journal of Medicine; 152:525-530, May 1990


Section 3) Scientific knowledge on marijuana's mechanism of action.

Most popular assertions about marijuana's affect on the human body and brain are based on what is now viewed by the scientific community as a discredited hypothesis.

The discovery of a cannabinoid receptor system in the human body began a scientific revolution that radically altered contemporary knowledge about marijuana's effects on the body and brain.

The cannabinoid receptor system accounts for almost all of marijuana's characteristic effects, as well as the substance's low toxicity.

The receptor has also been cloned, an endogenous ligand has been identified, and an antagonist has also been discovered. A structure-activity relationship for the ligand has also been established.

The cannabinoid receptor system responds to continued exposure to marijuana by reducing the number of receptors available for binding; the discovery of this tolerance mechanism for marijuana discredits the prior hypothesis that tolerance to marijuana resulted from a desensitization of brain cells, and supports the assertion that tolerance to marijuana does not contribute to a dangerous dependence liability.

The existence of the cannabinoid receptor system has clarified concern over marijuana's possible effects on the immune system, giving credence to claims that such effects pose no threat to human health.
The existence of the receptor system explains why marijuana has never been proven to cause brain damage.

The discovery of the receptor system and the resulting research provides great promise for development of a new class of effective pharmaceutical drugs, and may enable scientists to learn more about the chemistry of emotions.

These new research findings contradict many of the DEA's on-record findings of fact about marijuana, findings which have been used in the past to block reconsideration of marijuana's scheduling status.

References Cited in Section 3.


Mechoulam, R., "Interview with Professor Raphael Mechoulam, Codiscoverer of THC", *The International Journal of the Addictions*, 21(4&5), 579-587, 1986. (The interview was conducted by Stanley Einstein in Jerusalem on January 14, 1985.)


Thomas, B., Compton, D., Martin, N., "Characterization of the Lipophilicity of Natural and Synthetic Analogs of Δ⁹-Tetrahydrocannabinol and Its Relationships to


Section 4) History and current pattern of abuse.

It has long been recognized that marijuana is no more dangerous than alcohol, caffeine, and nicotine, other drugs whose use is far more prevalent in the United States than marijuana.

Marijuana use remains a widespread, persistent, and unregulated social practice among all age groups in the United States. Nearly 80% of marijuana users do not use other illegal drugs.

There is no evidence that this widespread use indicates equally widespread abuse of marijuana.

The credibility of government provided information about marijuana and health decreases as age and education increases, discrediting the hypotheses that marijuana use is inversely dependent on risk perception.

Marijuana's schedule I status has failed to keep marijuana away from school-age children.

The prevalence of alcohol and tobacco use by school-age youths exceeds and precedes marijuana use. Targeting marijuana use as a convenient battleground for the prevention of "drug abuse" is like closing the barn door after the horses have already left the barn.

Marijuana use alone results in less emergency room visits per 100,000 population than common household painkillers or benzodiazepines.
Marijuana law enforcement efforts persist as the dominant supportive force in the supply and distribution of marijuana in the United States.

Marijuana's schedule I status instigates international competition to supply illicit marijuana to American users.

Marijuana arrests continue to consume law enforcement resources; arrests continue on the level of several hundred thousand per year.

The efforts to legitimize marijuana's schedule I status at all costs results in several errors in reasoning popular in anti-marijuana warnings. Examples include: 1) National surveys do not support the assertion that people must be scared of marijuana not to use it, 2) Marijuana users are portrayed as polydrug users, when in fact a majority do not use other illegal drugs, 3) Unfounded and inaccurate comparisons are used to defend the erroneous assertion that marijuana is now more potent that the marijuana available in the 1970's, and 4) research hypotheses are presented to the public as findings of fact, such as claims that marijuana harms every biological system to which it is exposed.

References Cited in Section 4.


Section 5. Scope, Duration, and Significance of Use.

The legislative history of the Controlled Substances Act indicates that scheduling decisions must include consideration of the costs of law enforcement attendant to a drug or substance's scheduling, as well as a consideration of the impact of such law enforcement on the young.

The absolute yet unenforceable schedule I prohibition contributes to an unfavorable set and setting accompanying school-age access and exposure to marijuana. Not only are students provided access to marijuana, they are also grossly uninformed and misled about the substance and its use.

Adherence to the polarized and unscientific 'use = abuse' model obstructs the development of effective, research based policy and drug-abuse prevention programs; this restrains progress in protecting school-age youths from the dangers presented by all drugs, legal or not.

Marijuana prohibition makes criminals out of patients who use marijuana for legitimate therapeutic purposes, and forces patients to choose between honoring the law and honoring their own health.

The absolute yet unenforceable schedule I prohibition creates tremendous ethical problems for physicians and health-care-providers, professionals well-aware of the widening gap between existing governmental policies and the developing support for marijuana's therapeutic potential in scientific and medical literature, and professionals who are seemingly instructed by law to discourage their patients from using marijuana even if such use has obvious therapeutic benefits.
The failure of the Department of Health and Human Services, and of the National Institute on Drug Abuse specifically, to address this widening breach between recent research about marijuana and the findings required to sustain marijuana's schedule I status unfairly and inappropriately makes our federal law enforcement officials, particularly officials of the Drug Enforcement Administration, appear to be heartless, insensitive, self-serving idiots.

The federal failure to reconcile marijuana's schedule I status with contemporary medical and scientific evidence places an unfair and expensive burden on state criminal justice agencies and their limited budgets.

Marijuana's schedule I status and the high priority it places on domestic and international marijuana eradication has the unintended effect of transforming domestic law enforcement activity into a massive market and price support mechanism for entrepreneurs here and abroad.

Marijuana's schedule I status mandates high priority for domestic marijuana eradication efforts; the nearly impossible task presented to law enforcement results in extreme measures and increasing federalization of local and state judicial authority.

One of the results of the DEA's domestic marijuana eradication program is that in the mid 1990's domestic marijuana cultivation is now so extensive and decentralized that the DEA admits they can no longer estimate how much marijuana is grown in the United States. If they have lost hope of even estimating how much is grown, they have abandoned hope of ever eliminating marijuana cultivation in the United States, and of ever enforcing marijuana's schedule I status as a completely prohibited substance. The
purpose of schedule I is to regulate the manufacture of drugs and substances with the highest potential for abuse; without control of domestic marijuana cultivation such regulation is impossible.

References Cited in Section 5.


Alliance for Cannabis Therapeutics v. Drug Enforcement Administration. 15 F3d 1131 (1994, App DC)


Herkenham, M., "Cannabinoid Receptor Localization in Brain: Relationship to Motor and Reward Systems," In P.W. Kalivas and H.H. Samson (eds.), *The*


Mechoulam, R., "Interview with Professor Raphael Mechoulam, Codiscoverer of THC", The International Journal of the Addictions, 21(4&5), 579-587, 1986. (The interview was conducted by Stanley Einstein in Jerusalem on January 14, 1985.)


DAWN statistics indicate that marijuana does not present enough of a significant danger to public health to be considered a schedule I drug, as reflected by emergency room visits per capita and the inadequacy of the drug in contributing to suicide.

HHS asserts that youths who use marijuana ought to realize that their marijuana use will make them end up like all drug users, standing in line for emergency medical services.

The connection of marijuana use to the use of other illegal drugs, known as the gateway theory, is considered by its creator as a descriptive association, not a prediction of illegal drug use on the part of marijuana users.

Alcohol and tobacco are the first drugs used by school aged use, and it is likely that problem alcohol drinking occurs between marijuana use and the use of other illegal drugs in those individuals who do use other illegal drugs.

Social scientists believe the policy implications of their study of teenage drug use is that prevention policies must aim to delay the age of first use of drugs by school aged youths. Individuals who try marijuana for the first time after age 20 rarely if ever use other illegal drugs.

Marijuana users are not a homogenous group. Marijuana use is not a predictor in of itself of anything, and there is no research indicating that marijuana use is necessarily an indication of any underlying emotional or psychological deficit or syndrome.
The variables that most explain teenage use of alcohol, marijuana, and tobacco are availability and prior use.

Many common factors associated with the use of drugs by school aged youths have little if any correlation with teenage drug use in well constructed research studies, including (a) substance use by parents, (b) personality traits, (c) intelligence (d) social personality traits, (e) parental relations, (f) affect, (g) participation in structured activities, (j) self-esteem, (k) general values, (l) school performance, (m) stress management skills, (n) non-peer, non-family attitudes about drug use, (o) church attendance, (p) availability, (q) academic expectations, (r) drug use by extended relatives, (s) drug use by siblings, and (t) socioeconomic status.

Social science research provides empirical evidence to support the assertion that marijuana has a low potential for abuse unsuited for schedule I classification under the Controlled Substances Act. A recent convergence between pharmacology and behavioralism lend support to a theoretical model evaluating the effects of drug, set and setting on the use of drugs. Self administration is an indication that drug plays a predominant role among those three variables; the lack of self-administration in the case of marijuana, supported by the empirical social data, supports the assertion that in regards to marijuana abuse, set and setting play a more important role than the pharmacological substance itself.

Discussion of public health policies based on longitudinal studies of drug use includes consideration of harm-reduction policies which would require the end of marijuana's schedule I status to succeed.

References Cited in Section 6.


Section 7) Psychic or physiological dependence liability.

It was widely acknowledged when the Controlled Substances Act was passed into law that marijuana did not have the severe dependence liability required by schedules I or II, and that marijuana's placement in schedule I was meant to be temporary pending the review of current research by a forthcoming national commission, which recommended marijuana's decriminalization.

When marijuana's status as a schedule I drug was reviewed in the mid 1980's, marijuana's retention in schedule I was based on a presumption that marijuana may have a severe dependence liability.

The U.S. Court of Appeals has ruled that the Controlled Substances Act mandates that a drug's abuse potential is the primary criterion in determining a drug or substance's appropriate schedule.

Marijuana use has never fit the conventional definitions of drug dependence, and the some of the nation's most respected pharmacologists indicate that marijuana does not produce much of a drug dependency problem in the U.S.

The discarded cell membrane perturbation theory held that marijuana produced dependency by stimulating the pleasure centers of the brain.

Modern research has characterized the pleasure/reward system in the brain, and the key role of the neurotransmitter dopamine in this systems natural operation. Drugs which affect dopamine production have reinforcing characteristics which explain self-
administration in animal models. Research has indicated that heroin, cocaine, amphetamines, and many other drugs of abuse affect dopamine production in the brain.

Research made possible by the receptor system breakthrough and other advances in neurobiological research indicates that marijuana has no effect on dopamine production, explaining why animals will not self-administer marijuana and providing further support for the assertion that marijuana has a significantly low potential for abuse to justify lower scheduling under existing provisions of the Controlled Substances Act, and that schedule I status is in contravention of federal law.

References Cited in Section 7.


Institute of Medicine, Marihuana and Health. (Washington, D.C., National Academy Press,) 1982.


NORML v. DEA, 559 F.2d 735 (1977)


Section 8) Related or Precursor Chemicals

DEA maintains that the presence of numerous cannabinoid substances in marijuana makes it impossible to generalize about marijuana on the basis of cannabinoid research, and that marijuana and its constituent parts are more dangerous to use than THC, the principle psychoactive ingredient in marijuana.

Modern research firmly establishes the interrelationship of the cannabinoid family of chemicals unique to marijuana, bound together both by chemical similarity and by a common mechanism of action in the human body.

There are no significant reports of abuse of the synthetic THC pill approved by the DEA in the late 1980's for nausea associated with chemotherapy.

Modern cannabinoid research, including research on marijuana, is based on the validity of assertions based on scientific research on marijuana's separate cannabinoid constituents.

DEA is not authorized under the Controlled Substances Act to make scientific or medical determinations, and must accept the paradigms and conventions of the scientific community.

The scientific community recognizes the treatment of cannabinoids as a group for classification purposes. This relationship is explicit in all cannabinoid research, and is the basis for the development of new therapeutic drugs.
There is no scientific basis for an assertion that marijuana had a greater dependence liability than $\Delta^9$-THC.

There is no scientific basis for an assertion that any cannabinoid compound has a greater dependence liability than $\Delta^9$-THC.

There is no basis for distinguishing between the scheduling of marijuana, cannabinoids, and $\Delta^9$-THC on the basis of dependence liability or potential for abuse.

References Cited in Section 8.


Exhibit C.

A summary of any relevant medical or scientific evidence known to the petitioner, section 1 of 8 sections.

1) Actual or Real Potential for Abuse

According to the legislative history of the Controlled Substances Act:

a key criterion for controlling a substance, and the one which will be used most often, is the substance's potential for abuse.¹

The contemporary criteria cited in the legislative history include a definition used in the Federal Food, Drug, and Cosmetic Act for 'potential for abuse'. These include use of sufficient amounts to create a hazard to personal or public safety, diversion from regulated manufacturers, non-medical use, or similarity to known drugs of abuse.²

A 1965 House of Representatives Report discussed the term 'potential' and indicates that there must be:

a substantial potential for the occurrence of significant diversions from legitimate channels, significant use by individuals contrary to professional advice, or substantial capability of creating hazards to the health of the user or the safety of the community. .³

for such potential to exist.

A comparison of an authoritative 1987 review of marijuana's potential for abuse with these 1970 criteria will frame some of the issues addressed by this petition. Since a considerable amount of the research reported in this petition not only follow but confirm the assertions of this review, it provides a valuable baseline assessment.

The Merck Manual is one of the most widely used and respected medical texts in the world. Like the medical journal articles cited in this petition, its contents are subject to peer review prior to publication. The complete section on "Dependence of the

² ibid.
Cannabis (Marijuana) Type" from the 15th edition of the *Merck Manual of Diagnosis and Therapy* is as follows:

Chronic or periodic administration of cannabis or cannabis substances producing some psychic dependence because of the desired subjective effects, but no physical dependence; there is no abstinence syndrome when the drug is discontinued. Cannabis can be used on an episodic but continuous basis without evidence of social or psychic dysfunction. In many users the term dependence with its obvious connotations probably is misapplied.

Use of the drug is widespread. In the USA it is commonly used in the form of cigarettes made from the dried plant, Cannabis sativa, or as hashish, the pressed resin of the plant. Recently, synthetic ∆-9 tetrahydrocannabinol (THC), an active constituent of marijuana, has become available for research and limited clinical use; despite claims of dealers and users, it does not appear on the street.

Symptoms and signs: Cannabis produces a dreamy state of consciousness in which ideas seem disconnected, uncontrollable, and freely flowing. Time, color, and spatial perceptions are distorted and enhanced. In general, there is a feeling of well-being, exaltation, excitement, and inner joyousness that has been termed a "high." Many of the psychological effects seem to be related to the setting in which the drug is taken. An occasional panic reaction has occurred, particularly in naïve users, but these have become unusual as the culture has gained increasingly familiarity with the drug. Communicative and motor abilities are decreased during the use of these drugs. Difficulty in depth perception and altered sense of timing, both of which are particularly hazardous during automobile driving, have been demonstrated. There are now several published reports on the exacerbation of schizophrenic symptoms by marijuana even in patients being treated with antipsychotic medication (e.g., chlorpromazine).

Metabolic products of marijuana are retained in the tissues for a lengthy time. Lowered testosterone levels have been reported, although the biologic significance of this is uncertain.

In recent years, critics of marijuana use have become prominent and have enlisted much scientific data in support. A counter-reform movement opposed to decriminalization and the easy acceptance of the drug in American society has emerged. Many of the claims regarding severe biologic impact are still uncertain, but some other points are not. Despite the acceptance of the "new" dangers of marijuana, there is still little evidence of biologic damage even among relatively heavy users.
This is true even in the areas intensively investigated, such as pulmonary, immunologic, and reproductive function. The surveys that continually showed an increased prevalence and increasing daily use by high school students have in recent years shown a diminution of use. [This trend has reversed itself in the early 1990's]

Marijuana used in the USA has a higher THC content that in the past. Many critics have incorporated this fact into warnings, but the chief opposition to the drug rests on a moral and political, and not a toxicologic, foundation. 4

Until the late 1980's, physical dependence and the development of tolerance were considered the key criteria by which to evaluate a drug's potential for abuse. The Merck Manual, for example, defines the following terms in the introduction to its Drug Dependence section: drug dependence of a specific type, addiction, drug abuse, recreational drug abuse, psychological dependence, physical dependence, tolerance, and withdrawal syndrome. 5 While the Merck Manual utilizes these terms according to precise definitions, the widespread use of these terms among the general population has distorted their meanings from their original clinical origins. According to one expert writing in 1992:

This has been a major source of confusion in the scientific exploration of the dependence potential or liability of drugs and the manner society reacts to this problem. The terms drug abuse, drug addiction, drug misuse or drug dependence are often used interchangeably in defining the problem. 6

Thomas Cicero is the chairman of the Drug Evaluation Committee (DEC) of the College on Problems of Drug Dependency (CPDD). The CPDD evaluates drugs for dependence liability for the National Institute on Drug Abuse (NIDA). The CPDD's scientific task is to maintain and apply standardized tests for measuring the dependence

5 ibid. pg. 1476-77.
liability of drugs. The standardization of their tests provides a scientific database that facilitates equal application of the provisions of the Controlled Substances Act to pharmaceutical drugs and substances.

The problem with the term drug abuse is that it is far too subjective to have any true significance or validity in that it means different things to different people and it is difficult to establish definitive criteria to define it. For example, this term frequently conveys social approval of the use of a drug. Clearly, using social approval alone, drug abuse varies from culture to culture and from time to time. As an example . . . in many countries the use of marijuana is legal and/or condoned and is therefore socially acceptable behavior, although in scientific terms it fulfills all of the criteria for dependence potential. Finally, the use of certain drugs in our own culture has been viewed as abuse at certain times and socially acceptable at others; alcohol and cocaine use are good examples of this phenomenon and illustrate the danger associated with using social approval alone as a criterion to classify a drug as having a significant abuse potential.7

The term drug addiction suffers from many of the same problems. The term non-medical use of drugs "should be dropped from the scientific analysis of the dependence liability of drugs, since it confuses rather than clarifies any issues."8

This concern for terminology is not new. Joseph Brady is affiliated with the Behavioral Biology Research Center of the Johns Hopkins University, and is a prominent member of the CPDD. At the annual meeting of the CPDD in 1987, Brady complained about the deplorable state of the nomenclature in this muddled arena of drug and alcohol "addiction", "dependence", "abuse" or whatever! The interchangeable, quasi-technical use of these terms as referents for a bewildering range of phenomena and experimental pseudo-phenomena continue to produce a degree of semantic and taxonomic confusion that is perpetuated in even the most current and authoritative treatments of the subject by friends and relatives alike. The terms themselves, persistently reified as substantive noun "things" that enter into subject-predicate relationships with other "things" (and affect, as well as are in turn affected

7 ibid.
8 ibid. pg 3.
by these other "things"), are seldom accorded appropriate conceptual status as constructs emerging from observed relationships between specifiable antecedents (biological and social) and definable consequences (biochemical, physiological, and behavioral). Within this relational context, the analysis of interacting biological and behavioral events would seem to provide a basis for defining these constructs more operationally and specifying the conditions under which a unifying conceptual framework can be developed for this prominent aspect of substance use and misuse." 9 (emphasis added)

Any evaluation of marijuana's real or potential for abuse for scheduling purposes under the Controlled Substances Act (CSA) must rely on the legally and scientifically significant professional standards currently employed by the CPDD.

The CPDD's policy is that evaluation of dependence liability should be based on markers that reflect biological actions of the substance in question. The CPDD relies on animal models to test for dependence liability. A 1984 review of CPDD's animal testing procedures notes that:

It is important, however, in testing drugs for physical dependence liability, to ensure that the same test paradigm is employed throughout, so that the behavioral influences are kept constant for all drugs under comparison.10

Cicero described the College's work in a background paper for the Office of Technology Assessment (OTA) of the U.S. Congress. Cicero lists harmful, "compulsive drug self-administration" as the first of five characteristics of a drug with significant abuse potential. The second characteristic Cicero notes is a "preoccupation with drug

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seeking behavior to the exclusion of all other activities." Craving, tolerance, and withdrawal symptoms are the other three markers of drug dependence.\textsuperscript{11}

These criteria are "semi-quantitative" and are used to evaluate "the degree to which a drug possesses dependence liability."\textsuperscript{12} Tolerance and withdrawal symptoms develop for many compounds, but that does not qualify them as drugs with a significant dependence liability. Cocaine use, for example, lacks evidence of significant tolerance but satisfies the first three criteria.

Thus, it is essential that one look at the full spectrum of the drug's effects and the degree to which it satisfies the foregoing criteria before any conclusions regarding its dependence potential are drawn. However, it should be clear that the first three criteria mentioned above [harmful self-administration, compulsive drug seeking behavior, and craving] must be satisfied in all cases to classify a drug as having significant dependence liability.\textsuperscript{13}

Cicero explains that people self-administer many substances because of perceived beneficial effects. It is when this behavior results in adverse consequences that self-administration becomes an indication of drug dependence.

To summarize, self-administration of a drug to the point where the behavior becomes obsessive and detrimental to the individual is the primary criterion which must be met to classify a drug as one with significant potential for dependence.\textsuperscript{14}

The CPDD's conceptual framework for screening drugs for abuse potential is the same for opiates, stimulants, depressants, hallucinogens and inhalants.\textsuperscript{15} Animal models are used to evaluate self-administration, drug-discrimination, and tolerance or other neuroadaptation.

\textsuperscript{11} Cicero, 1992 pg. 3-4.
\textsuperscript{12} ibid. pg. 4.
\textsuperscript{13} ibid., pg. 4.
\textsuperscript{14} ibid., pg. 6.
Animal models are a powerful tool, and their use by CPDD creates legal standards by which the dependence liability of drugs is determined in comparison to other drugs.

Cicero concedes that animal models are not perfect.

It must be clearly recognized that the ultimate answer to the issue of whether a drug has significant abuse potential is long-term experience once the drug has become available. Specifically, when a drug is introduced into the general population, either legally or illegally, the true incidence of its relative abuse can be assessed with far greater precision than can be achieved using animal models or limited clinical screening. Nevertheless, animal models serve as the only practical means of initially screening drugs for dependence liability and have proven to be the most effective means of detecting whether there is likely to be a problem in humans.16

On the basis of Cicero's and other reports, the Office of Technology Assessment concluded that:

The capacity to produce reinforcing effects is essential to any drug with significant abuse potential, whereas tolerance and physical dependence most commonly occur but are not absolutely required to make such a determination . . . The predominant feature of all drugs with significant abuse potential properties is that they are self-administered . . . Animal models of self-administration provide a powerful tool that can give a good indication of the abuse liability of new or unknown drugs.17

Brady succinctly summarizes the significance of reinforcement:

If the abuse liability of a substance as defined by the likelihood of it supporting drug-seeking and drug-taking, is to be evaluated, an assessment of its reinforcing functions by self-administration is clearly the method of choice.18

At CPDD's 1989 annual meeting, a presentation on reinforcing characteristics of drugs also explains that this is the preeminent criterion:

18 Brady, 1988 pg 452
If the abuse liability of a substance as defined by the likelihood of it supporting drug-seeking and drug-taking, is to be evaluated, an assessment of its reinforcing functions by self-administration is clearly the method of choice.\textsuperscript{19}

Cicero's defense of CPDD's testing paradigms rests on a considerable foundation of published material, including the work of noted researchers such as Brady, Griffiths, Schuster, and Woods. Criticism of reliance on self-administration studies will be addressed below.

The Office of Technology Assessment reached the following conclusion about marijuana's abuse potential in 1993:

While marijuana produces a feeling of euphoria in humans, in general, animals will not self-administer THC in controlled studies. Also, cannabinoids generally do not lower the threshold needed to get animals to self-stimulate the brain reward system, as do other drugs of abuse.\textsuperscript{20}

The conclusion of OTA is widely acknowledged in the pharmacological literature.

Billy Martin has written extensively on marijuana related research, and conducts research at the Medical College Of Virginia. In a paper with colleague Mary Abood, Martin reports in 1992 that:

While self-administration of drugs has been taken as an indication of psychological dependence and/or abuse potential, few reports claim to have established experimental models for self-administration of $\Delta^9$-THC. . . This observation suggests limited potential for development of . . . limited psychological dependence due to the weak reinforcing properties of $\Delta^9$-THC.\textsuperscript{21}


\textsuperscript{20} U.S Congress, Office of Technology Assessment (1993) pg 34.

Miles Herkenham conducts research for the National Institute of Mental Health on the mechanism of action of marijuana's effects on the brain. Also in a 1992 paper, Herkenham's review of the literature produces this comment:

Animals generally will not self-administer $\Delta^9$-THC. Cannabinoids did not lower the threshold for electrical self-stimulation in one study. In another study they did, but apparently both this phenomenon and the enhancement of basal dopamine efflux from the [nucleus accumbens] by $\Delta^9$-THC are strain-specific, occurring only in Lewis rats.\textsuperscript{22}

According to Iwamoto and Martin, one of the criticisms of making self-administration a preeminent test of abuse potential is that:

The mechanisms underlying self-administration behavior in animals are not well-understood.\textsuperscript{23}

Another problem is presented by possible anomalies.

There are drugs, however, which are used by humans that are not self-administered by animals and include LSD, mescaline, DOM and [marijuana].\textsuperscript{24}

The challenge for the CPDD is to derive, utilize, and defend scientific standards for defining abuse liability. The tautological argument that a definition of abuse must include marijuana use because marijuana use must be drug abuse is exactly the misuse of terminology both Cicero and Brady have complained about above. Nonetheless, the question of validity is always important in evaluating scientific reasoning.

How can the self-administration model validated? First, . . .there must be concordance between animal and clinical results. In order to


\textsuperscript{24} ibid. pg. 459.
define the limitations of methodologies, more effort should be placed on
determining the reasons for discordant results. Secondly, there also must
be some sort of concordance between both the incidence and
perniciousness of street abuse on one hand, and the results of both animal
and clinical studies on the other. Because fads and trends play a major
role in drug abuse patterns, a good concordance can be expected only for
those drugs whose street abuse is well established.25

The validity of the conceptual model behind reliance on self-administration has
been established by research on the biological actions of drugs of abuse. Brady discusses
the synergy between biology and behavior in his acceptance of a lifetime achievement
award from the CPDD in 1990.

Laboratory procedures for the generation and maintenance of
drug self-administration have become the hallmark of abuse liability
assessment based upon the kind of functional models that have proven
most useful and productive in the experimental analysis of behavior. The
most important conceptual and methodological consequence of this
interactive research has been the analysis of relationships between the
biochemical/pharmacological properties of drugs and their
environmental/behavioral stimulus functions.26

The explosive advances in new knowledge of neurotransmitter and
receptor dynamics combined with the demonstrated specificity of action
and good correspondence with drug discrimination generalization profiles
now provide a more precise behavioral reflection of neurochemical
mechanisms.27

The significance of this neurobiological research on reinforcement mechanisms in
the brain will be discussed in section 7 of this petition.

New scientific knowledge on the mechanism of action of marijuana in the human
brain will be discussed in section 3 of this petition, after a review of pharmacological
knowledge in section 2.

25 ibid. pg. 461.
26 Brady, J.V. What's a Radical Behaviorist Like You Doing in a nice Pharmacology Club like CPDD?
Committee on Problems of Drug Dependence, Inc. Harris, L. (ed.), National Institute on Drug Abuse
27 ibid.
Scientific and medical evidence contrasting marijuana's mechanism of action in the brain with that of drugs of abuse such as heroin, cocaine, and amphetamine provide additional validity to the assertion that the non self-administration of marijuana or THC by animals is an indication that the drug does not have a significant dependence liability. This will be discussed in more detail in section 7. The relationship between marijuana and other cannabinoids will be addressed briefly in section 2 and more completely in section 8.

Sections 4, 5, and 6 of the petition will review data and reports which provide evidence of marijuana's actual use in society and its actual ramifications; this evidence will provide additional validity to the assertion that animal models are accurate in predicting marijuana's abuse potential.

Cicero makes it very clear that testing only addresses the issue of abuse potential.

Whether the severity of the abuse is a problem or not depends upon the extent to which self-administration of the drug represents a problem to the individual or society. A good example is caffeine. While most recent studies indicate that caffeine has abuse potential, as defined by the criteria outlined above, it seems unrealistic and irrational to assume therefore that it is equal to other drugs of abuse in terms of its effects on the individual or society. Ultimately, relative abuse potential and its severity must be considered in terms of the criteria outlined above.28

The Controlled Substances Act allows for realistic assessment of the practical application of its regulatory provisions. This will be discussed in more detail in section 5 of the petition. The key question is how are the provisions of the CSA applied? According to Cicero, the DEA application of the CSA is too "rigid."

The Drug Enforcement Agency (DEA) takes a much more restrictive view of drugs of abuse or potential dependence liability: drug abuse is defined as the use of any illicit drug, regardless of its consequences or frequency of use. While this definition is simple and makes enforcement relatively easy by allowing the scheduling of compounds under the Controlled Substances Act, it is far too broad and

lacks scientific validity. Many compounds are illegal in the United States, but clearly the consequences of their use poses no serious threat to society or the individual. Hence, this rigid definition does not allow for discriminating truly dangerous from non-dangerous drugs and, most importantly, there is little room for accommodating scientific evidence regarding relative abuse liability. However, there seems to be sufficient latitude under the current law to schedule compounds according to classes which appear to represent the largest threat to the public health. In these instances, scientific input concerning the dependence liability of drugs is desperately needed and must be incorporated into scheduling decisions.29

This petition seeks to utilize the "latitude under current law" to restore scientific validity to marijuana's scheduling under the Controlled Substances Act.

29 Cicero, 1992 pg 3.
Exhibit C.

A summary of any relevant medical or scientific evidence known to the petitioner, section 2 of 8 sections.

2. Pharmacology.

The DEA maintains that the chemistry, toxicology, and pharmacology of marijuana are not established. They assert that because marijuana is made up of over 400 chemicals, and that only a few of them have been individually tested, that existing studies are inadequate to explain the pharmacology of the substance. For example:

Because of the complex composition of marijuana, containing over 400 separate constituents (many of which have not been tested) varying from plant to plant, the chemistry, toxicology, and pharmacology of marijuana is not established.30

These studies are inadequate, according to DEA, because of differences between the studies and actual marijuana use, in that the studies tend to be with oral and intravenous THC, not with smoked marijuana plant material used by the public. For example:

Most pharmacological research with cannabis or its constituents has actually been conducted with orally ingested THC, rather than smoked marijuana. Although the pharmacologic effects are presumed to be similar, the studies with oral THC do not provide a complete picture of marijuana’s effects. Few of the other cannabinoids have been pharmacologically evaluated. The health consequences from smoking marijuana are likely to be quite different than those of orally ingested THC. Yet most of the chronic animal studies have been conducted with oral or intravenous THC.31

According to DEA, this lack of knowledge produces a lack of standardization of the drug which creates problems measuring the bio-availability, metabolic pathways, and pharmacokinetics of marijuana. Botanical variation in the relative amounts of the

constituent chemicals in marijuana compounds the problem. DEA continually asserts that marijuana is just far too complicated for scientists to understand. For example:

[M]arijuana's chemistry is neither fully known, nor reproducible. Thus far, over 400 different chemicals have been identified in the plant. The proportions and concentrations differ from plant to plant, depending on growing conditions, age of the plant, harvesting and storage factors. THC levels can vary from less than 0.2% to over 10%. It is not known how smoking or burning the plant material affects the composition of all these chemicals. It is not possible to reproduce the drug in dosages which can be considered standardized by any currently accepted scientific criteria.32

Regardless of this lack of knowledge, DEA asserts that marijuana use has acute and chronic side effects which render the substance dangerous for public use regardless of abuse potential. For example:

There is a need for more information about the metabolism of the various marijuana constituents and their biologic effects. This requires many more animal studies. Then the pharmacologic information obtained from the animal studies must be tested in clinical studies involving humans. The pharmacologic testing of cannabinoids in animals thus far has shown that while they do not appear to be highly toxic, they exert some alteration in almost every biological system that has been studied.33 (emphasis added)

This last assertion will be addressed near the end of this section.

All of these assertions by DEA were made as part of an administrative rule-making process, and serve as findings of fact that are part of the scientific justification for retaining marijuana in schedule I. These assertions of DEA rest on an evidentiary record that was closed in 1988. Perhaps in 1988 they were valid statements, perhaps they were not. That is beyond the scope of this review, which primarily concerns scientific findings published after this prior record was closed. These claims of DEA's are presented both as an indication of the agency's own apprehension of scientific research, and as a baseline

from which to understand the progress that has occurred in pharmacological research since the late 1980's.

The chemicals in marijuana can be divided into two categories, the unique family of chemicals named cannabinoids, and other chemicals commonly occurring in nature.

The combustion of this vegetable material into smoke and its inhalation into the lungs is inherently unhealthy. The extent to which an individual can make an informed decision to assume the risks of smoke inhalation can only be gauged by an assessment of the risks and dependence liability associated with the unique chemicals in the plant material. Considerable research has been done on the effects of marijuana smoke on the lungs by Donald Tashkin of UCLA and his colleagues.

A 1987 paper explains the research dilemma.

Evidence regarding the potential long-term pulmonary consequences of regular marijuana smoking is mixed. Several studies conducted during the past decade on whole animals and isolated cell systems exposed to marijuana smoke, as well as some clinical observations, suggest that marijuana can be harmful to the lung. Conversely, human studies carried out abroad have failed to find any evidence of respiratory dysfunction or disease in long term heavy users of marijuana.34

This study reviewed the history of heavy marijuana smoking on self-reported histories of symptoms of respiratory and pulmonary disease. Tashkin's findings in this review serve as a baseline for a great deal of his subsequent research; this review established marijuana and tobacco smokers had similar symptoms of respiratory problems.

A significantly larger proportion of smokers of marijuana and/or tobacco than nonsmokers reported chronic cough, chronic sputum production, more than 1 episode of acute lower respiratory tract illness within the past 3 years (increased cough and sputum lasting more than 3 wk), and wheezing. No significant differences were found when

prevalence of these respiratory symptoms was compared across the 3 smoking groups: smokers of marijuana alone, tobacco alone, and marijuana plus tobacco. Breathlessness was reported by relatively few subjects and was similar in frequency across the 4 subject groups, with 1 exception: tobacco smokers reported a higher prevalence of shortness of breath than did marijuana smokers.35

The author's basic hypothesis is that marijuana smoke, like tobacco smoke, is harmful to the lungs, and that exposure of the lungs to both marijuana and tobacco smoke is even worse. Their findings in this and subsequent studies provide no reason to reject this hypothesis. The public wants to know if marijuana smoking is more or less dangerous for the lungs than tobacco smoking. If one were to insist on a simple answer, that answer would be this: any smoke is damaging to the lungs, and continued exposure to smoke will likely cause lung cancer. However if the public insists on using tobacco smoke as a reference, Tashkin's research demonstrates that describing marijuana smoke in reference to tobacco smoke is complicated. On a simple numerical scale, in some areas marijuana produces higher indices of risk than tobacco, and in other areas, a lower indication of risk. The conclusion of this 1987 study is as follows.

We conclude that habitual, heavy marijuana smoking, irrespective of concomitant tobacco smoking, leads to symptoms of chronic bronchitis and an increased frequency of acute bronchitic episodes. In addition, heavy, habitual smoking of marijuana, whether alone or with tobacco, has an adverse effect on large airway function, but marijuana use alone, unlike regular tobacco smoking, has no demonstrable impact on small airways function or on diffusing capacity. The combination of heavy, habitual marijuana and regular tobacco smoking does not appear to worsen chronic respiratory symptoms or lung function abnormalities associated with smoking either substance alone. The implications of these findings with respect to the subsequent development of clinically significant chronic air-flow obstruction in continuing heavy smokers of marijuana is as yet unclear.36 (emphasis added)

Marijuana smokers smoke less material by weight per day than tobacco smokers, but they inhale the smoke deeper into their lungs and retain it longer. In a 1988 paper,

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35 ibid. pg. 211.
36 ibid. pg. 215.
Tashkin and his colleagues report on their attempts to establish that marijuana smoking delivers a greater quantity of smoke particulates and noxious gases to the lungs than tobacco smoke.

Marijuana smoking resulted in a tar burden to the respiratory tract that was 3.5 to 4.5 times greater than that produced by tobacco smoking in the same subjects. Furthermore, smoking a single marijuana cigarette caused a fourfold greater increment in carboxyhemoglobin saturation than did smoking a single tobacco cigarette.37

In view of the many similarities in the smoke contents of marijuana and tobacco, it has been argued that habitually smoking a few marijuana cigarettes a day may have a proportionately less harmful long-term effect on the lungs than regularly smoking several times more tobacco cigarettes. This argument assumes that the number of cigarettes smoked is directly proportional to the dose of smoke contents inhaled; however this assumption ignores the ways in which the characteristics of smoking may influence the delivery of the combustion products of cigarettes.38

One reason the authors provide to explain the delivery of greater tar to the lungs is that unlike tobacco cigarettes, marijuana cigarettes do not have filters. Also, they report that the increased carboxy hemoglobin levels are a result of the manner of smoking rather than the carbon monoxide content of the substances. This is very interesting in a public health context, because these factors can be addressed by changes in smoking techniques. Other factors that contribute to the differences in the tar and gas content is the density of the cigarettes. Tobacco cigarettes are tightly packed, providing more filtration. Marijuana cigarettes are comparatively loosely packed, and provide more complete combustion of the smoking material.

In a 1990 review article, Tashkin places these recent findings in perspective.

It is also noteworthy that most tobacco cigarettes currently in use are filter-tipped and have a relatively low tar content, but marijuana cigarettes do not contain filters and generate about twice as much tar as


38 ibid. pg. 349.
tobacco per unit of weight, assuming a similar smoking profile. Furthermore, the techniques for smoking marijuana and tobacco differ substantially: on the average, with marijuana the inhalation, or "puff," volume is about two-thirds larger, the depth of smoke inhalation about 40% greater, and breath holding about four times longer than those characteristics of tobacco smoking. These differences in filtration and smoking technique can result in about a fourfold greater amount of tar delivered to and retained in the lungs from the smoking of marijuana than from a comparable amount of tobacco, thus potentially amplifying the harmful effects of marijuana on the lungs.39

The exposure of the lungs to harmful particulates represents one of two possible health threats provided by marijuana use. The other possible threat is whether or not marijuana smoke affects the lung's ability to protect itself from harmful bacteria and clean itself of the harmful particulates produced by the smoke.

The results of various studies imply that marijuana smoking, like tobacco smoking, impairs the lungs' defense against microbial invasion, thereby increasing the tendency to respiratory tract infection.40

A 1991 study by this team addressed this second possible health problem. Here is an explanation of the function of alveolar macrophages.

Alveolar macrophages (AM) are the principle defensive cells of the lung against inhaled particulate matter and have a primary role in the inflammatory responses of the host lung. Therefore, increased numbers of AM in the lungs of cigarette smokers would be anticipated and, in fact, have been observed in the lungs of humans habitually exposed to the irritating fumes and particulates contained in the smoke of tobacco and/or marijuana cigarettes. Because AM are constantly being lost from the lung, their continued replacement would be important in maintaining the health and integrity of the host lung.41

This results of this study is that marijuana smoke stimulated macrophages to action, but not as aggressively as tobacco smoke. Many substances stimulate

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40 *ibid.* pg. 527.
macrophage production, macrophage cell division is a normal physiological response to foreign particles.

Overall, the total number of bronchoalveolar lavage (BAL) macrophages that were . . . labeled from either tobacco or marijuana smokers was significantly greater than that obtained from nonsmokers. . . . the nonsmoking group had the least number of . . . labeled macrophages (1.01) and the marijuana smokers had the next lowest number of dividing macrophages (2.90). The subjects who smoked tobacco had a nearly 19-fold greater number of . . . labeled macrophages (17.9) compared to nonsmokers, and the subjects who smoked both marijuana and tobacco had the second highest number of labeled macrophages (10.5), with a 10-fold increase.42 (numbers in parenthesis are x 10^-3)

These results illustrate the complexity of arguing that marijuana smoke is more harmful than tobacco smoke. It may even be the case in this area that marijuana smoke mitigates against some of the damage of tobacco smoke. This study contradicted an earlier study by the same team that showed a worse effect of combined marijuana and tobacco smoking on alveolar macrophages.

Interestingly, it appears that the substance(s) in marijuana smoke may be less stimulatory than the substance(s) in tobacco smoke, and, in fact, our data suggest that marijuana smoke may even inhibit tobacco induced proliferation. The reason for this phenomenon is unclear . . . [and] is based on only six individuals in the combined tobacco- and marijuana-smoking group and may be different with a larger sample.43

The same year Tashkin worked on a study on Pulmonary Alveolar Macrophages (PAM), considered one of the primary defenses the lung has to infection.

We conclude that marijuana smoking does not alter phagocytic behavior or the respiratory burst of human PAM, but marijuana smoking does decrease the ability of human PAM to destroy ingested Candida albicanus. These findings contrast with the effects of tobacco smoking, which not only decreases the fungicidal activity of human PAM but also increases their respiratory burst.44

42 ibid. pg. 1093.
43 ibid. pg. 1095.
44 Sherman, M.P., Campbell, L.A., Gong, H., Roth, M.D., and Tashkin, D.P. "Antimicrobial and Respiratory Burst Characteristics of Pulmonary Alveolar Macrophages Recovered from Smokers of"
However, the authors explain that Candida albicanus (a yeast) is a relatively large organism, and a decreased ability to destroy it may not indicate a decreased ability to destroy bacteria.

An appropriate question to ask is whether fungistatic or fungicidal activity by PAM bears any relationship to the intracellular killing of bacteria. As opposed to fungi pathogens, bacteria are more likely to be encountered during lung infections of MS or TS. Human PAM from healthy volunteers were recently compared with respect to their ability to ingest and kill Pseudomonas aeruginosa, Staphylococcus aureus, and Candida albicanus. Although bacterial killing was complete in 2 [hours], 4-6 [hours]. were needed for PAM to kill a stationary phase, agerminative strain of C. albicanus for PAM.

Returning to the issue of particulate exposure, Tashkin has also hypothesized in 1991 that "prolonged breathholding characteristics of marijuana smoking enhances THC absorption and possibly the associated rise in heart rate and the level of intoxication." If long breathholding determines intoxication efficiency, "then it may be difficult to modify this topographic variable in an attempt to reduce the cardiopulmonary hazards of marijuana smoking." These hypotheses were based on the findings of this study that the longer breathholding of marijuana smokers contributed to the greater exposure to tar and noxious gas quantified in earlier studies.

Tashkin and his research team have also characterized the differences in the delivery of tar, carbon dioxide, and $\Delta^9$-THC from the first and second halves of a marijuana cigarette:


48 ibid.

49 ibid. pg. 655.
An important clinical implication of the findings from this study is that smoking fewer marijuana cigarettes down to a shorter butt length to deliver more $\Delta^9$-THC and achieve a greater "high" will also result in the delivery of more tar and carbon monoxide to the smoker's respiratory tract that the consumption of a comparable amount of marijuana from more cigarettes smoked to a longer butt length. Because of the respiratory irritant and carcinogenic effects of some of the components of marijuana-derived tar, and the adverse effects of inhaled carbon monoxide on oxygen transfer in the lung, transport in the blood and delivery to the tissues, the common practice of smoking marijuana down to a short butt length may augment its potentially harmful effects on cardiorespiratory health.  

Another of Tashkin's teams has studied the impact of marijuana smoking on lung macrophage oxidant release, a mechanism that contributes to emphysema. In this study important differences were found between marijuana smoke and tobacco smoke.

In summary, pulmonary alveolar macrophages recovered from marijuana-only smokers have a spontaneous and stimulated release of oxidants that is equivalent to nonsmoker's macrophages. This finding coincides with the absence of small-airway dysfunction or diffusion abnormality in both groups of subjects. In contrast, pulmonary alveolar macrophages from tobacco smokers generate more oxidants under basal and stimulated conditions, and tobacco smokers do have demonstrable evidence of small-airways disease.  

Also in 1991, a team led by Gary Huber reported on "Marijuana and Tobacco Smoke Gas-Phase Cytotoxins." They note that PAM is depressed in vitro, but the results are not replicated in vivo (the same clash of theory and result Tashkin has clarified above.) The primary cytotoxins appear to be water soluble. Furthermore, stale smoke rapidly loses cytotoxic properties. The authors hypothesized that proximal airwaves remove the water-soluble cytotoxic constituents from the gas phase of the smoke. They created a model system that successfully tested this hypothesis.

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These results may explain to a significant degree, the discrepancies that exist in literature between in vitro and in vivo cytotoxicity of marijuana and tobacco smoke. These results also raise the consideration that the potentially injurious effects of water-soluble, gas-phase constituents on alveolar macrophages on lung explants may not be relevant to the health and integrity or the lung of the intact smoker in everyday life.\textsuperscript{53}

Certainly other aspects of marijuana or tobacco smoke may have an adverse effect on macrophages.

Although the gas-phase cytotoxins have received much of the earlier investigative attention; the data presented herein, however, would appear to render them less suitable culprits.\textsuperscript{54}

In 1992 a team of Tashkin's explored the effect of THC potency on respiratory functions.

The present study was carried out to investigate the effects of escalating doses of THC administered in smoked marijuana on the ventilatory and mouth occlusion pressure responses to both hypercapnia [high levels of CO\textsubscript{2}] and hypoxia [low levels of O\textsubscript{2}] and on resting minute ventilation and metabolic rate in young, healthy experienced male users of marijuana.\textsuperscript{55}

The study found no effect of THC on ventilation, oxygen consumption, carbon dioxide production, or metabolic rate. The only effects of THC noted were that:

The habitual marijuana smokers participating in this study exhibited a significant increase in heart rate, subjective intoxication (high), and decrease in airway resistance after smoking the active preparations of marijuana, but not placebo marijuana. These findings are consistent with the known cardioaccelerator, psychotropic, and bronchodilator effects of THC.\textsuperscript{56}

\textsuperscript{53} ibid. pg. 634.
\textsuperscript{54} ibid. pg. 634.
\textsuperscript{55} Wu, H., Wright, R., Catherine, S., & Tashkin, D. "Effects of Smoked Marijuana of Varying Potency on Ventilatory Drive and Metabolic Rate" \textit{Am Rev Respir Dis} 1992 146:716-721. pg. 716.
\textsuperscript{56} ibid. pg. 718.
This study used marijuana cigarettes from the National Institute on Drug Abuse of 0, 1.55%, and 2.65% THC. While the authors can not account for the possible effect of tolerance to marijuana, they do argue that the potencies used in their study are relevant to common use of the drug.

These doses of THC are comparable with those delivered from the recreational smoking of "street" marijuana (500 mg marijuana containing 1 to 6% THC) or the oral ingestion of U.S. Food and Drug Administration-approved synthetic marijuana (7.5 to 22.5 mg) for control of nausea and vomiting due to cancer chemotherapeutic agents. Our results therefore suggest that THC in doses commonly used either recreationally or medicinally neither stimulates nor depresses central or peripheral chemoreceptor-mediated ventilatory drive in habitual users of marijuana.57

In 1993 Tashkin and colleagues studied the effect of marijuana smoke on airway hyperresponsiveness (AHR), a risk factor for development of or a marker of airway injury in individuals susceptible to chronic airflow obstruction. There results:

In summary, in a convenience sample of 542 nonsmokers and habitual smokers of marijuana, cocaine, and/or tobacco, cocaine had no demonstrable influence on nonspecific AHR, whereas marijuana appeared to have an inconsistent effect and heavy tobacco smoking a modest but statistically significant positive influence in both men and women, independent of the effect of lung function on AHR. Neither marijuana nor cocaine appeared to potentiate the effect on AHR of other smoked substances, including tobacco.58

The fact that several studies indicate that marijuana smoke is not as harmful as tobacco smoke does not change the validity of Tashkin's original assertion that marijuana smoke is harmful to the human lungs, and that this harm is compounded in individuals who also smoke tobacco.

In a recent editorial, Tashkin argued that:

57 ibid. pg. 719.

Several lines of evidence suggest that marijuana smoking is also associated with an increased risk for the development of respiratory tract malignancy.59

Tashkin explicitly notes that advocates of the legalization of marijuana are wrong when they contend that no evidence exists linking marijuana smoking to serious health effects. Some diseases take a long time to develop, but other respiratory problems do not.

One might conclude from the dearth of information concerning marijuana-related morbidity [indicating acute respiratory illness such as bronchitis and pneumonia] either that such health effects are too infrequent to be measured or that such effects are occurring at greater than expected frequency but have not been documented because of the lack of a systematic effort to "capture" these events.60

One additional complication created by marijuana's illegality is that doctors and health care professionals do not ask patients about marijuana use, or patients are reluctant to disclose such use.62 While the research of Tashkin and others suggests that the harmful effects of marijuana could be minimized through introducing filtration and the idea honest disclosure and discussion with health care professionals to marijuana smokers. This introduces a critical issue which will be discussed in section 6, that is, what public policies will best reduce the harm associated with marijuana use.

Otherwise, the research of Tashkin and others on the effect of marijuana smoke on the lung contributes a great deal to understanding and characterizing the pharmacology of marijuana and its smoke. Marijuana smoke is the primary vehicle that introduces the active ingredients in marijuana into the human body; smoking is the primary route of administration. It is important in understanding the pharmacology of

60 ibid. pg. 636.
marijuana to distinguish between the effects of the smoke and the effects of the active ingredients, cannabinoids. Furthermore, understanding the absorption of the active ingredients from the smoke is crucial to understanding the effects of the constituent chemicals, the cannabinoids, on the rest of the body.

Mario Perez-Reyes has done considerable research on the pharmacology of marijuana. The paper he and his colleagues published in 1991 on "The Pharmacologic Effects of Daily Marijuana Smoking in Humans" is instructive beyond its findings, which concern tolerance.

Therefore, as long as marijuana is not used more than once daily, it appears that there is no need to escalate the dose to obtain the same degree of "high."

Acceleration of the heart rate is a consistent effect of THC. In this study, a trend toward diminished cardioacceleration and a significant decrease in the heart rate acceleration time response pattern were found to occur after the period of daily marijuana smoking. Taken together, these observations suggest that tolerance to the heart rate-accelerating effects of THC develops in response to modest daily doses of the drug . . .

That tolerance to the heart rate-accelerating effects of THC develops more readily than tolerance to its subjective effects is not understood . . . tolerance to cardio-acceleration may occur more readily as fewer neuronal circuits are involved.63

Like Tashkin's work, this study demonstrates that it is possible to use standardized marijuana is clinical experiments. The study used marijuana cigarettes provided by the National Institute on Drug Abuse (NIDA). The cigarettes were prepared from active and placebo material to obtain a standard 1% THC content, the average dose of THC was 8.8 mg per cigarette.64

This study also measured the bioavailability of marijuana by comparison with intravenously infused deuterated THC, with a calculation method that allowed for the

64 ibid. pg. 692.
different routes of administration. The direct estimation of bioavailability of THC from marijuana smoke has not been previously available.

Exposure to daily marijuana smoking did not alter the bioavailability of smoked THC. Wide individual variations were found, which confirms the observations of large individual variability of the manner in which marijuana cigarettes are customarily smoked.

THC is studied more intensely than other cannabinoids, and the pharmacokinetics and metabolism of cannabinoids were reviewed in 1986 by Agurell, Hollister, and colleagues. Hollister characterized this research during an acceptance speech for a lifetime achievement award from the College on the Problems of Drug Dependence, at which he once served as the chairman of the Drug Evaluation Committee.

Our studies of cannabinoids over the past 22 years have touched upon virtually every aspect of their actions. They constitute the largest series of studies of the human pharmacology of marijuana on record. Some have been concerned with drug interactions, most notably with other cannabinoids; we found none.

At some point in studying drugs, it becomes desirable to measure plasma concentrations to obtain a sense of the drug's pharmacokinetics and to try to relate these to clinical effects. The Swedish group, headed by Stig Agurell, was so far ahead in techniques of measurement that I despained of ever being able to catch them. So, following the old saying, "If you can't lick them, join them" we have collaborated with them during the past 10 years, the clinical work being done in the US and the laboratory measurements being done in Sweden. This cooperation has elucidated the patterns of drug availability from three routes of administration (smoking, ingestion and intravenous administration), has found that the kinetics of the inactive cannabinoids, CBD and CBN are similar to those of THC, has found that heavy marijuana use as compared

65 ibid.
66 ibid. pg. 694.
with light use does not much change the kinetics, and has correlated clinical actions with plasma concentrations.69

A closer look at Agurell and Hollister's 1986 review clarifies some basic background on the toxicology of cannabinoids.

(Agurell is from Sweden, and European scientists use a different labeling system for cannabinoids than scientists in the U.S. The system used by Agurell is a monoterpenic system, and refers to the active agent as delta-one THC. The U.S. uses the dibenzopyran system which refers to delta-nine THC.)

The major cannabinoids are the Tetrahydrocannabinols (THC), cannabinol (CBN) and cannabidiol (CBD).

Of more than 60 cannabinoids . . . only $\Delta^1$-THC has profound psychoactive properties. CBN i.v. shows about 1/10 the potency of $\Delta^1$-THC in man, whereas CBD is devoid of psychotomimetic properties. $\Delta^6$-THC is about equipotent with $\Delta^1$-THC but is usually present in very small amounts compared to $\Delta^1$-THC, CBD, and CBN. The latter three compounds occur in marihuana-type preparations in concentrations usually around 1 to 2%.70

Agurell and colleagues discuss the chemical aspects of THC, the influence of various routes of administration, their relation to blood plasma levels, and other pharmacological issues. They also conclude that:

In man it is unlikely that any active metabolite, such as 7-hydroxy-$\Delta^1$-THC, contributes in an important way to the effects of $\Delta^1$-THC after smoking or i.v. administration. After p.o. administration, however, we assume that 7-hydroxy-$\Delta^1$-THC contributes at least as much as $\Delta^1$-THC itself.71

Additional findings include the following. Agurell's team also measured bioavailability, and found a difference between heavy and light users. Plasma $\Delta^1$-THC profiles are similar after i.v. injection and smoking.

69 ibid. pg. 42.
70 Agurell et al (1986) pg. 22.
71 ibid. pg. 31.
The pharmacokinetics and metabolism of CBD and CBN in man and animals follow the pattern similar to that of $\Delta^1$-THC.\textsuperscript{72} The authors also note that:

Other studies suggest limited variation in pharmacokinetic parameters between heavy and light users, indicating that the development of tolerance to behavioral and pharmacological effects in THC users is most likely functional and not dispositional. $\Delta^1$-THC is initially metabolized in man in a way similar to that in most animals, i.e. by preferable allylic oxidation to 7-hydroxy-$\Delta^1$-THC.\textsuperscript{73}

These findings, and others, support the validity of the research paradigm applied by the research community to establishing the pharmacological actions associated with marijuana use. They validate comparisons between studies involving injected THC and smoked marijuana. They validate concentration on the study of the primary psychoactive agent, THC. They provide a basis for an assertion that research does not focus on the other constituents because there is not compelling evidence that they have either harmful or dependence-producing qualities.

The respiratory studies of Tashkin and the toxicological and pharmacological studies of Perez-Reyes, Agurell, and Hollister all indicate that it is an established research paradigm of the scientific community that valid assertions about the effects of marijuana can be based on studies of its constituent parts.

Additional recent research by Julian Azorlosa and his team at Johns Hopkins University School of Medicine provides more knowledge about the effects of THC content, puff volume, and breathhold duration.

One objective of pharmacological research has been to refine the measurement of the dose of marijuana delivered by smoking as the route of administration. A 1992 study by Azorlosa addresses this problem. Previous studies did not provide adequate measures of the volume of smoke delivered to the subjects, making it difficult to judge or compare

\textsuperscript{72} ibid. pg. 40.
\textsuperscript{73} ibid. pg. 40.
dose-effect relationships. Altering the THC content of NIDA produced marijuana cigarettes only produces a narrow range in actual dosages. Past studies did not measure post-smoking blood plasma levels of THC. These factors contributed to great uncertainty about the dosages delivered in various studies. This prevents establishing a relationship between dose, plasma THC levels, and the pharmacological effects of marijuana.

Azorlosa's study used a wide range of dosages, utilizing NIDA cigarettes of 1.75% and 3.55% potency, controlled delivery of the smoke, and measured plasma levels. All aspects of smoking behavior were controlled including number of puffs, puff volume, inhalation volume, breathhold duration and interpuff interval. Measurement of plasma THC levels after smoking thus provided an index of systemic delivery of a known volume and THC content of marijuana smoke. A complete profile of dose-response and time-course data was also obtained by measuring the effects of marijuana on physiological indices, subjective reports and performance on several cognitive and psychomotor tasks.74

The number of measured indices in the study provided a comprehensive array of data, all establishing "orderly dose-related increases as a function of cigarette THC content and number of puffs."75 The controls over delivery of smoke, number of puffs, and other aspects of smoking behavior allowed an accurate assessment of how a known volume and THC content of inhaled smoke translates into a measured plasma THC level.76

The study produced four dosage conditions:

a) 4 puff, 1.75% THC=57 ng/ml;

b) 10 puff 1.75% THC or 4 puff 3.55% THC=90 to 99 ng/ml;  
c) 5 puff 1.75% THC or 10 puff 3.55% THC=172 ng/ml;

d) 25 puff 3.55% THC=268 ng/ml.

75 ibid. pg. 120.
76 ibid. pg. 120.
Dose related effects were observed in plasma concentration, expired air carbon monoxide, heart rate, and a majority of subjective responses. Significant differences in acute doses were apparent between the highest and lowest doses delivered.

The results of the present study suggest that, under acute dosing conditions, human subjects may have difficulty discriminating between smoked marijuana doses that produce plasma levels in the range of 90 to 170 ng/ml.\(^{77}\)

At these doses, subjective measures are affected more by marijuana than performance measures; dose-related effects are observed in performance measures at higher doses.

Overall, this study provided a comprehensive assessment of the pharmacological effects of smoked marijuana over a wider and more precisely controlled dosage range than has been accomplished previously.\(^{78}\)

A study by Azorlosa's team in 1995 addressed the effects of puff volume and breathhold duration on plasma levels. Changes in puff volume produced significant dose-related changes in plasma, carbon monoxide, and subjective effects whereas changes in breathhold duration changed plasma levels but neither carbon monoxide nor subjective effects.\(^{79}\) The increases in plasma THC levels from breathholding are not statistically significant except at the lowest and highest doses.

Thus, the plasma THC data suggest that the stereotypic behavior of marijuana smoking is useful for maximizing absorption; however, our study suggests there are diminishing returns with longer breathhold durations.\(^{80}\)

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\(^{77}\) ibid. pg. 121.

\(^{78}\) ibid. pg. 121.


\(^{80}\) ibid. pg. 567.
As Tashkin determined in 1991, longer breathhold durations increase exposure to tar and carbon monoxide. The diminishing returns Azorlosa has established provides a basis for persuading marijuana smokers to alter their smoking patterns to reduce the harmfulness produced by prolonged breathhold durations. This is additional evidence that the harmful effects of the tars and carbon monoxide can be reduced through use of greater filtration and change in smoking techniques.

Additional work at the Addiction Research Center at NIDA provides more on the absorption phase of marijuana smoking.

Marilyn Huestis and her colleagues applied rapid blood collection, a paced smoking protocol and the timely collection of physiologic and behavioral measures for their 1995 paper on the "Characterization of the absorption phase of marijuana smoking."81

The rapid blood collection was assisted by use of a continuous withdrawal pump, and this allowed the team to produce sophisticated time lines for a variety of physical and behavioral indices.

This study was designed to characterize the absorption of Δ⁹-tetrahydrocannabinol during marijuana smoking and to define the onset, peak, and duration of the pharmacodynamic effects of marijuana.82

The study utilized six subjects who smoked placebo, 1.75% THC and 3.55% THC cigarettes obtained from NIDA. THC is found in plasma after the first puff, and plasma levels peaked at 9 minutes, before the last puff sequence began at 9.8 minutes. Plasma levels dropped by about one-third from their peak after 15 minutes, and levels at thirty minutes had dropped by about three-fourths. After 2 hours plasma levels flattened out at 5 ng/ml, and remained detectable for about 12 hours. The difference in the plasma drug

82 ibid. pg. 32.
concentrations varied significantly, and were characterized by the authors as "wide interindividual differences." 83

Heart rate increases of 46 and 56 beats/min. peaked at 17.4 minutes and 13.8 minutes for the low and high THC cigarettes respectively. The subject with the lowest THC levels had the greatest increase in pulse. Heart rate remains elevated for 3 hours after the highest dose, but the affects of the low dose disappear by this time.

Mean arterial pressure and systolic blood pressure also increased after marijuana smoking, but effects did not reach statistical significance. 84

Other physiological tests included skin temperature (decreased), and tests on the eyes measuring critical flicker fusion and pupil dilation (no changes.)

The study used visual analog scales to measure "feel drug" and "like drug". Large variations were present in the responses to "feel drug," but mean peak differences were reached after 16 and 10 minutes (for low and high dose, respectively). The subject with the lowest concentration (and highest heart rate change) also had the highest score on this index. The scoring of "like drug" was more consistent, and mean peak differences were observed at 8.4 and 10.2 minutes respectively. Effects were noticeable for 6 - 12 hours.

The visual analog scale "How much do you dislike the drug?" was not sensitive to the effects of smoked marijuana; there was no distinction in responses of the subjects between the placebo and active drug conditions. 85

The study used the Walter Reed performance battery to provide performance indices.

Three different parameters were assessed in each performance task; percentage of correct responses, throughput, and speed. None of the five tasks showed significant effects on throughput and speed after marijuana smoking. After smoking one 1.75% or 3.55% ∆-9-

83 ibid. pg. 35.
84 ibid. pg. 35.
85 ibid. pg. 37.
tetrahydrocannabinol cigarette, the percentage of correct scores on the logical reasoning task were significantly lower than after placebo. The mean peak decrease in accuracy for the logical reasoning task was observed at the time of first measurement at 22 minutes . . . The performance accuracy on the logical reasoning task had returned to baseline levels within 3 hours for all subjects. No significant differences in accuracy after marijuana smoking were noted in the matrix, serial addition and subtraction, manikin, and time wall performance tasks. In the time wall task, subjects had to estimate the completion of a 10-second time span. . .no significant differences in estimated time were observed after marijuana smoking. Response speed also was evaluated for all tasks and was not affected by marijuana administration.86

Only a few studies had previously attempted to collect blood during the smoking process, two of the three papers Huestis cites are by Perez-Reyes. While this paper hypothesizes that peak THC plasma levels are reached before smoking cessation as a function of puff volume, its real importance lies in the team's application of rapid blood collecting to the characterization of the absorption phase of marijuana smoking.

Studies that combine rapid blood collection, paced smoking protocols, and timely collection of physiologic and behavioral measures are essential for the complete characterization of the absorption phase of marijuana smoking.87

This study also found similarity between time-to-peak drug levels and effects for some measurements. It has previously been believed that time-delays existed between peak physiologic and behavioral effects.

An additional significance of the studies discussed above is that they demonstrate a tremendous degree of scientific specificity has been achieved in the study of the pharmacology and toxicology of marijuana smoke, and that extremely sophisticated technological innovations (such as allow measurement of puff volume and rapid blood collection) provide extremely accurate tools for controlled evaluation studies of the effects of marijuana.

86 ibid. pg. 38 - 39.
87 ibid. pg. 41.
Discussion will now turn from marijuana smoke, its harm to the lungs, and its delivery of a dose of cannabinoids to the body to the pharmacological profile of the cannabinoids.

The chemistry of the cannabinoids has been known for some time. The chemistry of marijuana\(^8\) and its biogenesis\(^9\) has been published by Raphael Mechoulam, a co-discoverer of THC. In the early 1980's researchers made great strides in associating changes in the chemical structure of cannabinoids with related changes in the observed effects, and in correlating this structure-activity relationship with various testing paradigms.

The structure-activity relationships of cannabinoids discovered by researchers were discussed and reviewed by Raz Razdan in 1986. Here is an extensive description of the pharmacological profile of marijuana.

The gross effects produced in man or animals cannot be classified pharmacologically as being primarily due to a stimulant, sedative, tranquilizer, or a hallucinogen, although they share some properties with each of these. In general, the effects produced by this drug are dose dependent. Thus in small doses, it produces subjective effects more typical of a hallucinogen and subjective effects more typical of a hallucinogen and somewhat resembling those of a small dose of lysergic acid diethylamide (LSD). However, unlike the latter, it produces sedative effects, with no significant sympathomimetic actions, and there is no cross-over tolerance to LSD. In addition, it is not a narcotic, and compared to many drugs such as the opiates, barbiturates, etc. it does not produce physical dependence. Interestingly, the user may be in a high state of intoxication, but to an observer, he may appear to be in a near normal state. Mild states of intoxication are generally undetected, and the mood may vary from being happy and gregarious to quiet and introspective. With high doses, notable signs are minimal, but the most reproducible signs include an increase in pulse rate and bloodshot eyes. Dryness of the mouth and throat and an increased appetite are common. In some cases, there may also be slurring of the speech. With moderate dosages, the user can perform simple physical and mental tasks, but the performance of more complicated physical and psychological tasks may

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be impaired. The most common subjective effect appears to be time distortion with other effects varying from pleasant relaxation to acute anxiety, loss of contact with reality, hallucinations, and panic. These latter effects are generally associated with large dosages. As with other psychoactive drugs, the effects vary greatly and are mostly dictated by the psychological makeup of the individual and the setting under which the drug is used.90

Razdan concludes that:

the concept of drug development from THC's and cannabinoids is based on very sound foundations, since unlike morphine, \( \Delta^9 \)-THC has a remarkable low toxicity in animals and humans. In addition, it has practically no respiratory-depressant activity, none or very low physical dependence liability, and, finally, a unique pharmacological profile compared to other psychoactive drugs.91

William Dewey also summarizes the pharmacological effects of cannabinoids as having two striking characteristics. One of them is the multiplicity of effects described above by Razdan. The other is the low toxicity of the chemical family.

Throughout this review, I have indicated that the minimal effective dose of \( \Delta^9 \)-THC for a particular pharmacological effect in animals was higher than that usually consumed by man. Yet, in almost all cases, it was much lower than the dose which produced toxic effects in the same species. The two characteristics of the animal pharmacology of cannabinoids carry over to humans. For instance, each of the cannabinoids tested in man causes many side effects at active doses and lethal effects of overdose by humans are nonexistent or rare. Toxicity following chronic use may be a different issue.92

The reason it may be a different issue is that at this time, the mid 1980's, no one knew what was marijuana's mechanism of action on the human brain. The popular research paradigm was that cannabinoid effects on the central nervous system were

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91 ibid. pg. 146.
produced by a cell membrane perturbation effect. A review of the biochemical research on possible mechanisms of action for cannabinoids was also included in the 1986 edition of *Pharmacological Reviews* by Billy Martin. Martin concluded his review of the "Cellular Effects of Cannabinoids" with this concerned and widely quoted observation:

> While the cannabinoids do not appear to be highly toxic, it is disconcerting that they seem to exert some alteration in almost every biological system that has been studied.

Martin's article is prefaced with a discussion of the problems caused by the solvents used to create THC solutions for biochemical research on its effect on cells. Razdan also notes that these solvents "are not without pharmacological activity." As discussion of the discovery of marijuana's mechanism of action in Section 3 below will explain, these problems resulted in the invalidation of may of the findings produced by the biochemical studies Martin reviewed in this 1986 article. Martin's article is cited frequently in 1990's cannabinoid research, not though for the alterations hypothesized above, but for his warnings and descriptions of the ultimately fatal flaws in this research paradigm.

Martin and co-authors realized in 1988 that a major change in research paradigms was looming on the horizon.

Two general mechanisms of action have been proposed for the cannabinoids. The first is that they act through a specific receptor as do the opioids and many other drugs. . . A second mechanism of action that has been proposed for the cannabinoids is that they alter the fluidity or ordering of biological membranes. This possibility was first investigated

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95 Razdan, 1986 supra pg. 75.
because of the highly lipophilic nature of most cannabinoids and their preferential association with biological membranes.96 (emphasis added)

Allyn Howlett, one of the co-authors of that statement, had made a breakthrough with a model neural system. One of her graduate students, William Devane, made a related breakthrough developing a radioimmunoassay that would allow researchers to conduct binding studies with a potent, experimental cannabinoid. The initial evidence that a cannabinoid receptor system existed was discussed in Martín and Howlett's presentation to the 49th annual meeting of the CPDD in 1988. The work of Howlett's team, especially due to the contributions of Devane, led to a major breakthrough in scientific knowledge about the effects of marijuana and their neural mechanism of action. This breakthrough will be discussed in Section 3 of this petition, which will also review the ramifications of this discovery on understanding the pharmacology of marijuana.

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A summary of any relevant medical or scientific evidence known to the petitioner, section 3 of 8 sections.

3) Scientific knowledge on marijuana's mechanism of action.

All rulemaking procedures involving marijuana and cannabinoids are based on the scientific record as it existed in 1988. Since then fundamental and profound discoveries have radically altered the way scientists consider and study marijuana and its constituent parts.

Between 1988 and 1993 a scientific revolution occurred in the field of marijuana and cannabinoid research. The epochal event of the scientific revolution was the localization and characterization of a cannabinoid receptor system in the human brain in 1990 by Miles Herkenham and his research team at the National Institute of Mental Health.97

William D.M. Paton is a distinguished British pharmacologist who has expressed great concern over the apparent harmful effects of marijuana on biological cells and systems. Along with Gabriel Nahas, another scientist noted for his concern over marijuana's effects on the human body, Paton helped to organize international symposiums on marijuana research. These excerpts from Sir Paton's summaries of these symposia make it clear that speculation about marijuana's effects on the brain was just that - speculation. At the time of these remarks, and indeed until Herkenham's breakthrough in 1990, all scientists had were theories about marijuana's effects on the brain.

1975: [M]any of these studies in cell biology are taking us toward an understanding of possible mechanism of action of THC. Should one

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think of a cannabinoid receptor? I prefer the idea of hydrophobic spaces in membranes or macromolecules, the average shape and dimensions of which limit their capacity to accept larger lipophilic molecules. Also, some investigators suspect that the characteristics of the site of action for the more toxic effects may differ from that for psychic effects. W.D.M. Paton

1978: At the neuronal level, the available evidence about THC remains tantalizing. . . [I]t appears reasonable to attribute the central stimulant effects of cannabis to generation of hypersynchronous neural discharge, but how this is brought about is still unsettled. THC depresses rewarding self-stimulation behavior, and tolerance develops to this. But we cannot yet reliably link these results to definite neurological changes. . . we still lack any well-defined type of neurochemical action by THC as a basis for all these effects. Although we must recognize radical differences between THC and general anesthetics, perhaps it is the case that the actions of both of them are to be defined not in terms of specific transmitters, but in terms of some other characteristic of the components of synapses such as size, geometry, or membrane composition. W.D.M. Paton

1984: Studies on the mechanism of action of delta-[9]-THC have still not resolved the question as to whether the drug acts mainly in a relatively non-specific way in cell membranes, at a receptor, or both. Much evidence is accumulating, however, to suggest that membranes are the preferred site and this is supported by the drug’s effects on a large number of organs and biochemical processes... D.J. Harvey & W.D.M. Paton

Until 1980 the cell membrane perturbation theory dominated scientific research on marijuana, and consequently the cell membrane perturbation theory formed the basis for policy decisions by the Department of Justice on the scheduling of marijuana under the CSA. Herkenham's 1990 discovery proved that the cell membrane perturbation

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theory was incorrect, and that this was due to technical flaws with the research. Ironically, Martin's 1986 paper which concludes with marijuana affects every biological system studied is now oft-cited as a reference to those technical flaws.

The primary technical problem is that it is hard to make a liquid cannabis solution to test on animals and cell tissue. Cannabinoids are not water soluble, and the creation of usable solutions for experimental research was fraught with problems. Even Gabriel Nahas took note of these difficulties:

Many different methods for suspending, solubilizing, or emulsifying delta-9-THC have been suggested. These include the use of surficants (Tween 80, Triton X-110, Pluronic), solvents (ethanol, propylene glycol, dimethylsulfoxide, olive or sesame oil), and suspending agents (resin, albumin, dextrans), as well as ultra sonic emulsifiers. None of these methods is entirely satisfactory, because they all influence the rate of absorption as well as pharmacological activity. The fact that all of these methods have been used by various investigators makes quantitative comparison difficult.101

This problem was also widely recognized by his contemporaries. Sir Paton warned as early as 1975:

A technical warning note that the pattern of extracting cannabinoids by different solvents varies with the tissue carries intriguing physiochemical implications.102

With hindsight, those two comments exhibit considerable understatement. According to Miles Herkenham of the National Institute of Mental Health, the early biochemical studies have three flaws:

Most of the biochemical studies employed concentrations of $\Delta^9$-THC that were in excess of physiologically meaningful concentrations that might be found in brain. In addition, the criterion of structure-activity relationship was not met -- that is, the potencies of the various cannabinoids in the \textit{in vitro} assays did not correlate with their relative potencies in eliciting characteristic behavioral effects. Particularly

\begin{itemize}
\item[102] Paton, (1976). pg. 552.
\end{itemize}
damaging to the relevance of these in vitro studies was the absence of enantioselectivity.\textsuperscript{103}

In simpler terms, it took incredibly unrealistic potencies to produce results, and there were no guarantees that the solutions did not alter the compounds being studied.

Cannabinoids are sticky, although scientists refer to this as a "tendency to adhere to glass and plastic in in vitro experiments." One problem is that this stickiness is not uniform. Different amounts of the compound precipitate out of various test solutions. British pharmacologist R.G. Pertwee explains that this feature contributes to variance in the concentrations of the cannabinoid compounds used in research, complicating interpretation of results.\textsuperscript{104} As explained in 1986 by B.R. Martin:

These properties of cannabinoids disallow an estimate of the concentration of agent at its site of action and hence compromise assessment of responsiveness.\textsuperscript{105}

Given the available evidence and technology, Martin's concerns had foundation. However technology changes, and as it changes it radically alters the evidence available to scientists for theory evaluation. As Herkenham reiterates in 1992:

Until recently, very little was known about the cellular mechanisms through which cannabinoids act . . . Without evidence that cannabinoids act through a specific receptor coupled to a functional effector system, researchers were prone to study the effects of cannabinoids on membrane properties, membrane-bound enzymes, eicosanoid production, metabolism, and other neurotransmitter systems in vitro.\textsuperscript{106}

This is a very confusing point for non-scientists to grasp, but conclusions based on many of the studies on membrane properties and the like are no longer scientifically valid. The researchers most responsible for the 1990 breakthrough explain.

\textsuperscript{105} Martin, B.R. (1986) "Cellular Effects of Cannabinoids." Pharmacological Reviews 38:45-74. pg. 46.
\textsuperscript{106} Herkenham (1992) pg. 19.
Because the cellular and biochemical mechanisms of action of psychoactive cannabinoids were not understood, neuroscientists were allowed great breadth to speculate upon the influence that these compounds might have on the neurons of the brain.107

For the same reason, policy making was also allowed the same breadth of speculation. Marijuana's current schedule I status is based on an FDA conclusion that abuse of the plant material may lead to severe psychological dependence in some individuals but the information was insufficient to determine with certainty whether the plant material produce physical dependence.108 (emphasis added)

In 1988, Howlett and Devane used radioimmunoassay techniques to characterize the existence of a cannabinoid receptor in a rat brain.109 In 1990, Herkenham and his team mapped the locations of a cannabinoid receptor system in several mammalian species, including man.110

Receptors are most dense in the basal ganglia, hippocampus, and cerebellum, and are sparse in the lower brainstem areas controlling heart and lung functions.

High densities of receptors in the forebrain and cerebellum implicate roles for cannabinoids in cognition and movement.111

Martin, in his 1986 review, acknowledged what many in the field suspected. Marijuana's effects might be produced by either membrane effects, or produced by a receptor system. A membrane-based mechanism was logical; like anesthesia marijuana's chemicals lodged in fatty cells.112 Some factors pointed toward a receptor based mechanism, but no technology existed to research this. There are several comments in

107 ibid., pg. 420.
108 51 FR 22947
111 ibid., pg. 1932.
112 Martin (1986)
the literature indicating two directions for research to pursue, but only one road to follow. According to Herkenham's research findings, they all traveled in the wrong direction.

Contemporaneous with the localization of the cannabinoid receptor in the brain came was the publication by a paper by Thomas, Compton and Martin that characterized the relationship of the lipophilic (fat-loving) nature of cannabinoids with their behavioral potency.113

The large number of cannabinoid compounds with which we have compared lipophilicity and pharmacological potency clearly indicates that a relationship does not exist between these two parameters. . . This lack of correlation between lipophilicity and CNS activity within the cannabinoids does not support a mechanism of action which involves only nonspecific membrane perturbation, but rather it suggest that the pharmacological effects of cannabinoids result from a more specific action . . .this lack of correlation does not entirely rule out the possibility that membrane partitioning cold contribute to some pharmacological effect of the cannabinoids.114

The location of cannabinoid receptors in the human brain correlate with the characteristic effects of marijuana. Of greater confirmation value, the receptor sites bind with cannabinoids and nothing else (at least none of the long list of drugs the researchers tried).115 Characterization of the receptor allowed Matsuda and colleagues to identify a previously cloned receptor gene of unknown identity as the endogenous cannabinoid receptor.116

Lichtman and Martin found that converging lines of evidence indicating that cannabinoids produce antinociception (pain reduction) through multiple mechanisms at

114 ibid. pg. 629-630.
115 Herkenham et al (1990)
both the spinal and supraspinal levels of the Central Nervous System. Further evidence indicates that discriminative stimulus and catalepsy are caused by two distinct mechanisms.

A 1991 report to the CPDD verifies that the work of Howlett, Devane, Herkenham, and Matsuda as responsible for the discovery of the new research paradigm.

Researchers today are working toward elucidating the mechanism of action of the cannabinoids. Recent work provides compelling evidence that its pharmacologic effects are caused by interaction with a specific receptor rather than by influencing membrane fluidity.

In 1992 Thomas, Wei, and Martin duplicated the localization of the cannabinoid receptor by Herkenham's team using a different autoradiographic assay.

In 1993 Roger Pertwee published a minireview in the British review General Pharmacology on "The Evidence for the Existence of Cannabinoid Receptors." Pertwee reviewed the criteria necessary to establish the existence of a receptor, and reviewed the evidence establishing a structure-activity relationship of the cannabinoids, their stereoselectivity, potency, binding sites and other areas.

It is clear from the available data that cannabinoid receptors do exist and that they are present in mammalian tissues in high concentrations. Particularly important factors in the discovery of these receptors, have been the detection of large amounts of specific, high-affinity cannabinoid binding sites, appropriately distributed in the brain, and the cloning of a functional cannabinoid receptor. These findings are

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backed up by evidence that cannabinoids show a remarkable degree of
chemical selectivity and stereoselectivity, that many of them are highly
potent agents, that cannabinoids can interact with certain classical second
messenger systems, and that the structural and geometric features of
cannabinoid molecules governing their ability to interact with cannabinoid
binding sites or second messenger systems closely resemble those thought
to account for their characteristic pharmacological properties. That the
cannabinoid receptor is a new class of receptor is indicated primarily by
the finding that its amino acid sequence differs significantly from that of
any other known type of receptor and by evidence that its recognition site
shows a high degree of selectivity for cannabimimetic agents.121

Also, Pertwee pounds another nail in the coffin of the cell membrane perturbation
theory.

In view of the strength of the evidence for the existence of
cannabinoid receptors, the once held idea that the psychotropic activity of
cannabinoids stems primarily from their known ability to interact with
membrane lipids is no longer tenable.122

Herkenham's research continued, and subsequently discovered the mechanism of
tolerance to marijuana.

Tolerance describes an adaptation by the brain to the continued presence of a drug
in which higher doses of the drug are required to obtain the effect of the initial dose.

The classic model holds that tolerance contributes to the development of
dependence, and that withdrawal symptoms reflect the brain's inability to function
without the accustomed drug. In this model the withdrawal symptoms are supposed to be
the opposite of the drug's effects.123

Gabriel Nahas has written about the cell membrane paradigm for describing
marijuana's effects since the early 1970's. His views have been very popular. Dr. Nahas
originally held that marijuana users do not develop physical dependence identifiable with

Pharmacology. 29:4 pg. 811-824. pg. 821.
122 ibid. pg. 821.
123 Pratt, J.A. (1991) "Psychotropic Drug Tolerance and Dependence: Common Underlying
Mechanisms?" In Pratt, J.A. (ed.) The Biological Bases of Drug Tolerance and Dependence. London:
Academic Press. 1991., pg. 4-5.
a specific withdrawal symptom. Later he characterized withdrawal from marijuana as mild and not always clinical noticeable. In 1990 withdrawal symptoms were described this way:

> Interruption of the regular use of marijuana is associated with an abstinence syndrome which is characterized by irritability, uneasiness and anxiety; nausea, diarrhea and sweating have also been reported. These symptoms are much less severe than those accompanying withdrawal from opiates which are quite unpleasant and anxiety laden resembling a very bad bout of flu.

According to Abood and Martin:

> Under the most intense exposure regimen, the symptoms of withdrawal are relatively mild in most subjects. There are few reports in which the abrupt interruption in marijuana use has led to incapacitation of the individual abusing the substance. The number of people who have difficulty in controlling their abuse of cannabis to the extent that they require professional treatment is relatively small.

Regardless on any link to withdrawal symptoms, some tolerance to marijuana does develop after regular, heavy use of the drug.

Tolerance is not a simple phenomenon, and only recently have its various mechanisms been described in the literature. Depending on the mechanism involved, three categories of tolerance can be distinguished. Dispositional tolerance results from a change in absorption of the drug. Pharmacodynamic tolerance arises from adaptational changes in the brain. Behavioral tolerance results from familiarity with the environment in which the drug is administered.

Dynamic tolerance also consists of subgroups, depending on the actual mechanism involved. According to one review:

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124 Nahas (1973)
125 Nahas and Frick (1981)
127 Abood and Martin (1992) pg. 204.
[A] number of adaptive processes can occur following repeated exposure to psychotropic drugs. In isolated tissues and cells, continuous exposure to some agonists (e.g. nicotine, opiates, and benzodiazepines) can produce a rapid desensitization. In brain tissue dissected from tolerant animals, downregulation of receptors and receptor uncoupling have been observed. The latter effect would appear to be a promising candidate for explaining tolerance to the effects of a number of psychotropic drugs. However, it is likely that no single neuronal adaptive process can account for the behavioral tolerance observed in vivo.\textsuperscript{130}

The Nahas paradigm includes the hypothesis that tolerance to marijuana can be described as "metabolic tolerance arising from decreased sensitivity of the target cells."\textsuperscript{131}

Through the use of autoradiographic assays, in 1993 Herkenham and his team discovered that tolerance to marijuana was produced by receptor down regulation.\textsuperscript{132}

The objective of this study was to explain the following conclusions the authors drew from pharmacological literature:

\textbf{E}xperienced users are capable of consuming enormous quantities of the drug with few or no obvious ill effects. Scores in cognitive tasks, both in human and non-human primate studies, show a paucity of measurable effects associated with chronic use.\ldots tolerance to most psychoactive and physiological effects does occur in humans when high doses are administered daily.\textsuperscript{133}

At the observational level, the animals in this experiment who received the most potent doses of cannabinoids developed tolerance the quickest, and returned soonest to normal levels of activity.

At the neuronal level, quantifiable reductions in the density of cannabinoid receptors were observed that correlated with the behavioral responses. The results were very dramatic.

\footnotesize
\begin{itemize}
  \item \textsuperscript{130} ibid., pg. 8.
  \item \textsuperscript{131} Nahas (1984) pg. 203.
  \item \textsuperscript{133} ibid., pg. 293.
\end{itemize}
[Indications of receptor regulation in other neuronal systems] stand in stark contrast to the massive and homogeneous changes in cannabinoid receptor levels found in the present [animal] study. The magnitude of the present effect, like the striking behavioral tolerance, may stem in part that, unlike other psychoactive agonist drugs, cannabinoids can be administered in very high doses. It is ironic that the magnitude of both tolerance (complete disappearance of the inhibitory motor effect) and receptor down-regulation (78% loss . . .) is so large, whereas cannabinoid dependence and withdrawal phenomena are minimal. This supports the claim\textsuperscript{134} that tolerance and dependence are independently mediated in the brain.\textsuperscript{135}

The conclusion of Herkenham's team on tolerance to cannabis is that:

The effect is selective to $\Delta^9$-THC (ruling out changes in second messengers), is time- and dose-dependent, and is reversible, and thus appears to be cannabinoid-receptor mediated. We propose by extension that cannabinoid tolerance \textit{in vivo} results, in [addition to behavioral factors], from cannabinoid receptor down-regulation.\textsuperscript{136}

These 1993 findings of Herkenham dispute the claim that tolerance to marijuana is the result of desensitized brain cells worn out from excessive exposure to accumulated cannabinoids.

Tolerance to marijuana was supposed to the a manifestation of desensitization of brain cells, and in addition to contributing to the supposed dependence liability this desensitization of brain cells was supposed to create an amotivational syndrome characterized by apathy and inactivity. The hypothesis was that this desensitization would impede normal brain operations and render individuals somewhat sluggish and unmotivated. The hypothesis has been challenged on both behavioral and pharmacological grounds.

In a widely respected review of the literature in 1986, Leo Hollister addresses the issues raised by the amotivational syndrome hypothesis:

\textsuperscript{135} Oviedo, et al. (1993) pg. 300.
\textsuperscript{136} ibid., pg. 300.
Whether chronic use of cannabis changes the basic personality of the user so that he or she becomes less impelled to work and to strive for success has been a vexing question. As with other questions concerning cannabis use, it is difficult to separate consequences from possible causes of drug use . . . The demonstration of such a syndrome in field studies has been generally unsuccessful. . . Laboratory studies have provided only scant evidence for this concept . . .

If this syndrome is so difficult to prove, why does concern about it persist? Mainly because of clinical observations. One cannot help being impressed by the fact that many promising youngsters change their goals in life drastically after entering the illicit drug culture, usually by way of cannabis. While it is clearly impossible to be certain that these changes were caused by the drug (one might equally argue that the use of drug followed the decision to change lifestyle), the consequences are often sad. With cannabis as with most other pleasures, moderation is the key word. Moderate use of the drug does not seem to be associated with this outcome, but when drug use becomes a preoccupation, trouble may be in the offing.137

In 1992, Abood and Martin has little more to offer, and in fact base their conclusion on Hollister's 1986 paper and a review by Fehr and Kalant published in the 1983 proceedings of a World Health Organization meeting. Martin concludes in 1992 that:

An 'amotivational syndrome' has been frequently described in the literature . . . Well controlled studies, however, have failed to provide strong evidence that an amotivational syndrome is a direct consequence of marijuana use.138

The hypothesis that the desensitization of brain cells caused by marijuana use explained both tolerance to the drug and an amotivational syndrome has been discredited by both natural and social science research.

Lawrence Melvin and Ross Johnson derived the experimental cannabinoid isomer, CP-55,940, that was essential to the discovery of the cannabinoid receptor system. In 1993 they joined with Martin, Razdan, Compton and Kenner Rice and Brian

De Costa to correlate the receptor binding with in Vivo activities and establish a Structure-Activity Relationship between the two.\textsuperscript{139}

The results presented in this manuscript clearly indicate that behavioral potency of cannabinoids in the mouse can be predicted by establishing the affinity of the cannabinoid receptor labeled by $[^3\text{H}] \text{CP-55,940}$.\textsuperscript{140}

The high correlation between binding and in vivo pharmacological effects:

suggest a lack of species differences in terms of receptor SAR, despite the fact that the pharmacological effects measured between each species do not necessarily appear to be related to one another. Additionally, these correlations were established using a set of cannabinoids incorporating a wide degree of structural diversity, and this set includes natural cannabinoids, cannabinoid metabolites, dimethylheptyl (or related) side chain analogs, nonclassical bicyclic cannabinoids, halegenated analogs and other synthetic analogs including stereoisomers. Thus, in the process of establishing these correlations, data presented here further enhance the body of knowledge concerning the structural requirements for binding to the cannabinoid receptor. . . Lastly, data presented here suggests that a single cannabinoid receptor exists to which almost all cannabinoids bind as a single recognition site. However some cannabinoids such as CBD may produce pharmacological actions either by interacting at this receptor at a different recognition site, or by another receptor mechanism altogether. No evidence is presented here which would suggest which is likely to occur.\textsuperscript{141}

Melvin and Johnson also published a study that elucidated the SAR's of bicyclic cannabinoid analogs in light of the receptor breakthrough.\textsuperscript{142}

A 1994 study indicated that $\Delta^9$-THC and kappa opioid agonists may share a common mechanism of action in the production of antinociception.\textsuperscript{143} Opiods affect

\begin{itemize}
\item \textsuperscript{140} ibid. pg. 222.
\item \textsuperscript{141} ibid. pg. 225
\end{itemize}
three distinct receptors, *mu*, *delta*, and *kappa*. Antagonists shut down receptor systems, closing the receptors to agonist or ligand binding. While *mu*-selective and delta-selective antagonists had no affect on the pain-killing effects of $\Delta^9$-THC, a kappa-selective antagonist also blocked the antinociception effects of $\Delta^9$-THC. This is the first evidence that cannabinoid antinociception has a different mechanism of action than the other behavioral effects of cannabinoids. This suggests that cannabinoids provide a means to activate pain-killing capabilities in the body previously accessible only through the use of opioid agonists or opioid drugs such as heroin and morphine, but without the significant safety risks that accompany opioid use. (Unlike opioids, cannabinoids to not depress the respiratory or pulmonary systems.)

Also in 1994, Herkenham's finding that down-regulation of cannabinoid receptors was responsible for tolerance to THC was replicated by a research team in Spain led by F. Rodriguez De Fonseca.144

However Dr. Herkenham's valuable discoveries did not end with the characterization of tolerance.

As noted above, the cannabinoid receptors in the brain account for most but not all of the effects of cannabinoids. Cannabinoids are lipophilic; they lodge in fatty tissues in the body, which are extensive. While this is not, as once believed, responsible for marijuana's characteristic effects on the Central Nervous System, the question remains as to what effect this has on other systems in the body.

The research literature indicates six areas of known or possible side effects from cannabinoid use that require explanation: pulmonary effects, immunosuppression, reproductive dysfunction, endocrine modulation, decreases in intraocular pressure, and effects on the digestive system.

Lynn and Herkenham utilized autoradiographic assay techniques to investigate non-Central Nervous System cannabinoid binding in a rat.145 Because of the difficulty in getting fat cells to adhere to a slide, they were not able to investigate lipid binding of cannabinoids. However this study makes important strides in three areas.

First of all, Lynn and Herkenham have determined and localized additional sites of specific and non-specific binding, that is, sites not in the brain.

Second, the locations of specific binding sites in areas that regulate the immune system help clarify prior research.

Third, the location of non-specific (unrelated to specific receptors) binding questions the basis for the "fat accumulation" concerns about cannabinoids.

It was not unexpected by the researchers to discover cannabinoid receptors in the immune system (the spleen, Peyer's Patches, lymph nodes, blood, and bone marrow), as there are close similarities between neural and immune cells. While some research has suggested cannabinoid suppression of T-cells, the receptors are actually located in B-lymphocyte cells. It is uncertain if macrophages (the killer cells of the immune system) are affected by cannabinoids.

Macrophages cannot be discounted and may contribute to binding; however, in other structures of the reticuloendothelial system besides the spleen, specifically the liver and lung, which have large numbers of macrophages, there is no specific receptor binding.146

Immune system suppression is a matter of great concern. Researchers have expressed concern about marijuana's use as an illicit therapeutic drug to induce appetite by AIDS patients.147 The possible effect of marijuana on the immune system has been a

146 ibid., pg. 1622.
special concern of Dr. Nahas for a long time. And indeed, a 1974 article by Dr. Nahas is cited along with many other papers in Lynn and Herkenham's consideration of cannabinoid effects on the immune system.

Leo Hollister reviewed evidence of cannabinoid immunosuppression in 1988 for the *Journal of Psychoactive Drugs.*

Despite the fairly large literature that developed during the past 15 years or so, the effect of cannabinoids on the immune system is still unsettled. The evidence has been contradictory and is more supportive of some degree of immunosuppression only when one considers in vitro studies. These have been seriously flawed by the very high concentrations of drug used to produce immunosuppression and by the lack of comparisons with other membrane active drugs. The closer that experimental studies have been to actual clinical situations, the less compelling has been the evidence.

Although the topic was of great interest during the 1970's, as indicated by the preponderance of the references from that period, interest has waned during the present decade. This waning of interest suggests that perhaps most investigators feel that this line of inquiry will not be rewarding. The AIDS epidemic has also diverted attention of immunologists to the far more serious problem of the truly devastating effects a retrovirus can have on a portion of the immune system. Persons infected with the virus but not diagnosed as AIDS have been told to avoid the use of marijuana and/or alcohol. This advice may be reasonable as a general health measure, but direct evidence that heeding this warning will prevent the ultimate damage to the immune system is totally lacking.

The significance of the location of cannabinoid receptors in the immune system concerns possible therapeutic drugs, not danger to human users of cannabis. The authors are quite specific about the significance of this discovery:

If cannabinoids do modulate B cell migration, proliferation, plasma cell morphogenesis, and immunoglobin production, such effects may have profound implications for the humoral immune response. Whereas suppression of B cell-mediated function could be detrimental (although there is little evidence that it is in vivo), cannabinoid suppression could

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play a positive therapeutic role in autoimmune disorders. [Research has shown] that Delta 9 THC is an effective prophylactic treatment for autoimmune encephalomyelitis (an animal model for multiple sclerosis) in Lewis rats and strain-13 guinea pigs, and they proposed a mechanism whereby lymphocyte migration and sequestration in the CNS are inhibited by the drug. Only subtle immune suppression has been noted in humans, which suggests a species difference in peripheral cannabinoid receptor distributions and densities.151

As if quite aware of the extrascientific debate over marijuana policy, Lynn and Herkenham place the external validity of their experimental animal findings in perspective.

Whereas this finding [of cannabinoid receptors in the immune system of a rat] has implications for human immunomodulation, it should be noted that rodents are more susceptible than humans to immunomodulation by cannabinoids, perhaps reflecting the substantially higher levels of receptor in their immune cells. In humans, immune suppression is subtle and in many cases insignificant. There is little evidence for cannabinoid immunosuppression as a causative agent in disease.152

Finally, Lynn and Herkenham have clarified some of the issues involving marijuana's effects on the rest of the body. As expected, non-specific binding is found in some structures with high lipid content. However high concentrations of non-specific binding were located in many structures without high fat contents. For example, the heart has high in non-specific binding, and without consequence, because the cardiovascular effects have previously been shown to be CNS-mediated. There is also noticeable non-specific binding in the pancreas.

Other factors besides lipophilia of cannabinoids must dictate the sites of nonspecific in vitro binding.153

Non-specific binding of cannabinoids may account for cannabinoid effects on the reproductive systems. The lack of non-specific binding in the testes suggests that the

152 ibid., pg. 1621.
153 ibid., pg. 1621.
effect of cannabinoids on sperm is due to action at some other site, perhaps the hypothalamus. Also:

Cannabinoids have not been shown to affect fertility adversely or to be teratogens, except in extremely high chronic doses. Such effects in part may be mediated at the level of the pituitary or brain, given the evidence about prolactin suppression in frequent female users of marijuana.154

According to Lynn and Herkenham, the effects of cannabinoids on the endocrine system, the digestive tract, and the cardiopulmonary system are all believed to mediated in part, by the CNS.

Scientific knowledge about marijuana has taken great strides since 1988. Even in 1988, though, there was considerable doubt to claims that marijuana caused brain damage, as claimed later by administrators of the DEA.

In 1986 a comprehensive review of research on "The Chronic Cerebral Effects of Cannabis Use" by Renee Wert and Michael Raulin appeared in the International Journal of the Addictions. Two papers examined neurological155 and neuropsychological156 findings to date, and the authors found "no evidence that marijuana produces gross structural impairment" and "little evidence that it leads to functional impairment, although subtle impairment cannot be ruled out."

In 1991 the Department of Health and Human Services (HHS) published the Third Triennial Report to Congress on Drug Abuse and Drug Abuse Research.157 Their report reviewed research published through 1988 and was written when it appeared likely from the work of Howlett and Devane that a cannabinoid receptor system may exist.

154 ibid., pg. 1621.
There is no discussion of brain damage, or the need for research to address the possibility. The focus of research in 1988 was two-fold. First, the objective of research was to discover the mechanism of action that marijuana has in the brain. Second, the critical issue of marijuana's dependence liability should be clarified by the discovery of the mechanism of action.

The research priorities suggested by the discovery of the cannabinoid receptor system have launched a new paradigm. The pioneers of this research elaborate on the new paradigm in the conclusion of a 1990 article on the cannabinoid receptor. Their summation is entitled "A challenge to neuroscientists" and is as follows:

Clearly, a plethora of questions about the actions of cannabinoid compounds in the CNS remain. Biochemical, anatomical and neurophysiological studies of the effects of cannabis compounds have been limited in the past due to the relatively low potency of $\Delta^9$-THC, its high solubility in membrane lipids, and its tendency to adhere to glass and plastic in in vitro experiments (see Martin, 1986 and Pertwee, 1988). The use of high-affinity cannabinoid agonists such as desacetyllevonantradol and CP-55,940 in these studies should allow rapid progress in addressing the unique and important actions of cannabinoid compounds in the CNS. Cannabinoid analgetics should be useful in studying novel mechanisms of anti-nociceptive at the level of the spinal cord as well as at higher levels in the CNS involved in processing of the response to pain. The anatomical and physiological properties of cannabinoceptive neurons in the hippocampus and cortex must be re-evaluated with respect to the role these neurons may play in cognition and memory. Study of the interactions of cannabinoceptive neurons with afferents to, efferents from, and interneurons within the basal ganglia must be re-evaluated. Additionally, the function of cannabinoid receptors in the cerebellum should be addressed. Renewed scientific interest in cannabinoid compounds would stimulate research within a broad range of neuroscience disciplines.\textsuperscript{158}

A 1991 report to the CPDD by several of the principle scientists responsible for the receptor breakthrough describes the research problems currently before the scientific community:

\textsuperscript{158} Howlett, et all (1990) pg. 423.
Much work is left to be done to unravel and utilize our knowledge of cannabinoids and how they work. The tools that allowed us to discover the receptor and pinpoint neuro-anatomical distributions coupled with the design of new tools (e.g. affinity ligands) will help us answer many other questions.

There are at least four major areas where we look for progress in the coming decades. The discovery of physiologically relevant receptor subtypes will aid the ultimate goal of separating the traditional activities of cannabinoids (specific agonists) in search of therapeutically useful drugs. The discovery of an antagonist will be a key event both as a research tool and to combat cannabis overdose. Recent findings of agonists and an antagonist in the aminoalkylindole (AAI) series gives us a hope that this goal will be attained soon. The third area ripe for new developments is the discovery of the endogenous ligand. Three separate groups (Howlett, Childress, and Mechoulam) are currently working on identifying the endogenous cannabinoid(s). Finally, new areas will evolve from this research, e.g., the discovery of peripheral cannabinoid receptors and new pain mechanisms.159

In 1992 William Devane and colleagues identified a naturally occurring chemical in a porcine brain that binds to cannabinoid receptors.160 In neurobiological terms, this substance is likely to be an "endogenous ligand", and it appears to share the pharmacological properties of ∆9-THC. Devane has named this chemical Anandamide, after the Sanskrit word for bliss. Martin summarizes the questions researchers began to face in the mid 1990's:

The future challenge is establishing the physiological role for the endogenous cannabinoids. Is anandamide a neurotransmitter or a neuromodulator? Does an entire cannabinoid family of amide derivatives of fatty acids exist, each of which has a distinct neurochemical role? If cannabinoids serve a normal physiological role, then what are the consequences of an imbalance in this system? Answers to these and

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related questions will likely provide an entirely new perspective on the way we view cannabinoids.161

Considerable progress is being made in advancing cannabinoid research. In 1994 Rinaldi-Carmona and her team found an orally effective cannabinoid antagonist, SR141716A.162 Along with advances in understanding anandamide, the endogenous ligand, the discovery of an antagonist will greatly accelerate development of new drugs based on the cannabinoid receptor system.

Progress has been made in discovering how anandamide is formed,163 and verifying its actions on the cannabinoid receptors.164 The pharmacological activity of anandamide has been tested and characterized, indicating distinct differences between the pain killing properties of anandamide and cannabinoids.165 Low doses of anandamides inhibit the pharmacological effects of Δ9-THC, perhaps on account of their partial agonist effects.166

In a 1986 interview Raphael Mechoulam, co-discoverer of THC, takes notice of how the different agendas of scientists and policy makers affect cannabinoid research:

Probably the major barrier has been the unwillingness, or fear, by companies to develop drugs that are based on cannabis. They are afraid, as I said before, of notoriety. They were afraid that they would get into a jam of sorts. So for the first ten years after our discoveries, essentially no work has been done whatsoever on the pharmaceutical properties of cannabis. Even afterwards the work that was done, was done very, very timidly and very slowly. Even when work done at a scientific level it was stopped at the corporate-administrative level... Most industries and

161 Martin, 1995 pg. 1761.
governments do not know how to make use of scientists and scientific ideas.167

Since then, Mechoulam, many of the scientists cited in this paper, and many others have brought about this revolution in cannabinoid research. Addressing a 1990 conference in Crete, Mechoulam reflected on the ultimate goal of their research:

Cannabis is used by man not for its actions on memory or movement coordination but for its actions on mood and emotions. . . From published work we know that there are Cannabis receptors in the limbic system. There is general agreement that the limbic system occupies a central position in the neural mechanisms that govern behavior and emotions. . . [These mechanisms require further study] . . . Let us hope, however, that through better understanding of Cannabis chemistry in the brain we may also approach the chemistry of emotions.168

The discussion of the relevance of this new scientific knowledge to marijuana's dependence liability will continue in section 7 below in relation to the psychic and physical dependence liability of marijuana.

These new findings by the scientific community, led by the research discoveries at the National Institute of Mental Health, contradict many of the "facts" upon which DEA has based prior consideration of marijuana's scheduling.

In 1989 DEA states that the possible effects of chronic marijuana use:

include: possible brain damage, sore throat, rhinitis, bronchitis and emphysema; suppression of luteinizing hormone secretion in women (which affects the production of progesterone); abnormalities in DNA synthesis, mitosis and growth; carcinogenicity; and genetic mutations.169

However the concerns about brain damage no longer have validity with the scientific community, and concerns about cellular processes were largely based on the

biochemical studies discussed above, now of questionable validity. The unfounded assertion that marijuana causes brain damage is repeated in 1992.\textsuperscript{170}

The Administrator states in 1992 that:

It is not possible to reproduce the drug in dosages which can be considered standardized by any currently accepted scientific criteria.\textsuperscript{171}

However, as demonstrated by the research of Tashkin, Perez-Reyes, and Azorlosa discussed in section 2 above, the National Institute on Drug Abuse provides marijuana in reproducible doses. According to the DEA's own findings of fact:

NIDA has shipped a total of 160,700 marijuana cigarettes for human studies from 1976 to 1988.\textsuperscript{172}

As noted above, DEA echoed the concerns of Billy Martin:

The pharmacologic testing of cannabinoids in animals thus far has shown that while they do not appear to be highly toxic, they exert some alteration in almost every biological system that has been studied.\textsuperscript{173}

DEA was mistaken about the validity of that observation, and about the scientific value of Martin's paper, as amply demonstrated by the criticism of methods of biochemical study by noted pharmacologists and researchers discussed above. As noted in a comment of Martin's above, there is a natural process in the body for reacting to cannabinoid drugs, and the question now is to assess the effects of disrupting that process.

DEA also has expressed considerable concern over the effects of marijuana and cannabinoids on the immune system.

Recent evidence also indicates that marijuana can depress an individual's immune function. The immune system's sensitivity to

\textsuperscript{170} 57 Fed. Reg. 10,499 (1992)
\textsuperscript{171} 57 Fed. Reg. 10,499 (1992)
\textsuperscript{172} 54 Fed. Reg. 53,774 (1989)
marijuana depends on the cannabinoid compound and varies among immune cell types. . .

Yet Lynn and Herkenham of the National Institute of Mental Health, far more qualified to draw conclusions from pharmacological literature than either this petitioner or the Administrator, expressly state their assessment that immunosuppression by marijuana is "subtle" and "insignificant."

Contemporary research findings discussed above also suggest fundamental errors in DEA's 1989 assessment of expected scientific findings. At this time, DEA believed that:

    Chronic marijuana use may also have a toxic effect on the human brain. Preliminary studies indicate that THC changes the way sensory information gets into and is acted on by the hippocampus. Chronic exposure damages and destroys nerve cells and causes other changes which are identical to normal aging and may be additive to the aging process. Therefore, chronic marijuana use could result in serious or premature memory disorders. The results of these studies are now being confirmed.

Despite the use of the words "may", "preliminary", "may be", and "could", this statement is a "finding of fact." Have the results of the studies alluded to by DEA in this finding been confirmed? No. These assertions, as many other DEA assertions, consist of hypotheses based on the cell membrane perturbation theory of action for marijuana's effects.

DEA also continually challenges the relevance of research on marijuana's constituent chemicals to an assessment of marijuana itself. For example:

    Although delta-9-THC is an active ingredient in the marijuana plant material, marijuana contains over 400 other chemicals. At least 61 of these chemicals are cannabinoids. All these chemicals could have some effect on the human body.
A discussion of this issue will continue in section 8 below addressing the issue of precursor chemicals.
Exhibit C

A summary of any relevant medical or scientific evidence known to the petitioner, section 4 of 8 sections.

4) History and current pattern of abuse.
   The illicit social use of marijuana is a widely studied phenomenon. Leo Hollister is a prominent veteran researcher in the field of drug abuse and dependency. Dr. Hollister once served as the chairman of the Drug Evaluation Committee for the CPDD. In a widely cited 1986 review of the "Health Aspects of Cannabis" in the *Pharmacological Reviews*, Hollister came to the following conclusion:

   Compared with other licit social drugs, such as alcohol, tobacco, and caffeine, marijuana does not pose greater risks. One would wonder, however, if society were given a choice based on current knowledge, whether these drugs would have been granted their present status of acceptance. Marijuana may prove to have greater therapeutic potential than these other social drugs, but many questions remain.177

   The scientific discoveries discussed above in section 3 address many of those questions. What does social science research have to report on marijuana use trends?

   There are five important annual indicators provided by the federal government to track the history and pattern of marijuana use in the United States: a) The National Household Survey (NHS) estimate of illegal drug use in the U.S.; b) The Monitoring the Future Project (MFP), which surveys drug use among high-school age children; c) The Drug Abuse Warning Network (DAWN) which provides data on emergency room mentions of drug use; d) the annual marijuana supply estimates of the National Narcotics Intelligence Consumers Committee (NNICC), and e) the annual estimates of total arrests in the U.S. in the Uniform Crime Reports (UCR) of the Federal Bureau of Investigation.

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These annual reports provide data sets which are generally accepted as indices of demand (NHS, MFP), dangerous results (DAWN), supply (NNICC), and law enforcement activity (UCR).

The significance of these data sets often relies on the policy objective of the individual or organizational beholder. In the context of this petition, these data sets provide significant information as to the extent of marijuana use, changes in marijuana use over time, and whether or not such widespread use provides indices of abuse. Discussion of the age on onset of drug use and the relation (if any) of marijuana to other drug use will be discussed extensively in section 6 on public health.

This review of these data sets will argue that their significance is threefold. 1) Marijuana use remains a widespread, persistent, and unregulated social practice in the United States. 2) There is no evidence that this widespread use indicates equally widespread abuse of marijuana. 3) Marijuana law enforcement efforts persist as the dominant supportive force in the supply and distribution of marijuana in the United States.

The persistence of marijuana use in the face of tremendous efforts to enforce the complete prohibition of marijuana causes major credibility problems for the nation's law enforcement and public health officials. These public servants are forced by law and policy to argue that any and all available evidence somehow supports and legitimizes marijuana's schedule I status as an extremely dangerous drug with one of the most severe dependence potentials known to modern science. This assertion is laughable, and the attempts of governmental agencies to package scientific research and findings in a way that supports prohibition are riddled with errors and flaws in scientific reasoning.

These reasoning flaws are extremely important to note. They are not isolated mistakes, but a systematic approach to science dictated by executive policy decisions rather than law. Is data on the prevalence of marijuana use an indication of a widespread
problem (marijuana abuse) or an indication of the unintended consequences of a failed policy (marijuana's schedule I status)?

An accurate assessment of the data is just as important with social science research as it is in the natural sciences. In biological research the now-discredited and abandoned cell membrane perturbation theory was based partly on the assumption that if marijuana had any effect on cell tissue or membranes, then that effect must be harmful. Eventually scientists discovered that many of the reactions produced by cannabinoids are the result of natural mechanisms. In the social sciences, the same simplistic polar analysis is applied to data on the prevalence of marijuana use; no distinction is made between use and abuse because marijuana's schedule I status provides the basis for a widely acknowledged presumption that any use of marijuana is abuse. As argued by Thomas Cicero and Joseph Brady of the CPDD, this simplistic approach has no scientific validity or usefulness.

Unless executive policy under the Controlled Substances Act is well-grounded in scientific theory and practice, there is no basis to conduct an evaluation of executive policy. Without policy grounded in scientific findings, analysts, advocates and legislators would be left with a mere tautology to justify continuation of a policy in which failed policies are used to justify their perpetuation.

Science, like policy, is also a social pursuit, and scientists are also subject to prejudice and unscientific bias.178 This, Stephen J. Gould argues, makes the examination of the basis for scientific assertions essential to the application of science to public policy. Gould examined the scientific basis for the use of intelligence tests to determine human fitness for reproduction and other social activity or opportunity, and presents a classic case study in mistaking a correlation between two social phenomena as

a causal relationship. One influence confounding scientific analysis in the research Gould reexamined was racism.

According to the U.S. Congress Office of Technology Assessment:

Historically, racial and ethnic minorities have been linked with, and often blamed for, many of the substance abuse problems within the United States.\(^{179}\)

OTA provides five examples of drugs and discrimination in U.S. history. In 1850 Irish immigrants were blamed for widespread problems with whiskey in Boston. In the 1880's Chinese immigrants in San Francisco were blamed for widespread, recreational opium use. In Ohio circa 1882 German immigrants were denounced by the state's governor as "sabbath breakers, criminals, and free thinkers" on account of their lively beer-garden Sunday meetings.\(^{180}\) In the Southwest during the 1930's "anxiety over competition for jobs shifted to wildly exaggerated fears of the effects of marijuana use customary among Mexicans."\(^{181}\) Finally, in the early 1990's, OTA points out that police forces are mostly white, and that inner-city residents are mostly African-American; the drug arrest rates for the inner cities far exceed the rates for suburban areas. Further evidence of the racist assumptions which form the historical basis for contemporary marijuana prohibition is presented by University of Virginia Law School Professor Richard Bonnie in a book on the history of marijuana prohibition in the U.S.\(^{182}\) In this historical context, attempts to blame teenage marijuana use on a notorious and evil pro-drug conspiracy consisting of the pro-pot media, rock musicians, drug paraphernalia


\(^{180}\) ibid. pg. 14.

\(^{181}\) ibid. pg. 14.

merchants, and advocates of marijuana law reform\textsuperscript{183} appears to be yet another example of a prejudicial, knee-jerk rush to blame complex social problems on unpopular or misrepresented groups.

\textbf{a) The National Household Survey}

The most extensive survey on drug use in the United States is now conducted annually. The National Household Survey is conducted by the National Institute on Drug Abuse and presents an impressive array of data on the prevalence of lifetime, annual, past month, and weekly drug use among various demographic categories and other occasional criteria. The NHS provides the official baseline for estimating the number of marijuana users in the U.S.

Generally the Household Survey indicates that marijuana use was falling steadily since 1979. Indeed, monthly use of marijuana has fallen 60\% since then, although this steady decline has just recently reversed.

The number of people who used marijuana in the past year increased from 17.4 million in 1992 to 18.6 million in 1993. Occasional users increased from 8.8 to 9.6 million, and monthly users increased from 8.6 to 9.0 million. Roughly, half of marijuana smokers use marijuana monthly, and half of those use marijuana at least on a weekly basis.

Of those aged 12 - 17, 9.9\% use marijuana, up from 8.2\% in 1992. Of adults, 8.9\% used marijuana in 1993, up from 8.5\% the previous year. Over two million kids between the ages of 12 and 17 used marijuana during 1993, a million of then on a monthly basis. These figures are unacceptable to all Americans, and indicate that marijuana's current scheduling under the CSA has not created the "closed system" envisioned by the legislation's authors.

The NHS estimates and reports a) the number of people who have taken any illicit substance, b) the number of people who have taken illicit substances other than marijuana and c) the number of people who have taken marijuana. To discover the number of people who only use marijuana and not other illegal drugs, one has to subtract figure b from figure a. The chart below summarizes this process and also provides a comparison of the number of people who only smoke marijuana to all those who use it.
Table 1. % of marijuana users who only use marijuana.

<table>
<thead>
<tr>
<th>Year</th>
<th>Only Marijuana</th>
<th>Lifetime Use</th>
<th>Past Year Use</th>
<th>Past Month Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993</td>
<td>only marijuana</td>
<td>35,059</td>
<td>11,682</td>
<td>7,073</td>
</tr>
<tr>
<td></td>
<td>all marijuana</td>
<td>69,923</td>
<td>18,573</td>
<td>8,992</td>
</tr>
<tr>
<td></td>
<td>% marijuana only</td>
<td>50.1</td>
<td>62.9</td>
<td>78.6</td>
</tr>
<tr>
<td>1992</td>
<td>only marijuana</td>
<td>34,348</td>
<td>10,286</td>
<td>6,737</td>
</tr>
<tr>
<td></td>
<td>all marijuana</td>
<td>67,525</td>
<td>17,400</td>
<td>8,950</td>
</tr>
<tr>
<td></td>
<td>% marijuana only</td>
<td>50.9</td>
<td>59.1</td>
<td>75.3</td>
</tr>
<tr>
<td>1991</td>
<td>only marijuana</td>
<td>33,699</td>
<td>11,104</td>
<td>6,932</td>
</tr>
<tr>
<td></td>
<td>all marijuana</td>
<td>67,379</td>
<td>19,235</td>
<td>9,721</td>
</tr>
<tr>
<td></td>
<td>% marijuana only</td>
<td>50.0</td>
<td>57.7</td>
<td>71.3</td>
</tr>
<tr>
<td>1985</td>
<td>only marijuana</td>
<td>26,303</td>
<td>13,963</td>
<td>11,017</td>
</tr>
<tr>
<td></td>
<td>all marijuana</td>
<td>60,883</td>
<td>28,590</td>
<td>17,844</td>
</tr>
<tr>
<td></td>
<td>% marijuana only</td>
<td>43.2</td>
<td>48.8</td>
<td>61.7</td>
</tr>
</tbody>
</table>

Table 1 supports several arguments. Most users of marijuana do not use other illegal drugs. The more someone identifies themselves with marijuana use, the less likely it is they use any other illegal drug. Over the last ten years, a group ethic against the use of more dangerous drugs has strengthened among regular marijuana users. At best less than one fourth of monthly marijuana users use other illegal drugs as well, hardly sufficient justification for the criminal persecution of all adult marijuana users.

Yet old "truths" die hard. It is true that in the early 1990's the perceived harm of marijuana use dropped among teens and teenage use of the drug increased. While this could mean that kids just haven't got the message yet, it could also just as easily mean...
they've heard the word and rejected it. Is there a credibility problem with anti-marijuana messages?

Historically, anti-marijuana campaigns have been the subject of ridicule and embarrassment. The classic example is a late 1930's movie, Reefer Madness, which is now a cult favorite on account of its ridiculous portrayal of marijuana's effects on a pair of school age teens. Ever self-conscious of this scurrilous tradition of propaganda, modern efforts are carefully prepared with claims promising faithfulness to the latest scientific evidence.

What percentage of adults report perception of great risk of smoking marijuana occasionally? How does this vary with the development of adult, independent reasoning skills?
<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 18-25:</td>
<td>&lt; High School</td>
<td>38.8</td>
<td>40.7</td>
<td>36.9</td>
<td>42.2</td>
</tr>
<tr>
<td></td>
<td>HS Graduate</td>
<td>31.8</td>
<td>32.1</td>
<td>32.3</td>
<td>33.5</td>
</tr>
<tr>
<td></td>
<td>Some college</td>
<td>28.3</td>
<td>22.8</td>
<td>22.9</td>
<td>24.9</td>
</tr>
<tr>
<td></td>
<td>College grad</td>
<td>16.6</td>
<td>21.6</td>
<td>18.1</td>
<td>25.2</td>
</tr>
<tr>
<td>Age 26-34:</td>
<td>&lt; High School</td>
<td>50.1</td>
<td>44.9</td>
<td>39.3</td>
<td>47.2</td>
</tr>
<tr>
<td></td>
<td>HS Graduate</td>
<td>33.8</td>
<td>34.9</td>
<td>32.0</td>
<td>32.6</td>
</tr>
<tr>
<td></td>
<td>Some college</td>
<td>24.9</td>
<td>25.5</td>
<td>24.0</td>
<td>30.1</td>
</tr>
<tr>
<td></td>
<td>College grad</td>
<td>19.9</td>
<td>20.6</td>
<td>19.9</td>
<td>20.3</td>
</tr>
<tr>
<td>Age 35+:</td>
<td>&lt; High School</td>
<td>76.5</td>
<td>67.6</td>
<td>67.5</td>
<td>72.6</td>
</tr>
<tr>
<td></td>
<td>HS Graduate</td>
<td>65.2</td>
<td>55.7</td>
<td>51.4</td>
<td>56.0</td>
</tr>
<tr>
<td></td>
<td>Some college</td>
<td>48.3</td>
<td>42.9</td>
<td>41.6</td>
<td>40.8</td>
</tr>
<tr>
<td></td>
<td>College grad</td>
<td>47.8</td>
<td>36.0</td>
<td>32.8</td>
<td>29.9</td>
</tr>
<tr>
<td>All Ages:</td>
<td>&lt; High School</td>
<td>67.8</td>
<td>60.4</td>
<td>58.7</td>
<td>64.6</td>
</tr>
<tr>
<td></td>
<td>HS Graduate</td>
<td>50.6</td>
<td>46.7</td>
<td>44.0</td>
<td>47.3</td>
</tr>
<tr>
<td></td>
<td>Some college</td>
<td>39.3</td>
<td>34.4</td>
<td>33.5</td>
<td>35.0</td>
</tr>
<tr>
<td></td>
<td>College grad</td>
<td>36.9</td>
<td>30.8</td>
<td>28.3</td>
<td>27.1</td>
</tr>
</tbody>
</table>


Source: National Household Survey  SAMSHA Advance Report #5 Table 9. 3/94.

The more education an individual has, the less likely they are to believe that the occasional use of marijuana is harmful. This observation holds up for any age group in
any year. People find less risk associated with marijuana use as their education and independent reasoning skills increase.

When kids are taught that marijuana users move on to other drugs, they also note the subtle suggestion that if someone likes marijuana, they’ll like the other drugs as well, and if they find marijuana exciting, other thrills await. This is the real danger of exaggerating the effects and dangers of marijuana use for adults, if the plan backfires there's no reason to avoid more dangerous drugs.

Many Americans clearly do not think marijuana use is dangerous, but still choose not to use the drug. This data is also available from the Household Survey, but like some of the data above requires a little mathematics. Table 2 presents the percentages of people who perceive harm from occasional marijuana use in various age groups. For each percentage that perceives harm, there is a complementary percentage who do not. For example, if 40% of a group think marijuana is harmful, then 60% of the group do not think it is harmful. Conventional wisdom would suggest that a high percentage of people who do not think occasional use of marijuana is harmful would also be regular users of the drug. Table 3 compares lists percentages obtained by comparing respondents who do not find great risk in occasional marijuana use with those who use the drug monthly.

<table>
<thead>
<tr>
<th>Education</th>
<th>Age 18-25</th>
<th>Age 26-34</th>
<th>Age 35+</th>
<th>All Ages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1993</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Levels</td>
<td>16.5</td>
<td>9.5</td>
<td>3.9</td>
<td>7.8</td>
</tr>
<tr>
<td><strong>1992</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; High School</td>
<td>24.2</td>
<td>18.0</td>
<td>5.8</td>
<td>12.7</td>
</tr>
<tr>
<td>High School</td>
<td>17.7</td>
<td>12.6</td>
<td>3.4</td>
<td>8.7</td>
</tr>
<tr>
<td>Some College</td>
<td>13.0</td>
<td>13.0</td>
<td>2.2</td>
<td>7.4</td>
</tr>
<tr>
<td>College Grad</td>
<td>7.3</td>
<td>7.9</td>
<td>3.0</td>
<td>4.0</td>
</tr>
<tr>
<td>All Levels</td>
<td>16.1</td>
<td>12.0</td>
<td>3.3</td>
<td>8.0</td>
</tr>
<tr>
<td>Year</td>
<td>Mj Easy to Get</td>
<td>1993</td>
<td>College Grad</td>
<td>Some College</td>
</tr>
<tr>
<td>------</td>
<td>---------------</td>
<td>------</td>
<td>-------------</td>
<td>-------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>78.6</td>
<td>73.3</td>
<td>55.6</td>
</tr>
<tr>
<td></td>
<td>1993</td>
<td>77.5</td>
<td>69.8</td>
<td>52.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4.1</td>
<td>5.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>12.3</td>
<td>9.0</td>
</tr>
</tbody>
</table>

Table 3. Ratio of percentages of monthly marijuana users to percentages of those who do not perceive great risk in occasional marijuana use, by year and demographic characteristics, with related availability data.


If marijuana use drops as perception of great risk increase, then one would expect increased use among those who perceive that the risk not to be great. Table 3 does not confirm that expectation (if it did the percentages would be considerable higher), and supports an argument that other factors than perceived risk contribute to avoidance of marijuana use. Only about 8% of people who do not think marijuana is dangerous use it monthly.

The National Household Survey does indicate that after a steadying decline, marijuana use is beginning to increase again in the United States. However it also demonstrates that nearly 80% of regular marijuana users do not use other illegal drugs, that adults lose confidence in government anti-marijuana information as the age and education increases, and that adults choose not to use marijuana despite a lack of harmful perceptions about the drug.

Monitoring the Future Project
This project is also known as the National High School Senior Survey, and is conducted for NIDA annually by the Social Research Institute of the University of Michigan. The purpose of the project is to closely monitor drug use by young people. While the project reports on drug use among school aged youths and college aged young adults, their data on high school drug use receives the most public attention.

In 1964 college marijuana use became a national media sensation, and by the 1970's marijuana use became a persistent feature among high school teen life. The trend toward decriminalizing marijuana was halted in the late 1970's. The existence of criminal penalties for marijuana sale and cultivation over the last forty years was supposed to have eliminated the threat of marijuana to school aged children. Concern over the dangers of exposing school aged children to marijuana led to federal mandatory minimum sentences for marijuana sales enacted in the mid 1950's.

While many of laws concerning possession of small amounts of marijuana were liberalized during the 1970's, severe penalties have always been available for other marijuana related crimes.

According to the Monitoring the Future Project, from 1975 to 1994 nearly all of 12th grade students, 85%, rated marijuana as easy to get. From 1976 to 1987 over 50% of high school students had used marijuana prior to graduation; since 1988 that figure has dropped to a low of 32.6% in 1992. In 1994 the project reported that 38.2% of 12th graders had tried marijuana.

The problem that has everyone concerned is that the age of first use of drugs is dropping. A significant percentage of school children are using inhalants, alcohol, tobacco, and marijuana by the time they finish the 8th grade.
<table>
<thead>
<tr>
<th></th>
<th>Lifetime</th>
<th>Last year</th>
<th>Last Month</th>
<th>Daily</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Marijuana Use:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8th Grade</td>
<td>16.7</td>
<td>13.0</td>
<td>7.8</td>
<td>.7</td>
</tr>
<tr>
<td>10th Grade</td>
<td>30.4</td>
<td>25.2</td>
<td>15.8</td>
<td>2.2</td>
</tr>
<tr>
<td>12th Grade</td>
<td>38.2</td>
<td>30.7</td>
<td>19.0</td>
<td>3.6</td>
</tr>
<tr>
<td><strong>More than a few sips of alcohol:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8th Grade</td>
<td>55.8</td>
<td>46.8</td>
<td>25.5</td>
<td>1.0</td>
</tr>
<tr>
<td>10th Grade</td>
<td>71.1</td>
<td>63.9</td>
<td>39.2</td>
<td>1.7</td>
</tr>
<tr>
<td>12th Grade</td>
<td>80.4</td>
<td>73.0</td>
<td>50.1</td>
<td>2.9</td>
</tr>
<tr>
<td><strong>5+ Drinks in the last 2 weeks:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8th Grade</td>
<td>14.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10th Grade</td>
<td>23.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12th Grade</td>
<td>28.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Been Drunk:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8th Grade</td>
<td>25.9</td>
<td>18.2</td>
<td>8.7</td>
<td>.3</td>
</tr>
<tr>
<td>10th Grade</td>
<td>47.2</td>
<td>38.0</td>
<td>20.3</td>
<td>.4</td>
</tr>
<tr>
<td>12th Grade</td>
<td>62.9</td>
<td>51.7</td>
<td>30.8</td>
<td>1.2</td>
</tr>
<tr>
<td><strong>Inhalant Use:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8th Grade</td>
<td>19.9</td>
<td>11.7</td>
<td>5.6</td>
<td>.2</td>
</tr>
<tr>
<td>10th Grade</td>
<td>18.0</td>
<td>9.1</td>
<td>3.6</td>
<td>.1</td>
</tr>
<tr>
<td>12th Grade</td>
<td>17.7</td>
<td>7.7</td>
<td>2.7</td>
<td>.1</td>
</tr>
</tbody>
</table>

Table 4. Prevalence of Marijuana, Alcohol, and Inhalant Use among 8th, 10th and 12th grade students.

Source: 1994 Monitoring the Future Results, 12/94
By the 8th grade, nearly 20% of students have tried inhalants, 25% have been drunk, 14.5% have had 5 or more drinks of alcohol within the last two weeks, and over 55% have had more than a few sips of alcohol in their very young lives. The fact that 16.6% of 8th graders have also smoked marijuana in their young lives should not come as much of a shock or surprise. Unacceptable, yes, surprising, no.

There is hardly much support for the argument that adult marijuana use contributes to teenage drug abuse. The predominant drug abuse problem among teenagers is the use of alcohol. While school age children are trying illegal drugs at increasingly earlier ages, their use of legal drugs are occurring at earlier ages and at even higher incidence.

It is true that teenage alcohol use has come under greater scrutiny over the last ten years, and prevention programs are increasingly treating the legal and illegal drugs with similar weight.

The use of alcohol, tobacco, and marijuana has become a routine part of high school life over the last twenty years. The high prevalence of alcohol and tobacco use among school aged youth could contribute considerably more to teenage marijuana use than the influence of adult marijuana use.

(The relationship of marijuana use to other drug use will be discussed further in section 6 below regarding the public health risk of marijuana use.)

The Monitoring the Future Project stopped providing data on tobacco use during the 1990's. Table 5 provides data from the Monitoring the Future Project during the years 1975 to 1990, when data on tobacco use was included in the report.

<table>
<thead>
<tr>
<th>Year</th>
<th>Ever Used</th>
<th>Last 30 Days</th>
<th>Daily Use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Al</td>
<td>Cig</td>
<td>Mj</td>
</tr>
<tr>
<td>1990</td>
<td>89.5</td>
<td>64.4</td>
<td>40.7</td>
</tr>
<tr>
<td>Year</td>
<td>Alcohol</td>
<td>Tobacco</td>
<td>Marijuana</td>
</tr>
<tr>
<td>------</td>
<td>---------</td>
<td>---------</td>
<td>-----------</td>
</tr>
<tr>
<td>1989</td>
<td>90.7</td>
<td>65.7</td>
<td>43.7</td>
</tr>
<tr>
<td>1988</td>
<td>92.0</td>
<td>66.4</td>
<td>47.2</td>
</tr>
<tr>
<td>1987</td>
<td>92.2</td>
<td>67.2</td>
<td>50.2</td>
</tr>
<tr>
<td>1986</td>
<td>91.3</td>
<td>67.6</td>
<td>50.9</td>
</tr>
<tr>
<td>1985</td>
<td>92.2</td>
<td>68.8</td>
<td>54.2</td>
</tr>
<tr>
<td>1984</td>
<td>92.6</td>
<td>69.7</td>
<td>54.9</td>
</tr>
<tr>
<td>1983</td>
<td>92.6</td>
<td>70.6</td>
<td>57.0</td>
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<tr>
<td>1982</td>
<td>92.8</td>
<td>70.1</td>
<td>58.7</td>
</tr>
<tr>
<td>1981</td>
<td>92.6</td>
<td>71.0</td>
<td>59.5</td>
</tr>
<tr>
<td>1980</td>
<td>93.2</td>
<td>71.0</td>
<td>60.3</td>
</tr>
<tr>
<td>1979</td>
<td>93.0</td>
<td>74.0</td>
<td>60.4</td>
</tr>
<tr>
<td>1978</td>
<td>93.1</td>
<td>75.3</td>
<td>59.2</td>
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<tr>
<td>1977</td>
<td>92.5</td>
<td>75.7</td>
<td>56.4</td>
</tr>
<tr>
<td>1976</td>
<td>91.9</td>
<td>75.4</td>
<td>52.8</td>
</tr>
<tr>
<td>1975</td>
<td>90.4</td>
<td>73.6</td>
<td>47.3</td>
</tr>
</tbody>
</table>


Source: NIDA
The Monitoring the Future Project also collects survey data on the intensity and duration of the highs experience as indirect measures of dose or quantity used, and to help characterize drug-using events. The drugs with the most intense highs tend to result in the longest highs; marijuana is once again an exception. The "Degree of (Marijuana) High Attained" by recent users in the class of 1990 were 5% not at all high, 25% a little high, 40% moderately high, and 30% very high.  

The highs achieved with marijuana, although intense for many users, tend to be relatively short-lived in comparison with many other drugs. Fewer than 6% stay high for seven hours or more. The majority of users usually stay high two hours or less, and the modal time is one to two hours (53% of users); however, one third (33%) report usual highs lasting 3-6 hours.

Interestingly, the duration of the highs obtained in practice by marijuana and alcohol are similar, however, more users sustain a stronger duration of high with marijuana than with alcohol.

For a given individual we would expect more variability from occasion to occasion in the degree of intoxication achieved with alcohol than with most other drugs.

These observations may explain why some individuals prefer marijuana to alcohol, especially when recognizing that the nausea does not accompany marijuana use.

This data on duration and intensity of high allows the project to make the following observation:

Not only are fewer high school students now using marijuana (in 1990), but those who are using seem to be using less frequently and to be taking smaller amounts (and doses of the active ingredient) per occasion. This is of particular interest in light of the evidence from other sources that the THC content of marijuana has risen dramatically during the eighties. The evidence here would suggest that users have titrated their

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185 ibid. pg. 120
186 ibid. pg. 122.
intake to achieve a certain perhaps declining level of high, and thus are smoking less marijuana in terms of volume.\textsuperscript{187}

The Drug Abuse Warning Network.

These reports serve as indications of the extent of emergency room admissions for drug-related episodes. The nature of the reporting data can be confusing. A visit to the emergency room is referred to, and counted, as an episode. Drug related episodes can involve one, or combinations of different drugs. Every time a drug is involved in an episode is a mention, and several drugs can be mentioned in a single episode. In this context a drug-related episode indicates the use of an illegal drug or the non-medical use of a prescription drug which results in an emergency room visit.

The DAWN network collects reports from a large sample of hospitals and provides data on the number of episodes and mentions, and on the number of mentions per 100,000 population or 100,000 emergency room visits.

In 1993 there were 466,897 drug-related episodes reported, and 808,233 mentions. Marijuana was the subject of 29,200 mentions, each a separate episode. Marijuana related episodes have increased 46% from 1988 to 1993, 22% from the 1990 to 1993.\textsuperscript{188}

However 50% of marijuana episodes included use in combination with alcohol. Use with cocaine was involved in 40% of the marijuana-related episodes, though some of those also involved alcohol. Of the 29,166 marijuana-related episodes, 50% or 14,853 were also alcohol related, 30% or 8750 involved the use of another drug besides marijuana, and only 20% or 5883 were the result of the use of marijuana alone. The number of marijuana alone episodes was similar to the number of episodes involving over the counter sleep aids (5,514). (In 1991 marijuana alone accounted for 20.3% of the

\textsuperscript{187} ibid. pg. 123
marijuana-related episodes, and 41.5% of the episodes involved 2 or more other drugs in addition to marijuana.) Only 23% of the increase in marijuana mentions from 1990 to 1993 was due to the use of marijuana alone.
<table>
<thead>
<tr>
<th></th>
<th>Number of Mentions</th>
<th>Mentions/100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total episodes</td>
<td>466,897</td>
<td>203.9</td>
</tr>
<tr>
<td>mentions</td>
<td>808,233</td>
<td>352.9</td>
</tr>
<tr>
<td>alcohol in comb.</td>
<td>145,394</td>
<td>63.5</td>
</tr>
<tr>
<td>cocaine</td>
<td>123,317</td>
<td>53.8</td>
</tr>
<tr>
<td>common analgesics*</td>
<td>72,496</td>
<td>31.6</td>
</tr>
<tr>
<td>heroin/morphine</td>
<td>62,965</td>
<td>27.5</td>
</tr>
<tr>
<td>benzodiazepines**</td>
<td>40,534</td>
<td>17.7</td>
</tr>
<tr>
<td>marijuana (all)</td>
<td>29,166</td>
<td>12.7</td>
</tr>
<tr>
<td>marijuana in comb</td>
<td>23,333</td>
<td>10.2</td>
</tr>
<tr>
<td>marijuana alone</td>
<td>5,833</td>
<td>2.5</td>
</tr>
</tbody>
</table>

* aspirin, acetaminophen and ibuprofen  
** alprazolam (Xanax), diazapam (Valium) and lorazepam

Table 6. Summary of selected mentions during emergency room visits from reporting sample in 1993.


According to the National Household Survey, there were an estimated 186 marijuana users per 100,000 people in the U.S. in 1993, and 2.5 of them (1.3%) had to go to the emergency room because of marijuana use alone. Marijuana use with other drugs, but not alcohol, resulted in 4.3 visits to the emergency room per 100,000 users. The Household Survey also estimates 1,378 users of alcohol per 100,000 people, and 63.5 of them (4.6%) had to go to the emergency room for various reasons as well.

Unlike alcohol and many other drugs, marijuana is non-toxic. It is impossible for someone to die from an overdose of marijuana; the drug has little effect on the heart or lungs. Excessively large doses produce long periods of sleep. Ironically, many marijuana-related visits to the emergency room involved perceived harm, such as
unexpected reactions, rather than actual harm to the individual, such as life-threatening overdose.

Compare with acetaminophen, which alone accounted for 35,000 episodes, 7% of the total and 15.3 visits per 100,000 population. Acetaminophen alone accounted for 42% of the episodes, 21% involved alcohol. Suicide attempts were the motive for 79% of the incidents, and an overdose was responsible for 90% of the emergency room visits. Aspirin alone accounted for 8.4 visits per 100,000 and Ibuprofen accounted for 7.9 episodes.

The use of marijuana alone results in relatively few emergency room visits. The use of marijuana with alcohol, or with other drugs, still provides relatively few visits in comparison to benzodiazepines, common household pain relievers, alcohol, cocaine, and heroin.

DAWN tracks the reasons patients give for taking the drugs responsible for their emergency room visit, and the reasons given for the visit. The reasons given for marijuana-related episodes is hard to interpret because only 20% of the visits were for marijuana alone. Nonetheless, the data is provided in Table 7, along with data for cocaine, heroin, and the entire group of emergency room visits.

<table>
<thead>
<tr>
<th>Use:</th>
<th>All Visits</th>
<th>Cocaine</th>
<th>Heroin</th>
<th>Marijuana</th>
<th>1988 Mj.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recreational</td>
<td>7.4</td>
<td>11.2</td>
<td>8.2</td>
<td>25.5</td>
<td>31.6</td>
</tr>
<tr>
<td>Dependence</td>
<td>29.2</td>
<td>63.42</td>
<td>76.0</td>
<td>37.2</td>
<td>37.6</td>
</tr>
<tr>
<td>Suicide</td>
<td>42.5</td>
<td>7.5</td>
<td>3.3</td>
<td>8.0</td>
<td>7.5</td>
</tr>
<tr>
<td>Other/Unknown</td>
<td>20.8</td>
<td>17.8</td>
<td>12.5</td>
<td>29.2</td>
<td>23.2</td>
</tr>
<tr>
<td>ER Visit:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unexpected reaction</td>
<td>11.1</td>
<td>22.9</td>
<td>11.0</td>
<td>30.1</td>
<td>27.7</td>
</tr>
</tbody>
</table>
Further evidence that present policy and scheduling regarding marijuana is based on inaccurate or outdated data about marijuana are these comments describing the significance of the DAWN data.

1993 Drug Abuse Warning Network, or DAWN survey . . . sends a clear message to our children. If you start doing drugs early -- there's a chance it will eventually lead you to the emergency room. . . young people [must] understand the serious health effects of marijuana and other drugs so they don't end up like so many of the long-term drug users in the DAWN survey -- chronically ill, in need of detoxification. . . This isn't hyperbole. . . The more young people know that all drugs -- including marijuana -- are harmful, the less likely they are to engage in the self-destructive behaviors that we see culminating in the DAWN data.189

A reality check is in order at this point in the discussion, and the reader can refer to the data cited above in reference to the following statements.

Marijuana used in conjunction with alcohol, or with other drugs, increases the possibility of adverse reactions and consequences, such as accidents, for the user.

Even when considered in combination with alcohol and other drugs, marijuana produces fewer visits to the emergency room per 100,000 population than alcohol, heroin, cocaine, benzodiazepines (tranquilizers), and common household pain killers.

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Suicide is the most frequent reason (42.5%) given by emergency room patients in drug-related episodes, and overdose is the most frequent reason (55.7% for an emergency room visit. While some people don't fully understand this, marijuana is non-toxic and can not produce death through overdose. Visits to the emergency room on account of marijuana use do not tend to be life-threatening.

Only 20% of marijuana mentions involve the use of marijuana alone, and over 3/4 of regular marijuana users do not use other drugs. Yet 40% of marijuana emergency room episodes also involve cocaine. A minority of marijuana users account for a majority of marijuana mentions in emergency room reports.

The majority of marijuana related visits to emergency rooms (30.1%) result from unexpected reactions to the drug. Novice users sometimes experience anxiety or panic attacks; the pharmacological literature refers to these episodes as self-correcting, meaning they are unlikely to reoccur in the same individual.190

Marijuana users are no more likely to seek emergency treatment for chronic effects of their use than any other visitor to ER for a drug-related episode.

Individuals seeking detoxification or other drug treatment services at an emergency room are there because they have no where else to turn for medical assistance. This is an indication of problems with the availability of treatment. Since 80% of marijuana related mentions involve the mention of other drugs (50% involve alcohol and 40% involve cocaine) it is impossible for DAWN data to support the argument that marijuana users are going to emergency rooms for detoxification in significant numbers.

When the DAWN data is rated against alcohol and marijuana drug using populations, marijuana with or without any drug except alcohol produces slightly less emergency room visits (4.3) per 100,000 users than alcohol (4.6). There is no evidence in the DAWN data to support the claim that marijuana use is a self-destructive behavior.

Like most users of alcohol, most users of marijuana are responsible and engage in moderate use of their drug under safe conditions.

Marijuana use does produce unexpected reactions, including accidents, which result in emergency room visits. Compared to other drugs, and considering marijuana's low or non-existent toxicity, it is difficult to use the DAWN data to support an argument that a danger index for marijuana exists and is on the increase.

If the theory that marijuana is too dangerous for un-supervised use is true, than one would expect there would be a greater incidence of marijuana-alone mentions in the DAWN data. Instead a closer examination of the DAWN data reveals that only a minority of marijuana users end up in the emergency, just as only a minority of marijuana users are actually polydrug users.

The National Narcotics Intelligence Consumers Committee.

The problems with making estimates about an illegal crop are immense. Analysts must estimate first total production in various areas of the world, and then estimate how much of that production is bound for the U.S. market. Brazil, for example, grows a lot of marijuana for domestic consumption and export to Argentina (entirely illegal, of course). Presumably most if not all of the marijuana grown in Columbia, Mexico, Jamaica, and Belize is intended for the U.S. market. Marijuana grown in Thailand and other South Asia and Pacific locations is sent to Australia, but considerable quantities reach the U.S. International marijuana production is reviewed annually by the U.S. Department of State.191 Canada, for example, also has marijuana consumers, many of whom ultimately receive theirs from the same overseas suppliers as the U.S. Finally, a considerable amount of marijuana is grown in the United States, for consumption in the United States.

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It is difficult to estimate how much because of the tremendous decentralization of the
domestic cultivation market.

According to NNICC, on average 39 million pounds of marijuana is available for sale in
the United States annually. According to the National Household Survey, there are less
than 20 million marijuana smokers in the United States. If one is to believe them both,
then the average marijuana smoker consumes 2 pounds annually. That is unrealistic.
Either a considerable amount of foreign produced marijuana does not make it to the
United States, or there are considerably more marijuana users in the U.S. than estimated
by the National Household Survey, or both.

The production figures for Mexico are volatile. Early in the 1980's the U.S. had
no idea how much marijuana was actually being grown in Mexico, and in the mid 1980's
U.S. pressure was on Colombia to reduce marijuana cultivation.
Mexico    7.72  8.05  10.39  66.59+  43.47  17.14  17.19  13.85
Colombia  6.72  9.81  15.11  6.17  3.31  3.64  9.09
Jamaica   3.09  .48  .72  .42  1.82  1.41  .58  1.11
Belize    1.10  .44  .13  .14  .13  .11  .11  .11
Other**   2.21  3.30  4.13  7.72  7.72  9.92  9.92*  9.92*

Gross Available  25.47  29.25  40.62  93.17  40.97  41.16  43.80
Less Seizures  7.72  7.72  8.82  8.82  8.82  8.82  8.82
Net Mj. Available  17.75  21.53  31.80  84.35  59.76  32.15  32.34  34.98

+ In 1989 DEA realized that Mexico had a lot more marijuana growing than was previously believed. the increase over 1988 reflects more accurate analysis rather than an increase in Mexican cultivation.
*1991 estimate
**includes S.E. Asia, and other Latin America Sources

Table 8. Net Marijuana Available for Sale to the United States, by source country, in millions of pounds.


In 1986 the U.S. and Mexican police discovered a network of several farms which produced 8 times more marijuana than was estimated for the entire country.192 When the U.S. began to focus on reducing Mexican marijuana cultivation in the early 1990's, the Colombian marijuana crop began to increase in production.

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There are few studies on actual marijuana consumption by U.S. citizens, however an estimate of one pound per person per year should be considered generous. By this standard, the 18 million users estimated by the NHS can't account for all the available marijuana. Deciding what happened to the millions of pounds of marijuana unaccounted for in the NNICC estimate can be a fanciful game; how much was diverted to other markets, how much was consumed by uncounted U.S. consumers?

Marijuana is a multi-billion dollar international commodity whose staying power is augmented by diverse demand within the United States and diverse competition around the world to respond to economic buying power of the U.S. marijuana consumers.

If U.S. marijuana consumption was limited to 20 million pounds consumed by 20 million people, at $1000 per pound (a conservative price), the U.S. marijuana market is worth $20 billion dollars. This is a very conservative estimate. Marijuana is a very large international market.

The Uniform Crime Reports

Many people believe that while illegal, no one gets arrested for marijuana any more unless they're selling it, or unlucky.
<table>
<thead>
<tr>
<th>Year</th>
<th>All Drugs</th>
<th>Marijuana</th>
<th>Mj/Drug</th>
<th>Mj. Poss.</th>
<th>Mj. Sales</th>
</tr>
</thead>
<tbody>
<tr>
<td>1965</td>
<td>60,500</td>
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</tr>
<tr>
<td>1966</td>
<td>75,900</td>
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<tr>
<td>1967</td>
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<td>61,843</td>
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<tr>
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<td>95,870</td>
<td>0.48</td>
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<tr>
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<td>0.41</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1970</td>
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<td>188,682</td>
<td>0.45</td>
<td></td>
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</tr>
<tr>
<td>1971</td>
<td>492,000</td>
<td>225,828</td>
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</tr>
<tr>
<td>1972</td>
<td>527,400</td>
<td>292,179</td>
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</tr>
<tr>
<td>1973</td>
<td>628,900</td>
<td>420,700</td>
<td>0.67</td>
<td></td>
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</tr>
<tr>
<td>1974</td>
<td>642,080</td>
<td>445,000</td>
<td>0.69</td>
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<tr>
<td>1975</td>
<td>601,300</td>
<td>416,100</td>
<td>0.69</td>
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<tr>
<td>1976</td>
<td>609,700</td>
<td>441,100</td>
<td>0.72</td>
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<tr>
<td>1977</td>
<td>642,700</td>
<td>457,600</td>
<td>0.71</td>
<td></td>
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</tr>
<tr>
<td>1978</td>
<td>628,700</td>
<td>445,800</td>
<td>0.71</td>
<td></td>
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<tr>
<td>1979</td>
<td>558,600</td>
<td>391,600</td>
<td>0.70</td>
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<tr>
<td>1980</td>
<td>580,900</td>
<td>405,600</td>
<td>0.70</td>
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</tr>
<tr>
<td>1981</td>
<td>559,900</td>
<td>400,300</td>
<td>0.71</td>
<td>344,339</td>
<td>55,990</td>
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<tr>
<td>1982</td>
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<td>455,600</td>
<td>0.67</td>
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<tr>
<td>1983</td>
<td>661,400</td>
<td>406,900</td>
<td>0.62</td>
<td>334,007</td>
<td>69,447</td>
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<tr>
<td>1984</td>
<td>708,400</td>
<td>419,400</td>
<td>0.59</td>
<td>342,157</td>
<td>73,674</td>
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<tr>
<td>1985</td>
<td>811,400</td>
<td>451,138</td>
<td>0.56</td>
<td>365,941</td>
<td>85,197</td>
</tr>
<tr>
<td>1986</td>
<td>824,100</td>
<td>361,780</td>
<td>0.44</td>
<td>296,676</td>
<td>65,104</td>
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<tr>
<td>1987</td>
<td>937,400</td>
<td>378,709</td>
<td>0.40</td>
<td>313,709</td>
<td>65,618</td>
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<tr>
<td>1988</td>
<td>1,155,200</td>
<td>391,600</td>
<td>0.34</td>
<td>326,921</td>
<td>64,961</td>
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<tr>
<td>1989</td>
<td>1,361,700</td>
<td>398,977</td>
<td>0.29</td>
<td>314,552</td>
<td>84,425</td>
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<tr>
<td>1990</td>
<td>1,089,500</td>
<td>326,850</td>
<td>0.30</td>
<td>260,391</td>
<td>66,460</td>
</tr>
<tr>
<td>1991</td>
<td>1,010,000</td>
<td>287,850</td>
<td>0.29</td>
<td>226,240</td>
<td>61,610</td>
</tr>
<tr>
<td>1992</td>
<td>1,066,400</td>
<td>342,314</td>
<td>0.32</td>
<td>271,932</td>
<td>70,382</td>
</tr>
<tr>
<td>1993</td>
<td>1,126,300</td>
<td>380,689</td>
<td>0.34</td>
<td>310,859</td>
<td>69,830</td>
</tr>
</tbody>
</table>
Table 9 provides a review of marijuana and other drug arrests from 1965 to 1993.

Historically, marijuana arrests have dropped as a percentage of all drug arrests, an indication of changing priorities for police departments. This is most evident in the 20% drop in marijuana arrests from 1985 to 1986, the year crack cocaine exploded onto the American scene. Total drug arrests grew little in 1986, as police simply redeployed their efforts to respond to crack. Then in 1987 drug arrests grew by over 100,000, marijuana arrests grew by a few thousand.

Cocaine-related arrests began to swamp the criminal justice system until the system reached maximum capacity in 1989. Since then marijuana arrests have remained relatively stable as a percentage of all arrests (about one third), which has also remained stable, at about 1.1 million arrests a year.

In 1993 an estimated 18.6 million people used marijuana and police arrested 380,689 of them. The arrest rate for marijuana offenses in 1993 was 2.04%. Marijuana users had a one in fifty chance of being arrested.

Actually, it is not that simple. Eleven states containing one third of the nation's population don't make arrests for possession of marijuana for personal use: Alaska, Oregon, California, Nebraska, Colorado, Minnesota, Ohio, Mississippi, North Carolina, New York, and Maine. These decriminalization laws were enacted during the 1970's and have resulted in considerable savings. Since 1980 there have been an average of 386,000 marijuana arrests a year.

In 1993 police made an estimated 14 million arrests in the United States. Using rounding of numbers to provide easy comparisons, the nature of distribution of arrests is as follows: Two million arrests were made for property crime, and three quarter million
arrests were made for violent crime. Another 1.1 million arrests were made for other assaults. Half a million people were arrested for cocaine and heroin related crime, half a million more for other drugs. One and a half million people were arrested for driving under the influence of alcohol, and the same number were arrested for drunkenness and disorderly conduct combined. There were a half million arrests for forgery and fraud, over 300,000 for vandalism and over 250,000 for weapons violations. Trafficking in stolen property resulted in 150,000 arrests. There were about 100,000 prostitution arrests, another 100,000 for sex offenses (not including rape). There were about half a million liquor law violations, 200,000 arrests of runaway kids, 100,000 curfew and loitering law violations, and 100,000 for offenses against families and children. All other offenses resulted in 3.5 million arrests.

Police did not solve 34% of murders, 44% of aggravated assaults, 47% of forcible rape cases, 85% of larceny-thefts, 76% of robberies, 86% of motor vehicle thefts, and 87% of burglaries in 1993.

One reason many of these crimes were not solved is lack of cooperation from the public. Sexual assaults are certainly a different matter and present different circumstances affecting reporting and crime investigation, and individual cases differ. But many crimes go unpunished because many citizens either fear retribution or look upon the police with suspicion rather than with trust. In 1972 the National Commission of Marihuana and Drug Abuse warned that continued arrests for marijuana possession would create disrespect for the law and the criminal justice system on the part of otherwise law-abiding citizens. What toll has continued marijuana arrests exacted from the credibility and stature of law enforcement officials over the last twenty years?

Once again, the significance of this indicator is in its persistence. Continued arrests have not and will not eliminate marijuana from our society, because its use is sufficiently widespread and well-established in the United States to acquire cultural significance.
According to Thomas Kuhn, the role of measurement in science is to isolate anomalies and make them unavoidable in theory appraisal.\footnote{Kuhn, T. "The Function of Measurement in Modern Physical Science" \textit{In The Essential Tension}, Chicago: University of Chicago. 1977. pp. 178-224.} One aspect of measurement error is inadequate study design, usually indicated by flaws in reasoning. Here are a few of frequent flaws that can be found in governmental defenses of marijuana policy based on rejected and outdated findings.

\begin{enumerate}

The surveys do not distinguish between use and abuse of drugs, the NHS has problems with underrepresented population segments, and the MFP has a problem with overreporting by young students. All of these provide serious problems for using the data as a policy diagnostic.\footnote{U.S. Congress, Office of Technology Assessment, \textit{Technologies for Understanding and Preventing Substance Abuse and Addiction}, OTA-EHR-597 (Washington, DC: US Government Printing Office, September 1994). pp. 37-38.}

During the early 1990's a downward trend in high school marijuana use reversed. As marijuana use was falling during
Marijuana: Trends in Perceived Risk of Regular Use and Prevalence of Use in Past Thirty Days for Twelfth Graders

Source: “A Synopsis of the Key Points in the 1994 Monitoring the Future Results”, The Monitoring the Future Study, the University of Michigan. Released by the Department of Health and Human Services 12/12/94.

Use: % using once or more in past 30 days (on left-hand scale)
Risk: % saying great risk of harm in regular use (on right-hand scale)
the 1980's perception of great risk associated with using marijuana increased. As marijuana use began to increase recently, risk perception dropped. (See Figure 1.) Federal policy is based on the assumption that use is inversely related to risk perception, and a graph of those two indicators is offered as the scientific justification for present policy, which is to increase risk perception.198

No null hypothesis is evaluated; there is no interest in trying to prove the theory false.

People who perceive great risk in using marijuana regularly can be recoded as believers, they believe that marijuana is harmful. There is a complementary percentage of the sample who are non-believers, who do not believe that regular marijuana use is harmful. According to the present policy paradigm, there should be little or no difference between the number of regular users and the number of non-believers.

One way to test this hypothesis is to compare the ratio of regular users to non-believers for the data presented in the NHS and the MFP and compare the ratios among different drugs. A generous standard is to define "little or no difference" as a ratio above .7, and the government paradigm would lead one to expect that little difference in the ratios between drugs, and an improving ratio as age and/or education increase.

Table 1 compares the ratios of users to non-believers for marijuana, alcohol, and tobacco. Regular use is defined as past month use for all drugs, and perceived risk was evaluated as to regular marijuana use, use of 5 alcoholic drinks or more in sequence within the last two weeks, and the use of a pack of cigarettes a day.

There is little or no difference between non-believers and regular users of alcohol and tobacco, and the difference between the two groups drops as age and education increase. (Table not included.) This does not provide sufficient data to reject the hypothesis that there should be little or no difference between the groups, and does not

contradict the theory that use is inversely related to perceived harmfulness. (The ratios in Table 1 for alcohol exceed 1.0, and suggest that many past month users agree 5+ drinks is risky and have milder consumption levels.)

There is a big difference between the ratio for marijuana and the ratios for alcohol and tobacco. With one interesting exception, the ratios for marijuana fall significantly below .7, and the ratios drop consistently as age and education increases. This provides sufficient reason to reject the hypothesis that there is no difference between non-believers and regular users.

Many people don't believe marijuana is harmful, and they don't use it anyway. The prominent exception is that during the 1980's, and only with high school students, the ratio was above .7 (though still below alcohol and tobacco). See Table
Table 1. Ratios of Users to Non-Believers

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Marijuana</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>used in past month</td>
<td>9.3</td>
<td>4.8</td>
<td>4.4</td>
<td>4.3</td>
</tr>
<tr>
<td>non-believers</td>
<td>25.2</td>
<td>22.2</td>
<td>22.3</td>
<td>23.3</td>
</tr>
<tr>
<td>ratio</td>
<td>.369</td>
<td>.216</td>
<td>.216</td>
<td>.185</td>
</tr>
<tr>
<td><strong>Alcohol</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>used in past month</td>
<td>58.3</td>
<td>50.9</td>
<td>47.8</td>
<td>49.6</td>
</tr>
<tr>
<td>non-believers</td>
<td>40.1</td>
<td>41.0</td>
<td>38.2</td>
<td>39.1</td>
</tr>
<tr>
<td>ratio</td>
<td>1.45</td>
<td>1.24</td>
<td>1.25</td>
<td>1.27</td>
</tr>
<tr>
<td><strong>Cigarettes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>used in past month</td>
<td>31.4</td>
<td>27.0</td>
<td>26.2</td>
<td>24.2</td>
</tr>
<tr>
<td>non-believers</td>
<td>43.2</td>
<td>36.5</td>
<td>35.9</td>
<td>34.5</td>
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<tr>
<td>ratio</td>
<td>.727</td>
<td>.740</td>
<td>.730</td>
<td>.701</td>
</tr>
</tbody>
</table>

Source: National Household Survey

Table 2. Ratios of Marijuana Users to Non-Believers, 12th Graders.

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>30 day-Mj</td>
<td>27.1</td>
<td>32.2</td>
<td>35.4</td>
<td>37.1</td>
<td>36.5</td>
<td>33.7</td>
<td>31.6</td>
<td>28.5</td>
<td>27.0</td>
<td>25.2</td>
<td>25.7</td>
<td>23.4</td>
<td>21.0</td>
<td>18.0</td>
<td>16.7</td>
<td>14.0</td>
<td>13.8</td>
<td>11.9</td>
<td>15.5</td>
<td>19.0</td>
</tr>
<tr>
<td>No Grt Risk</td>
<td>56.7</td>
<td>61.4</td>
<td>63.6</td>
<td>65.1</td>
<td>58.0</td>
<td>59.6</td>
<td>42.4</td>
<td>39.6</td>
<td>37.2</td>
<td>33.1</td>
<td>29.6</td>
<td>28.7</td>
<td>26.5</td>
<td>23.0</td>
<td>22.5</td>
<td>22.2</td>
<td>21.4</td>
<td>23.5</td>
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<td>35.0</td>
</tr>
<tr>
<td>Ratio</td>
<td>.478</td>
<td>.524</td>
<td>.557</td>
<td>.570</td>
<td>.629</td>
<td>.565</td>
<td>.745</td>
<td>.720</td>
<td>.726</td>
<td>.761</td>
<td>.862</td>
<td>.813</td>
<td>.792</td>
<td>.783</td>
<td>.742</td>
<td>.631</td>
<td>.645</td>
<td>.506</td>
<td>.564</td>
<td>.543</td>
</tr>
</tbody>
</table>

Source: The Monitoring the Future Study, the University of Michigan

Table 3. Ratios of Non-Believers to Regular Marijuana Users

<table>
<thead>
<tr>
<th></th>
<th>Age 18-25</th>
<th>Age 26-34</th>
<th>Age 35+</th>
<th>All Ages</th>
</tr>
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<tbody>
<tr>
<td>1993 Education</td>
<td>All Levels</td>
<td>.165</td>
<td>.095</td>
<td>.039</td>
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<tr>
<td>&lt; High School</td>
<td>.242</td>
<td>.180</td>
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<td>.127</td>
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<tr>
<td>High School</td>
<td>.177</td>
<td>.126</td>
<td>.034</td>
<td>.087</td>
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<tr>
<td>Some College</td>
<td>.130</td>
<td>.130</td>
<td>.022</td>
<td>.074</td>
</tr>
<tr>
<td>College Grad</td>
<td>.073</td>
<td>.079</td>
<td>.030</td>
<td>.040</td>
</tr>
<tr>
<td>All Levels</td>
<td>.161</td>
<td>.120</td>
<td>.033</td>
<td>.080</td>
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<td></td>
<td>1993</td>
<td>&lt; High School</td>
<td>High School</td>
<td>Some College</td>
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<tr>
<td></td>
<td>.253</td>
<td>.193</td>
<td>.040</td>
<td>.123</td>
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<tr>
<td>High School</td>
<td>.192</td>
<td>.122</td>
<td>.051</td>
<td>.098</td>
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<tr>
<td>Some College</td>
<td>.165</td>
<td>.081</td>
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<td>.090</td>
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<tr>
<td>College Grad</td>
<td>.094</td>
<td>.041</td>
<td>.021</td>
<td>.034</td>
</tr>
</tbody>
</table>

2. During the same years, the ratio would plummet as age and education increased.

Marijuana policy had high school students convinced marijuana was dangerous for a while, but then lost its credibility. This supports present policy. However marijuana policy loses credibility as people grow and exercise independent reasoning skills. See Table 3.

**Correspondence Rules**

What is a marijuana user? When the government announces that there are 18.5 million regular marijuana users, what do they mean? It means that the NHS estimates from its sample that 9.5 million admitted to using marijuana sometime during the last year, and 9 million others admitted to using marijuana during the last month. 199

Marijuana users are generally thought to be poly-drug users; certainly this is the implication of policy. Reduce marijuana and other illegal drug use will decline, because illegal drug users all use marijuana.

Policy presents scientific data to support its assumptions, but the indicators they discuss don't always measure up to the populations they actually represent.

According to the NHS, over 2/3rds of regular marijuana users do not use other illegal drugs. 200 This percentage has been increasing recently, suggesting that this is becoming a group ethic among marijuana users. When advocates of marijuana law reform refer to marijuana users, they refer to people who only use marijuana. When policy makers refer to marijuana users, they refer to people who use marijuana and other drugs. These are vastly disproportionate segments of the population of marijuana users.

The generalization, though, is very misleading. Illegal drugs are said to contribute to crime, and the Justice Department has published elaborate explanations of

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200 Ibid. Subtract 'use of any illicit drug other than marijuana' from 'use of any illicit drug' to produce indicators for 'marijuana use alone' and 'marijuana use w/other illicit drugs.'
The explanations are largely based on the research of Paul Goldstein, who finds that alcohol and cocaine contribute to a great deal of violent crime and that marijuana does not. However because marijuana is an illegal drug, and illegal drugs do contribute to crime, marijuana is also presumed to contribute to violent crime (other than the illegality of the drug use and sale itself).

**Self-Serving Comparisons**

Casual treatment of correspondence rules is not the only indication self-serving comparisons. The well-publicized accusation that marijuana has increased in potency over the last twenty years is classic. The primary reason marijuana prevention campaigns were successful with High School students in the 1980's was the declaration that marijuana was 10 times more potent than it was in the 1970's, and consequently more dangerous.

There are two problems here. For one thing, marijuana is a non-toxic substance; overdoses produce sleep, not death, because of a lack of cannabinoid receptors in the medullary region of the brain that controls breathing and heart rate. Marijuana users reduce consumption to compensate for increased potency. According to Lloyd Johnston of the University of Michigan Monitoring the Future Project,

> Those who are [using marijuana] seem to be using less frequently and to be taking smaller amounts (and doses of the active ingredient) per occasion.

By analogy, beer and whisky are both alcohol, and any danger is a function of the relative quantity consumed.

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203 See Herkenham and Lynn (1990)
The other problem is that the finding itself is false.

Tod Mikuriya and Michael Aldrich were among the first to document the fallacies of the allegation that increased marijuana potency rendered marijuana a dangerous drug regardless of past research.205

The story of the new allegedly stronger and more dangerous marijuana was rebirthed in January 1986 by the late Sidney Cohen, M.D., Professor of Psychiatry at UCLA. ". . . material ten or more times more potent than the product smoked ten years ago is being used, and the intoxicated state is more intense and lasts longer." In addition, Cohen asserted that "the amount of THC in confiscated samples averaged 4.1 percent THC during 1984. The sinsemilla [seedless] varieties were about 7% with some samples reaching 14 percent . . . all marijuana research to date has been done on 1 or 2 percent THC material and we may be underestimating present day smoking practices."206

After a careful consideration of historical records, reports of recent potency estimates, and the practice of marijuana smokers to self-adjust their dose, the authors reached the following conclusion.

While it may be true that sinsemilla is more widely available than 10 or 15 years ago, its potency has not changed significantly from the 2.4 to 9.5 percent THC materials available in 1873-1974, or the five to 14 percent sinsemilla of 1975. The range of potencies available then (marijuana at 0.1% to 7.8% THC, averaging 2.0% to 5.0% THC by 19750 was approximately the same as reported now. With such a range, the evidence simply cannot support the argument by Cohen that marijuana is "ten or more times more potent than the product smoked ten years ago." And to say that marijuana potency has increased 1,400 percent since any date in history is patent nonsense.

It is not legitimate to imply that average low potencies represent the full range of potencies available in reality. Neither is it valid to cite the low end of the range then as a baseline to compare the high end of the range now. The claimed baseline for THC content in the early 1970's would appear to be too low, probably because confiscated stored police samples were utilized; and this low baseline makes the claimed difference


206 ibid. pg. 47.
An examination of the government's actual potency data (rather than what they have reported in press releases) was conducted by Dr. John Morgan of the City University of New York Medical School, and indicated that the finding was based on a comparison of the highest THC percentage in the 1980's with the lowest percentage of the 1970's. Also, the data from the 1970's was derived from a sample of decaying, imported Mexican marijuana composed of leaf and flower; it was compared to recently harvested, domestically grown marijuana flowers. Finally, marijuana of similar potency to 1980's standards was available during the 1970's.

Morgan's debunking of marijuana potency findings relies on data presented by the NIDA potency project at the University of Mississippi. This data shows that the arithmetic average potency of *domestic cannabis* tested by the project has ranged from 1.5% to 4.75% THC. In 1973 Gabriel Nahas reports that the THC content of drug-type cannabis ranges from 3.4 to 4.8%. In 1975, before the emergence of high quality domestic marijuana cultivation in the U.S., John Langer of the DEA reports that:

Marihuana produced in the United States is considered inferior because of the low concentration of psychoactive ingredients, which varies between 0.2 and 2.0 percent. Marihuana of Mexican origin is known to be slightly stronger. The variety known as Jamaican ganja, which consists primarily of the flowers and breacts, has a THC content of 4 to 8 percent.

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207 ibid. pg. 53.
These citations from Nahas and the DEA independently demonstrate that a broad range of marijuana potencies was available in the 1970's, and provide additional evidence that assertions otherwise are without factual or scientific foundation.

It is important to understand the fallacy of the increased potency argument for several reasons.

1) It is just wrong. It is factually incorrect.

2) It is ironic that advocates of marijuana prohibition claim prior research is inadequate to explain the effects of this new, high potent marijuana when as explained in section 3, most of the contemporaneous research was later criticized for using extremely unrealistic potencies.

3) It is convenient. The hypothesis that marijuana is now much more potent than in the past provides convincing support for the assertion that any use of the drug is drug abuse. Rhetoric about marijuana potency substitutes for scientific findings in efforts to legitimize existing policy.

4) Most importantly, the scientific research reported in section 3 renders the potency question irrelevant to an assessment of the acute and chronic effects of marijuana use. Remember, in the mid 1980's when this hypothesis gained popularity, the dominant research paradigm was (incorrectly) based on cell membrane perturbation. Certainly, if marijuana produced dangerous effects by toxic seepage into cell membranes, than increases in potency represent increases in danger. Certainly if marijuana produced tolerance by desensitizing brain cells, a result of this toxic seepage, then increases in potency would increase the danger of adverse effects. However marijuana produces its results by way of a neural receptor system, not membrane perturbation, and the brain can tolerate extremely high potent doses of cannabinoids. Tolerance to marijuana develops through receptor down-regulation; the body's response to high potency marijuana is seek a manageable equilibrium through receptor down-regulation. The potency hypothesis
may have had some relevance in the 1980's, regardless of its foundation. However in the 1990's, the potency hypothesis has neither foundation nor relevance.

Misrepresentation of Research Findings

Scientific journals are not grocery stores where one can gather findings for a policy like ingredients for a soup.

Two or three letters show up in medical journals describing cases where doctors suspect a possible connection between marijuana use and tongue cancer.\(^{212}\) Tongue cancer then pops up in prevention literature as an additional danger research has indicated may be associated with marijuana use.\(^{213}\) This is not the way the validity of scientific assertions is established.

One study indicates a correlation between maternal marijuana use and lymphoblastic leukemia in new borns.\(^{214}\) Marijuana is well-known as an anti-emetic. Other anti-emetic drugs were shown in the same study to correlate just as highly as marijuana. Some prevention literature now indicates that marijuana has been linked with leukemia.\(^{215}\)

These warnings are consistent with policy, but do they reflect accurate science? Is there any evidence to predict that marijuana use will produce statistically significant incidence of tongue cancer and/or leukemia in children? The research data in these instances support hypotheses and further research, but they are not singularly persuasive and have been subject to critically negative review.\(^{216}\)

\(^{212}\) e.g. Almadori, G; Paludetti, G; et al "Marijuana smoking as a possible cause of tongue carcinoma in young patients." \textit{J Laryngol Otol} 1990 Nov.; 104(11):896-9. The article concerns a one patient, a 23 year old male regular marijuana smoker, and concerns marijuana as a possible new risk factor.

\(^{213}\) PRIDE, Inc. "Marijuana and Cocaine" (PRIDE: Atlanta, GA) 1990. "Marijuana . . . may lead to early development of head, neck and lung cancers."

\(^{214}\) Robison, LL; Buckley, JD; et al "Maternal drug use and risk of childhood nonlymphoblastic leukemia among offspring. An epidemiological investigation implicating marijuana (a report from the Children's Cancer Study Group)." \textit{Cancer} 1989 May 15;63(10):1904-11.

\(^{215}\) See PRIDE above. "Marijuana use during pregnancy may be linked to one form of leukemia in children."

The discovery of the cannabinoid receptor system occurred in 1990.\textsuperscript{217} Despite the invalidation of most of the biochemical research on marijuana in the 1980's, this didn't prevent the DEA from declaring in 1991 that marijuana was a dangerous drug because of its effects of cellular activities.

Cannabinoids . . . wreak havoc with the chemical process of cell division . . . cellular activity decreases. This interference can eventually stop cellular activity causing the cells to die . . . every function in the body is depressed.\textsuperscript{218}

This is apparently yet another incorrect use of Billy Martin's 1986 article in the *Pharmacological Reviews*.

**Conclusion.**

This section of the petition reviews recent data on the history and pattern of use of marijuana in the United States. While extensive data on the prevalence of marijuana use in the U.S. is available for analysis and discourse, considerable attempts have been made by officials of the U.S. government to misinterpret this data of evidence of widespread marijuana abuse. American adults use marijuana as a mild recreational intoxicant, and as a safe alternative to alcohol or cocaine. The popularity of marijuana is mentioned at the beginning of almost every journal article reporting on marijuana-related research. The persistence of marijuana's popularity in defiance of marijuana's 25 year old schedule I status is a testament to the failure of marijuana prohibition.

\textsuperscript{217} Herkenham, M., Lynn, A. et al. (1990).
Exhibit C.

A summary of any relevant medical or scientific evidence known to the petitioner, section 5 of 8 sections.

5. Scope, Duration, and Significance of Use.

The legislative history of the Controlled Substances Act establishes rationale criteria by which "scope, duration and significance of abuse" are considered.

In evaluating existing abuse, not only must the Attorney General know the pattern of abuse, but he must know whether the abuse is widespread. He must also know whether it is a passing fad, or whether it is a significant chronic abuse problem like heroin addiction. In reaching his decision, the Attorney General should consider the economics of regulation and enforcement attendant to such a decision. In addition, he should be aware of the social significance and impact of such a decision upon those people, especially the young, that would be affected by it.219

This clearly defines a cost/benefit analysis of the ramifications of scheduling decisions.

As demonstrated by the Monitoring the Future survey data discussed above in section 3, the current, prohibitive scheduling of marijuana has failed to create a closed system of distribution. Obviously, one impact of DEA's decision to maintain marijuana in schedule I has been the continued illegal and unregulated availability of marijuana in the nation's public and private high schools.

The social significance and impact of such a phenomenon is employed to justify continuation of prohibition, as discussed in section 4, however the legislative history insists that any possible benefits of prohibition (even moral benefits) be weighed against it social and economic costs.

This section will engage in a wider examination of a question raised in section 4: are the social costs correlated with marijuana use an indication of widespread abuse or an

indication of policy failure? Section 4 introduced three areas of social and economic costs--ready access to marijuana for school-age youths, a spiraling co-dependency between law enforcement and black market entrepreneurs, and an erosion of credibility for the nation's law enforcement and public health officials.

This section introduces six more areas of social and economic costs which the Controlled Substances Act mandates be reconciled with any possible benefits resultant from marijuana's schedule I status. These areas are as follows.

1) The absolute yet unenforceable schedule I prohibition contributes to an unfavorable set and setting accompanying school-age access and exposure to marijuana.

2) Adherence to the polarized and unscientific 'use = abuse' model obstructs the development of effective research based policy and drug-abuse prevention programs.

3) The absolute yet unenforceable schedule I prohibition creates tremendous ethical problems for physicians and health-care-providers, professionals well-aware of the widening gap between existing governmental policies and the developing support for marijuana's therapeutic potential in scientific and medical literature, and professionals who are seemingly instructed by law to discourage their patients from using marijuana even if such use has obvious therapeutic benefits.

4) The failure of the Department of Health and Human Services, and of the National Institute on Drug Abuse specifically, to address this widening breach between recent research about marijuana and the findings required to sustain marijuana's schedule I status unfairly and inappropriately makes our federal law enforcement officials, particularly officials of the Drug Enforcement Administration, appear to be heartless, self-serving idiots.

5) The federal failure to reconcile marijuana's schedule I status with contemporary medical and scientific evidence places an unfair and expensive burden on state criminal justice agencies and their limited budgets.
6) Marijuana's schedule I status and the high priority it places on domestic and international marijuana eradication has the unintended effect of transforming domestic law enforcement activity into a massive market and price support mechanism for entrepreneurs here and abroad.

Set and Setting:

One social cost is the impact this policy has on the young people exposed to marijuana. In 1984 Norman Zinberg of the Harvard Medical School argued that an assessment of drug abuse had to examine the individualized effects of Drug, Set and Setting. One assertion of Zinberg's was that drug abuse prevention efforts could learn a great deal from studying why many drug users do not have drug abuse problems.220 Interviews of marijuana and other drug users provided the data Zinberg used to develop his assertion, and he maintains that drug users develop sanctions and rituals to limit and guard against abuse. This is referred to as "controlled use." The illegality of many drugs has a dramatic influence over the scope, duration, and significance of marijuana use and abuse in the United States today. According to Zinberg, one unintended effect of marijuana prohibition of the 1970's and 1980's was as follows.

When parents, schools, and the media are all unable to inform neophytes about the controlled use of illicit drugs, that task falls squarely on the new user's peer group -- an inadequate substitute for cross-generation, long-term socialization. Since illicit drug use is a covert activity, newcomers are not presented with an array of using groups to choose, and association with controlled users is largely a matter of chance. Early in their using careers, many of our research subjects became involved either with groups whose members were not well schooled in controlled use or with groups in which compulsive use and risk-taking were the rules. Such subjects went through periods when drug use interfered with their ability to function, and they frequently experienced untoward drug effects. Eventually these subjects became controlled users, but only after they had realigned themselves with new companions -- a difficult and uncertain process.

Cultural opposition complicates the development of controlled use in another way: by inadvertently creating a black market in which the drugs being sold are of uncertain quality. With marihuana, variations in the content do not present a significant problem because dosage can be titrated and harmful adulterants are extremely rare; the most common negative effect of the black market economy is that the neophyte marihuana user pays more than he should for a poor product.221

Adolescents would be better served by a market that provided more control and regulation of adult marijuana use which also contributed to uniform social disapproval of teenage marijuana use, rather than perpetuate the existing policy which combines official disapproval with ample illegal access.

2) The effectiveness of the use = abuse model is now in question.

Zinberg's underlying assumption is that we can learn a lot about drug abuse by studying drug use. Of course, that requires accepting a distinction between the two. The Office of Technology Assessment of the U.S. Congress reported on emerging technologies for fighting substance abuse. One of these "technologies" is a different paradigm for studying drug abuse than that which currently drives policy, and one similar to Zinberg's position and that of other drug policy reformers. According to OTA, this emerging technology is called the "Public Health Model" for understanding abuse and addiction.

The legality or illegality of a drug is an artificial barrier that is not as relevant as the health-related considerations stemming from all types of drug use. Rather than using legal/illegal, the public health approach categorizes drugs by such characteristics as addictive potential and long-term health risks. . .Dealing with the drug problem primarily as a moral problem is considered inappropriate and counterproductive (as part of the public health model).222

The Office of Technology Assessment also notes movement towards Zinberg's advice to study drug use as well as drug abuse.

221 ibid. pg. 16.
What prevents some individuals from progressing from initial use to abuse to addiction? . . . Studying those individuals who do not progress from use to addiction may provide insights and lessons about how to prevent progression among those who do progress.223

This emerging trend has a name--harm reduction. In sharp contrast to existing policy, which self-consciously advocates increasing the consequences and harm of drug use, harm reduction policies pursue distinct obtainable objectives and are based on well-grounded analyses of scientific research and program experience. This trend will be examined in more detail in section 6 on the public health consequences of marijuana use. However it must be realized that harm reduction is not a new policy innovation.

The legislation creating the Controlled Substances Act also created a national commission to study marijuana and other drug abuse. The first report of this commission is well-known for recommending decriminalization of marijuana throughout the United States.224 The Commission issued a less-publicized second report a year later in 1973.225 Like Brady and Cicero 15 - 20 years later (see section 1), the Commission greatly objected to the unscientific and un-useful terminology employed to discuss public policy and drug-using behavior.

Drug abuse may refer to any type of a drug or chemical without regard to its pharmacologic actions. It is an eclectic concept having only one uniform connotation: societal disapproval.

The Commission believes that the term drug abuse must be deleted from official pronouncements and public policy dialogue. The term has no functional utility and has become no more than an arbitrary codeword for that drug use which is presently considered wrong. Continued use of this term, with its emotional overtones, will serve only to perpetuate confused public attitudes about drug-using behavior.

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223 ibid., pg. 75.
Drug abuse, or any similar term, creates an impression that all drug-using behavior falls into one of two clear-cut spheres: drug use which is good, safe, beneficial and without social consequence; and drug "abuse" which is bad, harmful, without benefit and carrying high social cost. From either a descriptive or an evaluative standpoint, the matter is much too complex to be handled in such a polarized fashion. The Commission urges that the public and its policy makers avoid such labels and focus instead on the relative risks and social consequences of various patterns of drug-taking behavior.226

Chapter One of the Commission's second report is one of the most lucid discussions on record in the last 25 years of the policy problems presented by prejudicial terminology. The Commission quite rightly predicted that a failure to distinguish between use and abuse in policy making and implementation would not help to reduce the various risks associated with different drugs and their use. The Commission endorses the cost/benefit analysis approach implicit in considering the scope of use in scheduling determinations.

In the Commission's view, problem definition should take into account the relationship between the maximum potential social cost of use of a particular drug under given conditions of availability, compared with the verified social costs at a particular point in time. In this context, the most serious concern in contemporary America should attach to the use of alcohol and heroin. Moderate social concern should attach to the use of amphetamines, barbiturates, hallucinogens, methaqualone and cocaine, the use of which is relatively well-controlled within the present time [1973]. Present trends do suggest, however, that the incidence of use of and dependence on barbiturates and cocaine may be increasing and may demand increased social attention.227

The Commission was influenced by the same scientific and extra-scientific theories and findings that resulted in the Controlled Substances Act which created it. This is not at all surprising. What is surprising is the increasing popularity of this analytical view among scientists twenty to twenty five years later.

226 ibid. pg. 13-14.
227 ibid. pg. 36.
In 1990 Joseph Brady was awarded the Nelson Eddy Lifetime Achievement award by the College on the Problems of Drug Dependence. In his acceptance speech, Brady directed his comments to the oddity this recognition posed--Brady is a behaviorist, and describes the CPDD as a "once exclusive opiod club" of pharmacologists. In what he describes as "the short answer" Brady describes the synergy between the two disciplines.

The short answer to the title question is that drugs interact in profound and broad-ranging ways with the transactions between individuals and their environment -- the unique domain of the behavioral sciences and the root subject matter of radical behaviorists. But let me reassure you about radical -- not to worry, neither violent nor terrorist proposals are in the offspring. Simply defined, radical means root and calls attention to an important difference between behaviorists, all of whom are not created equal. There are many, perhaps, most, whose interest in behavior is primarily methodological in the sense that what goes on at the interface between individuals and their environment is of concern primarily if not solely as a reflection of other activities of presumably greater import like central nervous system functions or so-called cognitive processes. Without denying these methodological claims to the territory, root behaviorists view the transactions as the interface between individual and environment as a legitimate subject matter in its own right and the source of an orderly and systematic body of empirical knowledge that does not require reduction to other levels of analysis or appeals to other levels of explanation.

It follows of course, that card-carrying root behaviorists tend to favor alternatives to the dominant "inner states" orientation of the "psych" disciplines. Among the most compatible of these alternatives is environmentalism which has two main tenets. The first of these is that knowledge comes from experience rather than from innate ideas, divine revelation, or other obscure sources. And the second is that action is governed by consequences rather than by instinct, will, beliefs, attitudes, or even the currently fashionable cognitions. These two constructs about the nature of human conduct -- the experimental basis of knowledge and the governance of action by consequences -- define a philosophy of social optimism that says if you want people to do certain things or to manage

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their lives in certain ways with respect for example, to drugs and alcohol, circumstances can be arranged. These two features of environmentalism also provide a productive framework for the analysis of drug-behavior interactions as well as an operational basis for the development of effective drug abuse treatment and prevention.229

It should be clear by now that self-administration of a drug indicates a situation in which the drug is having a stronger effect on the individual's behavior than mental disposition or environment. In therapeutic contexts, this is usually positive, whereas in some behavioral contexts this can be negative; this explains all the controversy over terminology. Language and theoretical choices indicate significance. The animal models used to evaluate a substance's dependence liability are part of a conceptual paradigm, developed by Brady and others, which holds that it is significant to separate the effects of the drug from the influence of set and setting. This is precisely what Norman Zinberg asserted was necessary for successful harm reduction policies.

In order to distinguish use from misuse, greater attention will have to be paid to how drugs are used (the conditions of use) than to the prevention of use. Researchers must study both the conditions under which dysfunctional use occurs and how these can be promulgated. The goal of prevention should not be entirely abandoned, but emphasis should be shifted from the prevention of all use to the prevention of dysfunctional use. When this new focus is adopted, policymakers may decide not to treat all intoxicating substances as if they were alike. Careful studies of the use of various kinds of drugs and of the varying conditions of use may reveal the need to create a different policy strategy for each type of drug.

To study the conditions of use for each drug will require consideration of the following topics: dosage, method of administration, pattern of use (including frequency), and social setting, as well as the pharmacology of the drug itself. Consider, for example, the question of frequency of use. It is only at the extremes that frequency is not necessarily related to the harmfulness of a drug, . . . A policy aimed solely (or mainly) at reducing frequency would not only mask the significant differences between the drugs themselves but would deny the importance of the social setting, including when, where, and with whom the drug is used. These social factors, which may vary across cultural and ethnic lines, combine with frequency and quantity of use to determine the quality of use. A policy aimed at encouraging a shift from those drugs that are

229 ibid. pg. 19-20.
generally considered to be the most harmful to those that on all counts are the least harmful (even though some may at present be illicit) would result in a considerable reduction of social cost.230

In 1994 OTA reported that

substantial U.S. ethnographic research on marijuana use in the United States has been generally lacking, despite the fact that marijuana has been the most commonly used illicit substance for decades.231

If ethnographic research existed, it would be the primary material for this section. However a policy based on marijuana's schedule I status holds that there is no use of marijuana to study; all use is misuse. Consequently, marijuana's schedule I status create obstacles to the development of effective research-based policy.

There is an extensive body of ethnographic material on marijuana's use as a therapeutic agent. Rather than recognize the valuable data such material presents, the U.S. government has been doing all it can to suppress marijuana's medical use and official study of the data that results from such use. The discussion below does not concern this ethnographic material, but the government's attempts to discredit it.

**DEA and the Therapeutic use of marijuana.**

Law, policy, history and circumstance have all contributed to the odd state of affairs in which the DEA maintains that unless they say so, marijuana use has no therapeutic benefits whatsoever, regardless of its observed effects on patients with various physical maladies.

A significant group of marijuana users affected by scheduling decisions are individuals who use marijuana for therapeutic purposes. Their use of marijuana underscores the importance of Zinberg's analytical perspective.

While the government has not acknowledged an accepted medical use for marijuana in the United States, significant numbers of citizens use marijuana as a

230 Zinberg, 1984 pg. 203-204.
231 OTA, 1994 pg. 124.
therapeutic agent at their own risk. The legislative history insists that the impact of scheduling decisions on these individuals also be considered in this rulemaking procedure, irrespective of findings regarding marijuana's medical use as a possible prescription substance. If marijuana does not have a significant dependence liability according to conventional medical standards, there is little justification for punishing medical use of marijuana by individuals on their own responsibility with criminal sanctions.

In 1993 Lester Grinspoon, also of the Harvard Medical School, published *Marihuana, the Forbidden Medicine* describing the illicit use of marijuana as a therapeutic agent. Among the patients who describe their therapeutic use of marijuana is Stephen Jay Gould, the widely respected expert on evolutionary biology and widely published on scientific topics and process.

In 1989 the Administrator of DEA rejected the recommendation of an Administrative Law Judge that marijuana be placed in schedule II because the substance had an accepted medical use in the United States and was safe for use under medical supervision. This decision was ultimately upheld by the U.S. Court of Appeals as within the Administrator's discretion.

In those proceedings, petitioners presented numerous affidavits and testimony regarding individuals' therapeutic use of marijuana. According to DEA this information has no value.

The evidence presented by the pro-marijuana parties regarding use of marijuana to treat various other ailments such as pain, decreased appetite, alcohol and drug addiction, epilepsy, atopic neurodermatitis, scleroderma and asthma was limited to testimony of individuals who had used marijuana for those conditions and the testimony of the psychiatrists.

233 54 FR 53,767 - 53,785.
234 Alliance for Cannabis Therapeutics v. Drug Enforcement Administration. 15 F3d 1131 (1994, App DC)
or general practice physicians mentioned earlier. There is not a shred of credible evidence to support any of their claims.235

Petitioners presented testimony of patients with multiple sclerosis whose use of marijuana allowed them to get up out of their wheelchairs and walk, when without the drug, they could not. According to DEA, these patients are suffering from drug-induced delusions.

Why do scientists consider stories from patients and their doctors to be unreliable? First, sick people are not objective scientific observers, especially when it comes to their own health. We have all heard of the placebo effect. Second, most of the stories come from people who took marijuana at the same time they took prescription drugs for their symptoms. Third, any mind-altering drug that produces euphoria can make a sick person think he feels better. Fourth, long-time abusers of marijuana are not immune to illness. Many eventually get cancer, glaucoma, MS and other diseases. People who become dependent on mind-altering drugs tend to rationalize their behavior. They invent excuses, which they can come to believe, to justify their drug dependence.236

The credibility of patient anecdotes depends on two corroborative factors. First, if marijuana does not have a significant dependence liability, then it does not have reinforcing effects that contribute to denial, which, as expressed by DEA, is when users "invent excuses, which they can come to believe, to justify their drug dependence." The primary assessment of a drug's ability to produce reinforcing effects is self-administration. As Cicero explains not all self-administration is harmful. Testimony of sufficient weight for an Administrative Law Judge to conclude that marijuana has an accepted medical use is of great relevance to the separate question of evaluating marijuana's abuse potential.

DEA argues that expert testimony from scientists should concern the field of the scientist's expertise.

In reviewing the weight to be given to an expert's opinion, the facts relied upon to reach that opinion and the credentials and the experience of the expert must be carefully examined. The experts presented by the pro-marijuana parties were unable to provide a strong scientific or factual basis to support their opinions. In addition, many of the experts presented by the pro-marijuana parties did not have any expertise in the area of research in the specific medical area being addressed.\textsuperscript{237}

A psychiatrist from the Harvard School of Medicine such as Dr. Lester Grinspoon is certainly qualified to evaluate the extent to which drug dependence has prejudiced a patient's account of the therapeutic use of marijuana. Consequently his recent book on marijuana's medical use is an expert's account of the incidence of non-abusive use of marijuana in the United States. Grinspoon's book and the full record of testimony in the case ultimately decided in \textit{ACT v. DEA} provide valuable evidence of the scope, duration and significance of marijuana's use as a therapeutic agent in the United States.

As this petition establishes, the dependence liability of marijuana is not a settled scientific issue; indeed this petition argues that there is substantial evidence that marijuana does not have a sufficient dependence liability to justify schedule I or II placement under United States law.

The second corroborative factor is the evidence provided by the discovery of the cannabinoid receptor system in the human brain, which provides a scientific explanation for the mechanisms of action behind marijuana's therapeutic effects. As described above by the pioneers of the cannabinoid revolution, research on cannabinoids is now focused on developing the considerable therapeutic potential of this system and cannabinoid drugs.

When Hollister prepared his 1986 paper for the \textit{Pharmacological Reviews}, he also reviewed the issue of marijuana's therapeutic use. As cited above, he concluded that marijuana may prove to have greater therapeutic potential than other social drugs. In this passage, he elaborates on the therapeutic potential of marijuana.

Therapeutic uses for marijuana, THC, or cannabinoid homologs are being actively explored. Only the synthetic homolog, nabilone, has been approved for use to control nausea and vomiting associated with cancer chemotherapy. While little doubt remains that marijuana, THC, and nabilone are effective for this use, the advent of other drugs that are equally effective but with fewer adverse effects may make this use moot. Use of marijuana to reduce intraocular pressure in patients with glaucoma requires a feasible topical preparation of cannabinoids. Although some cannabinoids have analgesic activity, the abundance of new opioid analgesics with little dependence liability provides tough competition. The use of marijuana as a muscle relaxant, though promising, has not yet been studied. Clinical studies to establish the efficacy of cannabidiol as an anticonvulsant or to compare it with other anticonvulsants are still to be done. Other therapeutic uses, such as treatment of bronchitis, migraine, anorexia, and alcoholism, are most unlikely prospects.²³⁸

Hollister once served as the chairman of the Drug Evaluation Committee of the CPDD. In this 1986 passage he refers to "competition" between marijuana and other analgesics. Hollister states that there is "little doubt" that marijuana is effective as an anti-nausea agent. He refers to ongoing research on cannabidiol, one of the non-psychoactive constituent chemicals, regarding convulsions.²³⁹ These comments establish that it is an underlying assumption of contemporary research that marijuana has therapeutic benefits, regardless of whether or not it has a legally defined "accepted medical use in the United States."

Also in 1986, Raphael Mechoulam, in an interview with the International Journal of the Addictions, also confirms that marijuana has therapeutic potential.

In summary, THC or cannabis may have important effects in the areas of pain control, as antiasthmatics, to treat glaucoma, and as part of cancer treatment as an antiemetic during chemotherapy. All these are important activities. Unfortunately, not much work is being done, certainly not when one compares it with what needs to be done...

Knowing what I know today, I would have worked more on the therapeutic aspects of cannabis. This area apparently needs a major push

²³⁸ Hollister, (1986) pg. 17.
that it has not had up 'till now, particularly given that it has therapeutic potential. One of the reasons that it has not been pushed was that most pharmaceutical companies years ago were afraid to go into that field. Companies were "burnt" working on amphetamines and LSD.240

The 1990 article by Miles Herkenham, Allison Lynn and colleagues on the "Cannabinoid receptor localization in brain" also verifies that the therapeutic potential of marijuana is a fundamental assumption supporting modern cannabinoid research, and begins to provide a basis for understanding how this potential is realized.

There are virtually no reports of fatal cannabis overdose in humans. The safety reflects the paucity of receptors in medullary nuclei that mediate respiratory and cardiovascular functions.

Anticonvulsant and antiemetic effects of cannabinoids have therapeutic value. The localization of cannabinoid receptors in motor areas suggests additional therapeutic applications. Cannabinoids exacerbate hypokinesia in Parkinson disease but are beneficial for some forms of dystonia, tremor, and spasticity.241

In a 1992 article published in the *Annals of the New York Academy of Sciences*, Herkenham made additional comments.

The localization of cannabinoid receptors in motor areas suggests therapeutic applications. Cannabinoids exacerbate hypokinesia in Parkinson's disease but are beneficial for some forms of dystonia, tremor, and spasticity. The association of cannabinoid receptors with GABAergic striatal projection neurons suggests roles for cannabinoids in control of movement, perhaps therapeutic roles in hyperkinesia and dystonia. Cannabinoids have been shown to be beneficial for some forms of dystonia and spasticity. . . Further work may show the basis for reported usefulness in controlling nausea and stimulating appetite in patients receiving chemotherapy for cancer or AIDS.242

Abood and Martin confirm that:

There have been reports to indicate that the cannabinoids may be effective in treating pain, convulsions, glaucoma, muscle spasticity,

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bronchial asthma, nausea and vomiting. These disorders are currently treated with drugs that are structurally distinct from cannabinoids . . . Obviously, new strategies are crucial for treating patients who are unresponsive to current therapy or suffer severe side-effects.243

Martin and Abood express concern about the use of marijuana by individuals with already compromised immune systems. They note "the lack of conclusive evidence" of any adverse effect on the immune system, but express concern that findings from experimental research could be a source of alarm. Abood and Martin's concern should be balanced by the statements of Herkenham above, and the explicit comments on marijuana's effect on the immune system by Lynn and Herkenham above.

Further evidence that the therapeutic potential of marijuana is a fundamental assumption supporting contemporary research can be found in the newsletter of the National Institute on Drug Abuse, NIDA Notes. In an article discussing the discovery of "Marijuana's Natural Counterpart", the author points out that:

Other NIDA-funded researchers are uncovering what appear to be other naturally occurring compounds that act like marijuana. Investigators believe that they will be able to show that these compounds help the body cope with stress, pain, and nausea.244

Certainly when these scientists refer to therapeutic potential they mean that useful drugs can be developed from the study of marijuana. However their comments have additional value in that they verify that marijuana has therapeutic mechanisms of action. It is these mechanisms which scientists seek to better understand in order to unlock the pharmaceutical drug making potential of the cannabinoid family of chemicals.

Regardless of the status of scientific knowledge about the action of marijuana on these therapeutic mechanisms, science has proved that these mechanisms actually exist. They are not figments of the dependence-produced craving of marijuana users experiencing serious organic illnesses.

243 Abood and Martin (1992) pg. 205.
Once again, regarding reports from marijuana users of medical benefits DEA maintains that "there is not a shred of credible evidence to support any of their claims." There is in fact substantial evidence to support their claims, as the above comments from professional pharmacological and medical journals indicate.

Policymakers have a legal obligation to consider the impact of prohibitive scheduling of marijuana on individuals who use the drug for its therapeutic potential at their own risk. Prohibitive scheduling calls for the criminal prosecution of patients who grow marijuana for personal medical use for the crime of manufacturing a controlled substance. Instead of arresting medical marijuana patients, their medical use of marijuana should be studied by the medical community to aid researchers in developing effective cannabinoid therapeutic agents.

**Burden on State and Local Governments**

During the 1980's mandatory/minimum sentences for distribution of schedule I drugs, including marijuana, were reinstated by the Congress.

Most drug possession offenses end up in the local courts, primarily county or city courts. However, the volume of drug cases in the federal courts has been increasing, and this increases the economic costs to the criminal justice system produced by marijuana's schedule I status. This scheduling status requires that state and local authorities give marijuana use, sale, and cultivation equal enforcement status with other schedule I and II drugs, such as heroin and cocaine. At the federal level the significance of devoting resources to the ongoing prosecution of marijuana-related offenses amidst increasing demands on the criminal justice system must be rationally addressed by the executive branch in accordance with this aspect of the legislative history of the Controlled Substances Act.

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Drug cases not only consume resources, they also divert them. For example, the federal courts must give preferential scheduling to criminal over civil cases. Consequently, the increasing caseload of drug filings inhibits, if not paralyzes, the courts' ability to handle civil matters in anything resembling a timely fashion.

While there is much to study about the effect on the courts of drug cases in general, the savings attributed to decriminalizing marijuana possession cases in California has been studied. A history of California's marijuana laws and its enactment of decriminalization notes what prompted consideration of this now longstanding policy.

As California entered the 1970's, it was clear that marijuana law enforcement had become an immense legal and social problem in the state. For the first time, policymakers began to seriously question the underpinnings of the prohibition-based public policy toward marijuana.246

The following data was compiled in a successful attempt to preserve California's policy of issuing a fine of $100 for marijuana possession.247,248:

In 1974 one fourth of all the adult felony arrests in California were for marijuana. Huge jumps in the number of felony marijuana arrests since the mid-1960's caused a logjam of felony marijuana cases in the courts, over 38,000 in 1975. In 1969 the legislature responded to the increasing case loads by throwing marijuana cases into the lower courts, then as they filled up in the 1970's they tried to ease the pressure with programs to divert offenders into treatment programs. Rather than decriminalize completely, the Moscone Act (creating a $100 fine for possession of one ounce or less) kept marijuana as a criminal offense but out of the courts. The number of marijuana cases were down to less than 8000 in 1978.

In 1985, 40,761 citations were issued in California, producing over $4 million in fines. It would have cost $2875 each to arrest and try those offenders. It is estimated that the Moscone Act has saved California $100 million annually since its enactment.

These are the estimated savings for the period 1976-1985: $464 million in arrest costs, $441 million in court costs, $38 million in prison costs, and $14 million in parole costs.249

A proposal to recriminalize marijuana in California by providing an alternative six month prison sentence and/or a $500 fine would have increased court costs six times what they were for California in 1985 when the proposal was made.

These figures illustrate the burden marijuana's present restrictive scheduling places on the criminal justice systems of individual states. All states must enforce marijuana cultivation laws.

**Federal Marijuana Eradication Efforts and Their Influence on Marijuana Cultivation.**

A cost/benefit analysis of law enforcement resources applied to enforcing laws related to marijuana's schedule I status must include a review of the DEA Domestic Cannabis Eradication/Suppression Program. DEA and other government reports suggest that domestic marijuana cultivation can neither be eradicated nor suppressed.

The DEA has misrepresented the significance of the number of cannabis plants they have eradicated, the potency and profit potential for the average marijuana plant, the effect of their program on the price of marijuana, and the extent of their success in affecting the availability of marijuana.250

The DEA has claimed that their program has substantially increased the price of marijuana over the years, when actually most of the increases are attributable to inflation.

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249 ibid. pg. 79.
250 Gettman, J. *Cannabis Suppression and Marijuana Crop Value.* (Washington, D.C.: NORML.) 1993. Most of the material in this part of section 5 has been excerpted from this 1993 NORML report, with the permission of the author.
Throughout this time period the DEA's actions have encouraged more decentralized cultivation, with fewer plants grown on increasingly more plots. The DEA's actions have also led to a tremendous growth in the number of people who grow marijuana indoors, under lights.

The DEA has not been content to let state police and courts handle marijuana cultivation problems, and has given federalizing marijuana cultivation prosecutions and investigations a great amount of consideration.

The DEA claims about the seriousness of the marijuana problem have been used to involve the National Guard and the military in eradication efforts. The National Guard is quite straight-forward about how the law allows them to get around historical traditions and laws which keep the military out of domestic law enforcement.

Throughout this period the DEA constructed their own annual estimates of marijuana production in the United States based on assumptions of plant quality, yield per plant, and seizure success estimates.

Marijuana remains the nation's number one cash crop. Throughout the last eleven years the DEA has not been able to reduce the value, and therefore the market incentive to grow, marijuana. In fact, the DEA has often stated that rising prices for marijuana is a sign their program is working.

The DEA's war against domestic marijuana cultivation is a failure. Domestic cultivators have increased, proliferated and prospered since the program's inception.

In 1982, the DEA made this startling discovery: The strategic intelligence estimate for 1981 domestic marihuana production was 1200 metric tons. Therefore, the program shows that:

in 1982, 38% more domestic marihuana was eradicated than was previously believed to exist. Although a total U.S. marihuana production figure is not easily determined, the statistics obtained from this program
reveal, without doubt, that the United States is becoming a major source for the drug.251

By their own standards, the program is a dismal failure.

In 1982 the goal of the eradication program strategy was:

   to deter both commercial sinsemilla or high grade marihuana cultivation and to suppress the proliferation of that cultivation in areas which have not yet developed a large or sophisticated growing or marketing capability.252

DEA documents show that marijuana cultivation, in fact, proliferated widely throughout the United States, often in response to the DEA's program itself. For example, compare the statement above with this statement from 1992:

   Domestically grown marijuana accounted for 10% of all marijuana in 1980 this has increased to 25% in 1992, with a production estimate of 4500 - 5300 metric tons.253

   By the DEA's own estimates, domestic marijuana production has increased four-fold between 1982 and 1992.

And this from 1990:

   A large measure of the U.S. marijuana market will be captured by domestic growers, individual entrepreneurs and well-organized, multi-state cooperatives. Sinsemilla . . . will dominate the domestic market. Indoor and public land cultivation are the most common methods of cannabis production. Domestic cultivation may account for as much as 50% of the U.S. market by 1995.254

Eradication and the Price of Marijuana.

The DEA claims that the increase in the price of marijuana over the years is an indication of the success of their program to discourage marijuana cultivation and use. For example:

The results of this program in 1992 have been impressive and are reflected dramatically by the soaring price of marijuana in the United States. 255

255 DEA, 1993, pg. iii.
Marijuana Prices Per Pound 1982 - 1992

The DEA brags about raising the price of marijuana. Yet Sinsemilla cost $2000 a pound in 1981. In a 1990 report price for Sinsemilla at $3000. Correcting for inflation, in 1982 dollars that 1990 pound only cost $2,086, a real increase of the Domestic Cannabis Eradication program is a price support program. The value of marijuana comes from its relative content within the price supported by DEA eradication.

Reports of Domestic Marijuana Prices:

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<td>$2,417</td>
<td>$2,520</td>
<td>$2,610</td>
<td>$2,675</td>
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<td>High Times</td>
<td>$2,220</td>
<td>$2,435</td>
<td>$2,275</td>
<td>$1,685</td>
<td>$1,735</td>
<td>$1,805</td>
<td>$1,950</td>
<td>$1,915</td>
<td>$2,060</td>
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<tr>
<td>DEA I (combined index)</td>
<td>$830</td>
<td>$1,057</td>
<td>$1,248</td>
<td>$1,982</td>
<td>$1,425</td>
<td>$1,476</td>
<td>$1,935</td>
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<tr>
<td>DEA II (top prices)</td>
<td>$2,300</td>
<td>$3,500</td>
<td>$3,000</td>
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<tr>
<td>NNICC I (top prices - sinsemilla)</td>
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<td>$2,100</td>
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<td>$4,100</td>
<td>$6,000</td>
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<td>NNICC II (top prices - commercial)</td>
<td>$600</td>
<td>$700</td>
<td>$1,450</td>
<td>$1,800</td>
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About the Sources for the Price Indexes:

**Baseline:** This index reflects the growth in the price of marijuana due to the rate of inflation. The price of $2000/lb of Sinsemilla was widely reported in the newspapers in 1981. These baseline prices were calculated by raising that price by the inflation rate for each subsequent year.

**High Times Magazine:** Readers of this magazine send in price reports for marijuana along with descriptions. Multiple price quotes (for different quantities of the same product) allow the derivation of formulas to convert price quotes for smaller quantities into comparable quotes for a one pound quantity. Quotes used were for domestic marijuana, and taken from the period of July through December for each year.

**DEA I:** DEA reports on their eradication program provide ranges for the price of both commercial grade marijuana and Sinsemilla grade, and data which allows an estimate of the ratio of the two grades. A composite index was created by midpoints of the price ranges and weighting accordingly.

**DEA II:** These figures are the extreme figures quoted by DEA to represent the top prices commanded by the grade domestic marijuana, usually grown in California, Hawaii.

**NNICC I:** These figures are the high end of the price for Sinsemilla quoted by NNICC, the government group responsible for maintaining drug supply data.

**NNICC II:** These figures are the high end of the price for Commercial grade marijuana quoted by NNICC, the government group responsible for maintaining drug supply data.

Marijuana cost more in 1992 than it did in 1982, but so did most consumer goods. Using the *New York Times* report for 1981 as a baseline, and using the consumer price index to adjust for inflation each year, the sinsemilla that was $2000 a pound in 1981 would be $3300 a pound in 1992 dollars. Yet the DEA never considers inflation in their reports; they report inflationary increases in the price of marijuana as proof of their own effectiveness.

This claim was especially acute in 1986:

Prices, with few exceptions, however, had doubled over those of 1985 . . .

Heretofore, the availability of domestic marijuana supplies may have offset the "dry spell" created by the seasonal fluctuation of imported marijuana. With the expansion of the U.S. eradication program, and its continued overall effectiveness nationwide, this "dry spell" may have been prolonged this year. . . Indications are the lessened availability of marijuana is of a temporary nature and will be alleviated as foreign crops are harvested and smuggled into this country. 257

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257 ibid., pg. 25.
It should be noted that price increase may not be only due to lessened availability but also to the preference by growers to specialize in Sinsemilla.\textsuperscript{258}

In 1987, though, availability improved while prices remained steady.

In contrast to the 14 Divisional Offices which noted diminished availability of marijuana in the 4th quarter of 1986, only one DEA Divisional office noted diminished supply of marijuana for the same time period in CY 1987.\textsuperscript{259}

Even so, the suppression program was still considered to be a major factor:

Generally, in those states in which supplies were reported as diminished, the situation appeared to reflect a localized occurrence. That is to say, there appeared to be either (1) a lack of established foreign cannabis distribution networks within specific areas, (2) an effective domestic cannabis eradication and suppression program which impacted on availability within those states, and/or (3) geographic and climatic constraints within the state which inhibited production.\textsuperscript{260}

Marijuana has remained widely available throughout the period of this program, and domestic cultivation has continued to increase. There is a connection between THC content and market value, and the DEA activities have encouraged more growers to produce more potent marijuana. For example:

Although marijuana appeared to be more readily available at a national level in CY 1987, prices remain high for domestic commercial marijuana.\textsuperscript{261}

Prices have remained high because the DEA has annually supported a high marijuana price by removing large amounts of the crop from the market.

The chart above compares various price indexes with the baseline established by the 1981 \textit{New York Times} quote and inflation. It is hard to support claims that the price of marijuana has increased dramatically throughout the 1980's. One index is derived

\textsuperscript{258} ibid., pg. 24.
\textsuperscript{260} ibid., pg. 21.
\textsuperscript{261} ibid., pg. 21.
from reports of marijuana consumers directly to *High Times* magazine. This data suggests that when adjusted for inflation, the price of marijuana stabilized and dropped in the late 1980's, only to rise again recently.

The volatility of the price of any agricultural commodity is the basis for the complex trade in agricultural futures. This is a formidable testament to continuing fluctuations in commodity prices. 

**Effects of Eradication Program on Cultivation Trends and General Availability**

In the 1970's marijuana bound for the American market was grown extensively in vast fields overseas and imported. By the 1980's, much of the marijuana consumed in the United States was grown intensively, in small plots, and much of it was grown in the United States itself. The utilization of intensive agricultural techniques is as old as antiquity, and is one of the technologies which made civilization possible.

One factor encouraging this trend was the 1978 use in Mexico of the herbicide paraquat, and fear among consumers in the United States that the undetectable paraquat might poison them. On account of this fear, and diffusion of knowledge about cultivation, by 1978 domestic marijuana cultivation in the United States had become a problem.262

The DEA and marijuana growers are locked in an unending game of cat and mouse. At first marijuana was grown in a few states on private land. The government came in with paramilitary operations, and the cultivation diffused, all over the country. The paramilitary campaigns followed. The growers began cultivation of more potent plants to increase profitability per plant, and in smaller plots to avoid detection. Intensive cultivation began to replace extensive cultivation. When Congress enacted forfeiture statutes, growers moved to public land. As paramilitary eradication efforts increased, growers moved indoors. All commentators within and external to the government agree

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that the dominant trend in marijuana cultivation in response to the DEA’s program has been the promotion, decentralization and atomization of marijuana cultivation in the United States.

To repeat, In 1982 the goal of the eradication program strategy was:

   to deter both commercial sinsemilla or high grade marihuana cultivation and to suppress the proliferation of that cultivation in areas which have not yet developed a large or sophisticated growing or marketing capability.263

This is reiterated again in 1985.

The goals of the program are: to suppress cultivation in established areas, to deter cultivation in potential growing areas, and to minimize product availability through crop destruction.264

Recent analysis by the DEA suggests that marijuana cultivation is well-rooted in American culture, and continuing to grow.

A large measure of the U.S. marijuana market will be captured by domestic growers, individual entrepreneurs and well-organized, multi-state cooperatives. Sinsemilla . . . will dominate the domestic market. Indoor and public land cultivation are the most common methods of cannabis production. Domestic cultivation may account for as much as 50% of the U.S. market by 1995.265

The DEA realized as early as 1982 the extent of their influence on marijuana cultivation. They knew that eradication efforts encouraged growers to maximize their efforts and preserve their investment. Knowledge is a form of technology, and Sinsemilla was the technology that enabled growers to keep ahead of the DEA. "This resulted in marihuana of greater potency and higher value, thus providing a compelling incentive to the grower."266

263 DEA 1983, pg. 1.
265 DEA 1991a, pg. 32.
266 DEA 1983, pg. 1.
Hawaii, California, Oregon and Washington became the agricultural trendsetters for the marijuana boom.

(In California, Washington and Oregon) cultivators strive for a high quality product in small remote plots to avoid detection. Other states average larger plots. These may become smaller in subsequent seasons with increased law enforcement activity . . . (in) Hawaii . . . the plants tend to be scattered through the jungle, rather than in defined plots.267

As early as 1983 the DEA realized not only that marijuana cultivation was a nationwide problem, but that their efforts were having the same effect nationwide as they were having in the Pacific area.

Large seizures should not . . . be considered a trend involving the plot size of domestic cultivation. To the contrary, a definite trend involving the shift towards smaller cultivated plots was again noted during 1983. . . . This shift is viewed as a further attempt to deter aerial detection as eradication pressures increase.268

Also in 1983, the DEA realized that eventually growers would go so far to escape detection as to move indoors. "Further increases in the utilization of greenhouses are anticipated as producers seek new means to deter detection."269

Indoor marijuana cultivation had other advantages than security. Indoor cultivation can decrease the time required to produce flowering tops for market.

In a hydroponic operation cannabis seedlings are transplanted into plastic pipes through which a solution of water and fertilizer flows. The plants are nourished by the solution and are subjected to artificial lighting 24 hours a day thereby maturing into eight to ten foot plants in less time than conventional open field operations.270

These decentralizing trends toward smaller plot size and indoor cultivation continued noticeably through 1984 and 1985.

267 ibid., pg. 4.
269 ibid., pg. 4.
270 ibid., pg. 5.
In 1984, the median plot size was computed to be 128 plants per plot. This shows a continuing trend toward smaller cultivated plots.271

Indoor growing operations accounted for an increased number of sightings and destructions in 22 states in 1984. Standard greenhouses, as well as converted residences, barns, basements, and attics were encountered.272

By 1985 the median plot size had dropped to 100 plants per plot, and indoor sightings increased in 26 states.273

Before Congress established the Office of National Drug Control Policy, the Reagan Administration coordinated drug policy through the National Drug Enforcement Policy Board (NDEPB). Their 1984/85 report indicates awareness of another aspect of focusing on marijuana interdiction and eradication.

The continuous, concerted effort to attack marijuana smuggling, a key element of the drug smuggling problem, has had considerable impact. Decreases in the amounts of marijuana seized and other indications show that interdiction efforts have made it more difficult for the marijuana smuggler to conduct business.274

By effectively bottling up and diminishing the competition from the Colombian marijuana crop in 1984, the government further contributed to a bull market for domestically grown marijuana. Unfortunately, many of the international smugglers were given market incentives to switch from marijuana to cocaine. "Compared with marijuana, the high value, low volume nature of cocaine often makes interdiction difficult."275


272 ibid., pg. 6.

273 DEA. 1986.


275 NDEPB 1986a, pg. 144.
Another effect of eradication efforts that was apparent by the mid 1980's was that the DEA programs were removing the amateurs and casual growers from the market, leaving it to more hard-core and/or experienced elements.

The NDEPB ordered a staff report on the Cannabis Problem in 1986. One of the problems they reported was that after several years of eradication and suppression activity, the market provided "a stronger product at a lower price per milligram of THC".276

The inevitable trend toward indoor cultivation was confirmed.

Although the extent of indoor cultivation is not known, the technical advantages, combined with continuing law enforcement pressure on outdoor plots, appear to have accelerated the trend toward indoor growing.277

The trend toward indoor growing appears to be gathering momentum.278

The DEA has always tried to portray marijuana growers as violent and dangerous, often conjuring images of extensive booby-traps and/or the classic image of the moonshiner protecting his still with a shotgun. However the NDEPB observed otherwise:

violence . . . directly conflicts with most growers' political agenda of building popular support for legalizing the cultivation and consumption of marijuana.279

The major trend is capitalization, attracted by the high price/crop removal/protectionist policies of the federal government. Fortunately this came from urban capitalists rather than organized crime.

A convicted grower interviewed by NDEPB staff reported that the biggest change in the last five years has been the influx of urban money
into rural cultivation operations. . . there appears to be little or no traditional organized crime (La Cosa Nostra) in domestic cannabis production.  

Another trend acknowledged by the NDEPB was that the Americans were beginning to make a strong dent in the competition's share of the American market. "In an effort to reverse this trend, foreign growers appear to have made a decision to upgrade the quality of their product." In 1989 the National Narcotics Intelligence Consumers Committee (NNICC) increased their estimate of the amount of marijuana grown in Mexico nearly nine-fold on account of "improved estimation methodologies and a review of cultivation areas that had not been included in previous years." In other words, marijuana cultivation was booming in Mexico between 1985 and 1989.

The NDEPB report devoted considerable attention to describing who these domestic growers are. They distinguish between commercial and personal use growers, with each category having amateurs, journeyman, and horticulturalists. The NDEPB cites an estimate derived at by the DEA, the IRS, and the GAO estimating that as of 1985 the country had 90 - 150,000 commercial marijuana growers, and that personal use growers probably exceed one million.

The result of the various trends instigated by the eradication program was a very decentralized, well capitalized and diffuse marijuana production capability to meet demand for high quality, domestically grown marijuana. According to the NDEPB:

The best indication of how these basic needs (to avoid detection and produce a high quality product) will be met are the scope and management structure of the illegal operation. Small plots generally need little more than a network of friends for advice and distribution. In many areas, friendship networks have become formalized as cooperatives. Labor, costs, profits and, in some cases, losses are shared. In areas of

280 ibid., pg. iv.
281 ibid., pg. 7.
283 NDEPB 1986b, pg. 17.
284 ibid., pg. 24.
extensive eradication efforts, losses by individual growers are absorbed partially by these organizations. Nearly two/thirds of the growers are "small-time independents."285

In perhaps the most succinct description of why eradication efforts are not successful, the NDEPB observes that: "commercial growers are well-motivated to adapt to changes in tactics."286

The DEA began to comment extensively on this point in 1987. They report on the still continuing trend of decreasing plot size, and cite a magazine popular with growers, *Sinsemilla Tips*, to the extent that this change of tactics has preserved harvestable crops for many growers.287

Other efforts to avoid detection were described.

The employment and sophistication of camouflage techniques to avoid detection were again noted in almost all states surveyed. Camouflage techniques ranged from the standard intercropping of cannabis plants among existing vegetation to such unique practices as hoisting potted plants up to the center of trees in what are termed "tree plots."288

By 1989 the DEA had changed its tune. Ignoring their own role in the diffusion of marijuana cultivation in the United States, the DEA put a new spin on the issue. At this point, technological developments had enabled the U.S. to become a major source of marijuana, and the indoor marijuana cultivation becomes portrayed as the symbolic root of the problem.

For example, here is how the DEA describes the changes in the marijuana market during the period described above:

Prior to the late 1970's, domestic cultivated marijuana was considered inferior to Mexican or Colombian grown marijuana . . . U.S. growers experimented with seeds from various countries and improved

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285 ibid., pg. 24/25.
286 ibid., pg. 48.
288 ibid., pg. 22.
horticultural techniques which resulted in the development of high grade domestic marijuana. The most significant discovery ...produced a stronger marijuana known as "sinsemilla."\(^{289}\)

The emerging party-line is reflected in these comments:

During 1987, indoor cannabis cultivation emerged as a significant and increasing problem. During 1988, DEA developed ..."Operation Green Merchant" to address covert indoor cannabis cultivation.\(^{290}\)

The trend for the last several years is the increased seizure of indoor operations.\(^{291}\)

DEA proudly reports a 65 percent reduction in marijuana cultivation in Colombia in 1989. ...due to this increase, the United States has emerged as the second leading producer of marijuana in the world behind Mexico.\(^{292}\)

An estimated 25 percent of the marijuana consumed in the United States is produced domestically. Indoor growing of cannabis is escalating both in the number of operations and in the quantity and quality of plants cultivated.\(^{293}\)

By 1990 the DEA was implying that outdoor marijuana cultivation was under control, and that now all the action was going after indoor grow rooms. Once again indoor cultivation is held up as the dominant trend.

High yielding, potent, hydroponic cultivations are becoming very popular among illicit entrepreneurs because the profit margin is lucrative. Sinsemilla buds sells for up to $3000 per pound. One hundred marijuana plants can produce a profit of over $250,000 per harvest. Many of these plants yield several crops a year. Modern cultivation methods produce a potent plant which averages 8 percent tetrahydrocannabinol (THC) as compared to 1-2 percent in the 1970's. The THC content of some sinsemilla plants is as high as 19 percent.\(^{294}\)

The 1990 DEA report also contains the frank acknowledgment that marijuana's staying power is world-wide. "Worldwide consumption will steadily increase causing a


\(^{290}\) ibid., pg. 1.

\(^{291}\) ibid., pg. 4.

\(^{292}\) ibid., pg. 4.

\(^{293}\) ibid., pg. 22.

global upswing of cannabis production. Therefore, foreign-source threats cannot be ignored."295

By 1990, the program to eradicate and suppress marijuana cultivation had acquired law enforcement powers and capability unprecedented in the history of the United States, which will be reviewed below. Despite this accumulation of power, the DEA, by this time, was owing up to the realization that marijuana would be a fact of life in the United States for a long time to come. As cited earlier, the DEA was not forecasting victory in this war anytime soon.

A large measure of the U.S. marijuana market will be captured by domestic growers, individual entrepreneurs and well-organized, multi-state cooperatives. Sinsemilla . . . will dominate the domestic market. Indoor and public land cultivation are the most common methods of cannabis production. Domestic cultivation may account for as much as 50% of the U.S. market by 1995.296

In an echo of the observed trend to smaller plots in the mid 1980's, the 1991 DEA report observes that: "The successful crackdown of DEA's eradication efforts is driving cultivators to public lands, smaller plots, and indoor grow operations."297

The reiterate their new priority of investigating indoor grow operations, showing great skill in capitalizing on a trend they helped to start.

The decrease in availability of foreign source cannabis and the high demand for sinsemilla quality marijuana are indicators that indoor cultivation of cannabis in the preferred method. Statistics for the past three years show that indoor marijuana seizures have increased at a rate of 20% per year, a trend that is likely to continue.298

Despite their 1982 goal of preventing the proliferation of marijuana cultivation, the DEA acknowledges in 1992 that "Domestically grown marijuana accounted for 10%
of all marijuana in 1980 this has increased to 25% in 1992, with a production estimate of 4500 - 5300 metric tons. "299 And, to no one's surprise by now, the DEA also points out that "Mexican growers are adapting new growing methods to produce a higher potency drug to compete in the American market."300

This comment from the 1992 report sums up the whole program.

The program, includes all 50 states and is constantly evolving to counter the illegal drug growers efforts. We're changing from the initial "Whack and Stack" operations, to sophisticated interstate cooperative criminal investigations. Marijuana farmers have become more and more resourceful and mobile, and so have we.301

The cannabis eradication/suppression program represents lifetime employment for agents of the Drug Enforcement Administration and other law enforcement officials.

Federalization of Marijuana Cultivation Offenses

The domestic cannabis eradication suppression program has been used by the federal government to usurp state criminal justice systems. In 1983, it was rare to make a federal case out of a marijuana cultivation incident.

Almost all the arrests were prosecuted at the state level with the exception of eight cases, which due to the size of the cultivation or significance of violator, were prosecuted in federal court. . . Of the subjects sentenced, all but one was sentenced to time in prison, with one individual receiving an eight year prison term.302

By 1984, this had begun to change.

More cases were prosecuted in the Federal Court system than reported in previous years. The increase in total prosecutions at both state/local and Federal levels seems to be attributable to the increase in the capabilities of state and local agencies to expend more time in the investigative phases of incidents of cultivation.303

300 ibid., pg. 1.
301 ibid., pg. 2.
302 DEA 1984, pg. 5.
303 DEA 1985, pg. 6.
The exact same comment is included in the 1985 DEA report. Interestingly
the report dwells on the increase in prosecutions, not the trend towards federal over state
prosecution. The 1986 NDEPB review reports on a local backlash to the DEA program
which had been developing among local residents. The eradication activity polarized
many areas, and drove away business and tourists. In California, the annual eradication
program "is viewed by many residents as an annual trauma." The report noted that 23% of the public favored legalizing marijuana, and that the
public generally frowns on locking up marijuana users. It was believed that the general
public held that cocaine presented a more serious problem than marijuana, and that the
courts were too crowded to handle marijuana cases. "Most respondents believed that if
the federal government withdrew its support, state and local operations would shrink to
token levels."

The report describes some of the unintended results of eradication activity. For
example: "In a bizarre case in Hawaii, the . . . helicopter flew so close to a rabbit farm
that the noise caused a panic and fighting among its inhabitants. More than 7000 bunnies
died in this incident." Another problem is that the heavy-handed nature of their
paramilitary operations created bad press and damaging political fallout. "CAMP [the
California program] has unintentionally increased the visibility of pro-legalization
arguments and their sponsors because of the extended debate over costs and tactics."

This review of cannabis eradication efforts listed four reasons why they haven't
worked:

1) Law enforcement agencies feud and compete.

304 DEA 1986, pg. 5.
305 NDEPB 1986b, pg. 41.
306 ibid., pg. 34.
307 ibid., pg. 41.
308 ibid., pg. 42.
2) They aren't being hard enough on offenders. Although the Program is frequently referred to as the 'Eradication' Program, the word 'Suppression' in the title is of equal importance. The goal of the program is to deter the cultivation of cannabis in the United States.

3) Sentences are too light, there is a lack of federal prosecutions, and light sentences are doled out in local prosecutions.

4) "Anti-federal sentiment is often high in rural southern and western states. Since many communities consider growers an economic benefit to the area, there is little enthusiasm for prosecution."309

Furthermore, the report argues, it is unrealistic to pursue full enforcement of marijuana cultivation laws.

The limits of law enforcement are set by practical realities and public support. It is simply not feasible to investigate and establish the ownership of the 40,000 plots eradicated last year. Seizing eight houses on a block of ten for growing a few plants in the backyard is feasible but imprudent. Federal drug efforts must remain sensitive to public opinion. Pro-drug organizations have demonstrated their ability to use the media and would certainly exploit efforts that might appear disproportionate to the situation. Effective law enforcement in any area requires the good will of the people.310

The DEA, though, remained insensitive to public opinion and proceeded full steam ahead with prosecutions and property seizures. In 1988 the DEA began to advocate stiffer sentences for marijuana cultivation.

The overall 1988 Domestic Eradication Program was a success. In 1989, the program will strive for increased follow-up investigations and increased asset seizures. Additionally, DEA will strive for an increase in federal prosecutions of cultivators under the new federal minimum mandatory sentence provisions.311

309 NDEPB 1986b
310 ibid., pg. 51.
The DEA had come to the conclusion that they weren't going to get convictions or deterrent sentences in state and local courts.

Most arrests and prosecutions for marijuana cultivation are at the state and local level. Conviction rates are high with many growers entering pleas to lesser included charges. Sentences are usually a term of probation and or fine. A marijuana grower is more likely to be sentenced to prison if convicted in Federal Court. Among the states surveyed, prison overcrowding was consistently mentioned as a reason convicted growers are not sentenced to jail.312

To put it simply, the DEA's position was that this situation could not be allowed to stand, and that our heritage of local discretion over law enforcement had to be disregarded, or their program would grind to a halt.

The criminal justice system's laxity in dealing with offenders does not encourage defendants to cooperate with authorities. Growers are aware that they face a minimal chance of conviction and incarceration. Fines are viewed as a cost of doing business. There is no deterrence when the profit potential exceeds the potential loss. The lack of defendants cooperating detracts from the intelligence data base regarding marijuana cultivation activities.313

By 1988, the DEA was ready to disregard issues such as male plants, plant potency, value, and personal use on account of new legislation passed by Congress. The number of plants become the sole legal issue for sentencing.

The Anti-drug Abuse Act of 1988 includes provisions for mandatory Federal prison sentences, depending on the number of marijuana plants involved. For one hundred plants or more, the statute provides for mandatory 5 year prison sentences. For more than one thousand plants, a mandatory 10 year prison sentence is provided. The DCE/SP will emphasize Federal prosecution for cultivation investigations involving 100 plants and more.314

1988 also marks another turning point in federal involvement in the anti-marijuana war. The Anti-Drug Abuse Act of 1988 also provided "authority for the Civil

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312 ibid., pg. 20.
313 ibid., pg. 20.
314 ibid., pg. 20.
Air Patrol to assist in drug eradication and interdiction. The 1988 Defense Appropriation Bill gave additional funding to the National Guard and the Department of Defense for drug eradication and interdiction.  

By 1989 the DEA was ready to acknowledge the federalization of marijuana cultivation offenses as a fait accompli.

In the past, DEA considered the growing of domestic marijuana as a state and local law enforcement problem. . . . A review of the domestic cannabis situation by DEA's Cannabis Investigations Section (OM) indicated that DEA had to change its domestic marijuana enforcement policy. It is imperative that DEA continue to lead a unified state, local and Federal enforcement effort directed toward the arrest and conviction of marijuana growers.

By 1990 it was clear that many aspects of the cultivation issue had not changed since the NDEPB report in 1986.

In many areas of the country, with depressed economies and high unemployment, cannabis cultivation has proliferated. Particularly in rural areas, money from marijuana trafficking has a significant impact on local economies. Advanced agronomic techniques, a preference for a more potent seedless marijuana, a lessened fear of arrest, and high profits have all contributed toward an increase in cannabis cultivation.

Also by this time the DEA was well into Operation Green Merchant, in which they seized customer records from various vendors in order to create investigative leads regarding possible indoor marijuana cultivation. In 1989 Green Merchant produced 30,000 investigative leads. By 1990 Green Merchant produced 57,000 leads, with no state in the country providing less than 100 leads. These figures are indicators of just

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316 ibid., pg. 22.
318 DEA 1990, pg. 22.
319 DEA 1991a
how widespread indoor marijuana cultivation is, as well as an indication of how the DEA spends a lot of its time - looking for small-time indoor marijuana growers.

Despite the history of the program and its obvious failures, the DEA has maintained every year since 1982 that the program is a great success. If measured against the goal of acquiring power and authority for the DEA, the program has been very successful. According to their 1991 report, the new excuse for greater police powers will be derived from the entry of "criminal organizations" into marijuana cultivation.

The Domestic Cannabis Eradication/Suppression Program has been such a success that in 1992, the Cannabis Investigations Section will again focus on asset seizures as well as intensify efforts to dismantle and disrupt criminal organizations that are cultivating marijuana in the United States. Likewise, efforts will be directed toward increased arrests and Federal prosecution of cultivators under the Federal minimum mandatory sentencing statutes.

**Paramilitary and Military Operations Expand**

The number of federal agencies involved in eradication efforts has been steadily increasing. By 1992 the DCESP was coordinating activities by U.S. Forest Service, the Bureau of Land Management, the Fish and Wildlife Service, the National Park Service, the Bureau of Indian Affairs, the National Guard and the Civil Air Patrol. The use of the National Guard deserves special attention.

There has been a consistent escalation in federal efforts to eradicate marijuana. In 1979 the DEA helped with eradication efforts in California and Hawaii. In 1981 the program was expanded to include Oregon, Florida, Georgia, Missouri, and Kentucky. In 1982 the program was expanded to include 25 states. In 1983 they had 40 states, by 1984 - 48 states, and finally 50 state participation in 1985. This program growth was good for

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320 DEA 1991b, pg. 4.
the DEA payroll. "The total number of DEA employees dedicated to the program has increased in proportion to the number of states participating in the program."322

The program grew in other ways, as more and more government agencies became involved. This aspect of the program became particularly acute after forfeiture provisions were passed in 1985, providing an incentive to grow on public rather than private lands for those growers who wished to remain outdoor cultivators.

The National Guard was involved in marijuana eradication efforts as early as 1982, providing helicopter support in Hawaii and Arkansas.323 It was becoming clear during 1983, as the scope of domestic cultivation was becoming fully appreciated, that the National Guard provided interesting opportunities for further escalation of eradication efforts.

The National Guard Bureau has recognized the significant contribution they can provide to the domestic eradication effort in the areas of intelligence production and sharing. Additionally, under state activation, the insertion of law enforcement personnel into raid sites and the extraction of personnel and drugs using helicopters can be of critical importance to the success of the campaign. During 1983 definitive guidance was provided to all Guard units clarifying the terms and conditions under which they can properly support the eradication campaign. This resulted in a number of states executing letters of agreement for intelligence hearing. Additionally, the Guard units in Hawaii and California directly supported the program through the commitment of helicopter and other resources.324

In 1984 attempts to use herbicides within the United States to eradicate were prevented by legal challenges brought by the National Organization for the Reform of Marijuana Laws. The DEA maintained that they did not have to file an Environmental Impact Statement before using herbicides for marijuana eradication, NORML and the courts believed otherwise. DEA was enjoined from using herbicides such as paraquat

322 DEA 1986, pg. 2.
323 DEA, 1983.
324 DEA 1984, pg. 12.
and glyphosate pending completion of an Environmental Impact Statement (EIS). This left the DEA looking for other ways to compensate for the labor intensive aspects of eradication. The EIS was published in July, 1985 (DEA EIS-1), and limited spraying on two sites occurred in 1985 using the herbicide glyphosate. The EIS process indicated that it would be difficult to use herbicides on a widespread basis in the U.S., and they have not been a major tool for the DEA since.

The manpower required to accomplish the physical destruction of cannabis sightings has been, and continues to be, one of the primary contributing factors toward overall difficulty in eradication efforts. Intelligence is a necessary component . . . it is also understood that a labor-intensive effort is required to minimize the availability of domestically grown cannabis.

Integrating the Guard into eradication activities continued throughout 1984. The National Guard Bureau continued its cooperative efforts with DEA in the cannabis eradication/suppression program in 1984 through the issuance of specific instructions and guidelines to state National Guard units stressing cooperation with law enforcement agencies and providing the methodology to facilitate the state units responses to requests for assistance in this program.

In 1985 the DEA enlisted Department of Agriculture field personnel, with representatives in over 3000 counties, to report cultivation "detected during their normal duties." This program was tested in 1984. The use of the National Guard was becoming more direct. "Several state National Guard units under state activation status

325 DEA 1985, pg. 21.
326 DEA 1986, pg. 22-23.
327 DEA 1985, pg. 6.
330 ibid.
provided direct support to state law enforcement efforts in this program during 1985.”331

Both programs continued throughout 1986.332

Military involvement continued to expand in 1988, with the DEA noting that "the 1989 eradication program will be enhanced through support provided from the Department of Defense."333

In 1989 they acknowledged another desirable aspect of using the National Guard. "NG personnel are under the command of each state governor and are not restricted by the Posse Comitatus Act" which forbids the use of the military in domestic law enforcement.334

The Posse Comitatus Act was passed in 1879, and forbids federal troops from entering private land or dwellings, and from detaining or searching civilians. In 1988 Congress passed a law authorizing Guardsmen to work under Title 32 of the United States Code in an "Active Duty for Special Work" status. The result is federally paid soldiers under state control. Guardsmen under this status receive combat pay, and can undertake searches of vehicles, buildings and enter private property without consent.335

Army Chief of Staff Gen. Gordon R. Sullivan told the 1991 National Guard Association convention that

You represent us in uniform in ways the active forces cannot unless certain laws are changed. You are part of a Total Army dedicated to protecting our values and our way of life.336

Colonel Richard R. Browning III, the chief of the drug demand section of the National Guard Bureau has described the Guards role this way.

331 ibid., pg. 14
332 DEA 1987
334 DEA 1990.
336 ibid.
America is caught up in the most pervasive drug epidemic in history. An epidemic that transcends the health, economy, and general well-being of our nation. The rapid growth of this drug scourge has shown that military force must be used to change the attitudes and activities of Americans who are dealing and using drugs. The National Guard is America's legally feasible attitude-change agent.337

The National Guard is currently cleared for 16 counterdrug missions according to their newspaper *On Guard*, including reconnaissance, ground radar support, cargo inspection, vehicle detection, marijuana eradication, drug lab detection, film processing, and weapons support, which includes everything from M16A2 automatic rifles and 9 mm semi-automatic Beretta pistols to Hawk missile radar and OV/ID infra-red detection equipment.338

Clearly, the Army views the Guard involvement in eradication and other anti-drug activities as a precursor to its own involvement. In an active Army publication titled *Tomorrow's Mission*, Lt. Gen. J.H. Binford Peay III, the Army Chief of Staff for Operations and Plans, asserts that in the Army of the 90's

> military forces are required to provide domestic nation assistance such as internal peacekeeping and anti-drug operations and support of civil authorities to maintain stability in a rapidly changing America.339

Speaking at a 1991 conference of the Association of the United States Army, Stephen M. Duncan, Assistant Secretary of Defense spoke explicitly on the subject.

> We can look forward to the day when our Congress repeals the Posse Comitatus Act and allows the Army to lend its full strength toward making America drug-free. 340

**Self Evaluation by the DEA**

The DEA thinks that if they go out and seize millions of marijuana plants, they're doing a good job. Every year the program is a success, often because their self-created

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337 ibid.
338 ibid.
339 ibid.
340 ibid.
indicators have gone up - more plants, more grow rooms, more seizures, etc. For example:

The increase in the number of plots and plants eradicated during 1985 is attributable to an increase in eradication efforts (manpower/financial) and refined reporting procedures as well an increase in public awareness and public participation in the overall drug abuse prevention program.\(^{341}\)

At this time the NDEPB was warning of the dangers in getting caught up in too zealous of a prosecution policy, a warning that was to be ignored. "The systematic destruction of illegal plots requires an extensive commitment of manpower, which cannot be siphoned off by futile attempts to determine the ownership of each plot."\(^{342}\) They provided a 20 point prescription for greater program success:

1) look for large organizations
2) target significant states
3) keep 50 state program
4) make the locals get the ditchweed
5) upgrade intelligence
6) increase aviation
7) states should pick up surplus DOD equipment
8) encourage states to use more small aircrafts
9) encourage growers to inform on patch pirates and violent growers
10) enhance prosecutions
11) increase penalties for cultivation over 100 plants
12) exempt from liability from loaned DOD equipment unless grossly negligent
13) DEA staff get less brownie points for cannabis eradication- change that
14) standardize sentencing
15) improve inter-agency cooperation
16) expand training program
17) prevent leaks like the Delta 9 leaks in 8/85
18) build public support with PR
19) invite foreign media to view eradication efforts
20) use herbicides, if they can\(^{343}\)

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\(^{341}\) DEA 1986, pg. 4.

\(^{342}\) NDEPB 1986b, pg. 48.

\(^{343}\) ibid.
The DEA incorporated most of these points into their activities in subsequent years, except they zealously continued increasing prosecutions and asset forfeiture. They still measured success by increasing indicators, such as:

In 1987 we had an increase . . . in the number of sinsemilla plants that were destroyed . . . in the number of cultivated plants eradicated . . . (and) in the total number of arrests, greenhouses operations, weapons and assets seized . . . The overall 1987 Domestic Eradication Program was a great success. In 1988 we will strive for increased follow-up investigations and to increase the value of assets seized.  

While the DEA portrays their work with a sense of pride and accomplishment, every now and then they publish comments that indicate the enormity of the task before the cannabis eradication program and the inadequacy of their efforts. For example:

"Also there were not enough resources available to eradicate all the marijuana plants that were located."  

In 1988 they admitted that "more fields were located through citizen complaints than by random aerial searches," bringing into question the cost effectiveness of aerial searches, despite the strategic reliance on helicopter and fixed wing flights.

The DEA has continually had problems with the physical eradication of discovered marijuana.

The manpower required to accomplish the physical destruction of cannabis plots continues to hamper DEA's eradication efforts. The expansion of intelligence gathering and labor-intensive eradication efforts are essential for minimizing the availability of domestically grown cannabis.

By the late 1980's legal challenges to herbicide use had been exhausted, though the litigation had established stringent rules and regulations for herbicide use. In many

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344 DEA 1988, pg. 1.
345 ibid., pg. 4.
346 DEA 1989, pg. 21.
347 DEA 1990, pg. 4.
respects, the desire to use herbicides in the U.S. was driven as much by foreign policy considerations as by addressing the DEA's manpower problems.

Foreign countries have turned to the United States for leadership in narcotic and drug enforcement because of its support for herbicidal eradication of opium and cannabis in source countries throughout the world. The United States resolve is to employ these same eradication techniques, which have been questionable to some against domestic produced marijuana. During the past year the traditional manual eradication of cannabis was supplemented with an ambitious herbicidal spray operation in Hawaii. These techniques should send a strong message to cannabis producing countries.348

Despite the use of forfeiture, mandatory/minimums, herbicides, and the use the National Guard and other federal agencies, and after over ten years of zealous eradication activity, the DEA is left by 1990 to defending its defining concept rather than its accomplishments.

It is estimated that about 25 percent of the marijuana consumed in the United States is produced domestically. Adequate effort and resources must be expended to deal with the threat. The concept of this program must be pursued. Continued support from all will ensure a proactive posture in dealing with this illicit phenomenon.349

Nonetheless, "DEA's goal is to significantly reduce the availability of cannabis in the United States."350 In a complete shift from the seizure driven policies of the mid 1980's, the new forfeiture driven eradication program favors arrests.

DEA's suppression policies will require a near-term focus on pursuing the producers, rather than the product. If successful, this policy will change to targeting distribution networks. The emphasis will be to vigorously eliminate organizations by increased arrests and seizures.351

From the DEA's perspective, no one really understands how important it is to prosecute and incarcerate marijuana cultivators. So, the "DEA will educate Federal and

348 DEA 1991a, pg. 3.
349 ibid., pg. 26
350 ibid., pg. 32
351 ibid., pg. 33
state prosecutors and the judiciary on the importance of deterrence in national and international cases."352 They will also "assist domestic demand reduction efforts by raising public awareness about the harmful effects of marijuana use. DEA, in cooperation with the National Institute of Drug Abuse (NIDA), will aggressively publicize research findings on the hazards of high-THC products."353

In his 1990 National Drug Strategy William Bennett called the domestic marijuana cultivation situation "intolerable" and called for an increase in funding from $8 million to $16 million in 1990 to wipe it out. He claimed that success against domestic cultivation "should be a benchmark of national anti-drug resolve." 354 The DEA was able to triple their funding of local eradication efforts in 1991 and 1992, with no appreciable increase in the number of seizures either year.355

Despite all the problems detailed above, and the need to involve so many other agencies and resources over the years, the DEA has always maintained that it seized a large percentage of the marijuana grown in the United States. "Officially, the DEA maintains it eradicated half the U.S. crop, although privately law enforcers say they snagged only 10 to 40 percent of the total."356 A California based DEA agent claims that outdoor growing in the state has been reduced by 3/4 .357

Kentucky state police believe they seize no more than half of the marijuana grown in the state, and they have the most aggressive campaign in the country after Hawaii's.358

352 ibid., pg. 33
353 ibid., pg. 33
354 U.S. News & World Reports, 11/16/89.
355 DEA, 1993.
356 Insight Magazine 7/1/91, pg. 13.
357 Insight Magazine 7/1/91, pg. 17.
358 Wall Street Journal 12/24/92. "Appalachian Kentucky Relies on Marijuana To Buttress Economy" by Joe Davidson.
Statistically speaking, if one of the most aggressive programs only seizes half of the cultivated marijuana, it is impossible for the entire program to seize half of the country's production. Cultivation is too diffuse to average 50% in every eradication program, and few states will boast of eradicating that much of the marijuana crop. Perhaps it is for this reason that the DEA claims they aim to get 70% of the Tennessee marijuana crop annually, and that it is the fourth most successful in the country.359

Regardless of the DEA's success rate, or lack thereof, "Domestically grown marijuana accounted for 10% of all marijuana in 1980 this has increased to 25% in 1992, with a production estimate of 4500 - 5300 metric tons."360

Under these circumstances, with no end in sight, the DEA still maintains that:

the program is working. We are doing a measurable good job in most of the states. With continued dedication, next year we can plan to strike even harder and keep even more of the marijuana from reaching the market.361

DEA estimates of domestic marijuana crop

The DEA does not have a good track record in estimating the size of marijuana crops. "Tip of the iceberg" anecdotes are common, suggesting that any estimate offered by the DEA be increased several fold.

The DEA method for estimating domestic marijuana production was first stated in 1983.

Using a relatively accurate plant count and conservative weight per plant factors, it is estimated that 1653 metric tons of marketable marihuana were eradicated. The strategic intelligence estimate for 1981 domestic marihuana production was 1200 metric tons. Therefore, the program shows that in 1982, 38% more domestic marihuana was eradicated than was previously believed to exist. Although a total U.S. marihuana production figure is not easily determined, the statistics obtained from this

360 DEA 1993, pg. 1
361 ibid., pg. 28
program reveal, without doubt, that the United States is becoming a major source for the drug. 362

They also explicitly listed the plant yield criteria they attributed to current cultivation.

To arrive at an estimated weight of marketable marihuana for that which was eradicated, the following factors are used: One sinsemilla plant yields two pounds of marketable material; one regular marihuana plant yields one pound of marihuana. These factors are considered conservative. 363

The DEA regularly prints a disclaimer in its reports suggesting that such estimating was only acceptable when the DEA itself engages in it. "It should be noted that the total figure of sightings in this report by no means represents the total number of plots under cultivation in the united States and no attempt should be made to correlate the two." 364 A revised comment shows up in every subsequent report.

However, consider this:

In 1989, 5,605,460 marijuana plants weighing approximately 2,548 metric tons (MT), were eradicated. DEA estimates that 50% of the domestic marijuana is being eradicated. This would indicate that approximately 5,096 MT of marijuana was cultivated in the United States in 1989. 365

This is making a correlation between the number of plants seized and the total number of plants grown in the United States.

Furthermore, the statement is just wrong. In every other context except this specific report, the DEA domestic estimate in expressed as a net figure, what was not seized. In this context, they present the figure as a gross figure. This incorrectly minimizes the size of the market in comparison to other years. The NNICC report for 1989 tactfully ignores this slight of hand, and publishes a net figure of 5000 to 6000

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362 DEA 1983, pg. iii (emphasis in original)
363 DEA 1983, pg. 5
364 DEA 1984, pg. 5
365 DEA 1990, pg. 4
metric tons. This indicates that they hold that roughly 8000 metric tons were grown, the DEA eradicated 2500 MT, and 5500 MT was harvested. This places the DEA's seizure percentage at about 30% of the crop, not the 50% they claim in their own report. Perhaps they made a mistake, and it is only a coincidence that it is so self-serving.

A recent report by a DEA agent in California calculates the value of cannabis in California assuming that they only seize 10% of the actual crop.

The DEA's ability to seize a large percentage of the marijuana grown in the U.S. was called into question above. Their estimates of U.S. production are called into question here.

In the mid 1980's the DEA maintained that U.S. production was only 12% of the country's consumption.

Anecdotal evidence suggests that the 12% estimate may be low. Projections made by a senior U.S. Forest Service official indicate that domestic production could be about 50% of U.S. supply. In addition, the Oregon Deputy Attorney General, in testimony before the House Select Committee on Narcotics Abuse and Control, stated that the correct figure "may be as high as 50%." During the interviews conducted, officials offered estimates ranging from 30% to 60%. It is important to emphasize that these high estimates are impressions rather than conclusions based on firm data.

When the DEA estimated that domestic cultivation provided 12% of U.S. consumption in 1984, they estimated production at 2100 metric tons. In 1984 the Mexican police raided five separate large scale growing sites in Mexico belonging to a consortium reputedly led by Caro Quintero. They seized over 2000 metric tons of marijuana, "8 times more marijuana than Mexican and American authorities at the time believed was produced annually throughout Mexico."

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368 NDEPB 1986b, pg. 15,16.
369 President's Commission on Organized Crime, 1986.
Regardless of the historical accuracy of DEA's estimates, there is no dispute today that domestically grown marijuana represents tens of billions of dollars of economic activity. "At minimum, this business is worth $20 billion to $30 billion a year," says John Sutton, chief of DEA's cannabis investigations branch (KY) 370 The DEA has estimated that domestic growers have harvested 10 million pounds annually since 1988. Their data, without corrections, would place the 1992 crop value at $26.8 billion.

**Recent Critiques of DEA Eradication Program Data**

A recent report from the Office of National Drug Control Policy estimates that only $9 billion is spent annually on marijuana in the United States, whether foreign or domestic. 371 The estimate is based solely on National Household Survey data estimating the prevalence, frequency, and amount of marijuana use in the U.S. The author's admit the $9 billion figure is conservative.

These estimates are probably low. Users are likely to underreport socially disapproved behaviors even when those behaviors are legal. They would seem to have even more incentive to underreport illegal behaviors. Some readers might find it reasonable to inflate these estimates for marijuana consumption by about one-third. 372

Another problem for consumption estimates based on the National Household Survey is presented by the limitations of the data. While the survey does solicit data about the gross amount of marijuana used by the respondent in the last month, it triangulates that information with data on the average number of joints used in the same time period. This sort of analysis assumes that every marijuana user smokes marijuana by way of a cigarette, ignoring the popularity of waterpipes among marijuana users, especially college-aged consumers. Smokers of marijuana cigarettes are likely to consume more marijuana than waterpipe or pipesmokers to achieve the same subjective

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372 ibid. pg. 22.
high because, as discussed in section 2, the delivery efficiency of each mode of smoking varies. This may seem like a small problem, and perhaps it is, however the NHS data set has a lot of missing data in it, and this data is replaced with data that is "imputed" from the available data. Depending on the amount of imputed data used in the estimate, assumptions about usage patterns could become very significant to the accuracy of the estimate.

Gettman has analyzed DEA Eradication program reports for the National Organization for the Reform of Marijuana Laws, and based on these reports has formulated estimates of the size and value of the domestic marijuana crop. These reports have been highly critical of the data used by DEA in estimating marijuana prices in the United States, and in DEA's self-serving estimates of the domestic marijuana crop size. A 1994 paper from the Office of National Drug Control Policy voices many of the same criticisms about the price data presented by DEA, and like the 1993 NORML report incorporates price information reported in High Times magazine. This report is also critical of DEA's crop estimates:

Clearly, DEA estimates of domestic marijuana production are not consistent with the consumption-based estimate. Not only is the DEA estimate of 1992 production approximately triple the consumption-based figure, but DEA data also suggests a roughly fifty percent decline in domestic marijuana cultivation from 1990 to 1992. By comparison, user surveys indicate only a twenty percent drop in consumption over the same period.

If we take the 1992 total eradication figure, and use a conservative yield estimate of one half pound for commercial grade and one quarter pound per plant for sinsemilla (DEA estimates a yield of a full pound per plant regardless of type), the eradication and suppression program appears to have prevented about 1,475 metric tons from being harvested. When combined with the estimate of total domestic marijuana production, this

373 Gettman, 1993.
375 ibid. pg. 45.
implies that roughly sixty percent of domestically grown marijuana is eradicated. This seems unlikely. A plausible explanation for the apparent inconsistency is that a substantial fraction of the marijuana eradicated by authorities and reported as sinsemilla or commercial grade is in fact "ditchweed", a very low potency generally less than 1 percent THC) variety of marijuana that grows wild in much of the U.S.376

The DEA has easily withstood such criticism from NORML, and has since the mid 1980's. However such negative criticism from the ONDCP could not be ignored; the DEA gave up trying to estimate the size of the domestic marijuana crop in the United States. According to a note in the 1995 ONDCP report:

The DEA no longer estimates the amount of marijuana under cultivation in the United States. The DEA also notes that indoor marijuana cultivation continues and that there is no way to estimate the extent of this practice.377

Consequently, without an estimate of U.S. domestic marijuana supply it is impossible to develop a supply-based estimate of the retail marijuana market in the U.S. with which to compare the $9 billion consumption based estimate.

It is difficult to develop an estimate of the size of the U.S. retail market for marijuana from estimates of available supply. First, the amount of marijuana that Americans cultivate for personal use is impossible to estimate. Second, even though a large amount of the domestic marijuana market is grown in the United States, countries in South and Central America, the Caribbean, Asia, North Africa, and the Middle East also supply cannabis to the domestic market. Unfortunately, the data needed to develop better estimates are not available, and without the independent ability to assess the reliability of the marijuana cultivation estimates, we cannot develop a plausible supply-based estimate of the retail value of the marijuana market in the United States.378

In other words, the scope of marijuana cultivation in the United States is so immense that the government has just admitted that it exceeds characterization. If it is impossible to even estimate personal cultivation, then it is patently absurd to believe that marijuana's schedule I status can ever be enforced by law enforcement officials.

376 ibid. pg. 46.
378 ibid. pg. 38.
Enforcement of the Controlled Substances Act is premised on control and regulation of drug manufacture and supply.

Summary:

Marijuana's schedule I status presents more problems and costs to society than the substances persistent, widespread use. To reiterate, Section 4 introduced three areas of social and economic costs--ready access to marijuana for school-age youths, a spiraling co-dependency between law enforcement and black market entrepreneurs, and an erosion of credibility for the nation's law enforcement and public health officials.

This section introduced six more areas of social and economic costs which the Controlled Substances Act mandates be reconciled with any possible benefits resultant from marijuana's schedule I status.

1) The absolute yet unenforceable schedule I prohibition contributes to an unfavorable set and setting accompanying school-age access and exposure to marijuana.

2) Adherence to the polarized and unscientific 'use = abuse' model obstructs the development of effective, research based policy and drug-abuse prevention programs.

3) The absolute yet unenforceable schedule I prohibition creates tremendous ethical problems for physicians and health-care-providers, professionals well-aware of the widening gap between existing governmental policies and the developing support for marijuana's therapeutic potential in scientific and medical literature, and professionals who are seemingly instructed by law to discourage their patients from using marijuana even if such use has obvious therapeutic benefits.

4) The failure of the Department of Health and Human Services, and of the National Institute on Drug Abuse specifically, to address this widening breach between recent research about marijuana and the findings required to sustain marijuana's schedule I status unfairly and inappropriately makes our federal law enforcement officials, particularly officials of the Drug Enforcement Administration, appear to be heartless, self-serving idiots.
5) The federal failure to reconcile marijuana's schedule I status with contemporary medical and scientific evidence places an unfair and expensive burden on state criminal justice agencies and their limited budgets.

6) Marijuana's schedule I status and the high priority it places on domestic and international marijuana eradication has the unintended effect of transforming domestic law enforcement activity into a massive market and price support mechanism for entrepreneurs here and abroad.

The scope of marijuana use in the United States has far exceeded the government's ability to enforce the substance's schedule I status, and this existing scheduling status does far more harm than good to the social fabric of our nation.
Exhibit C

A summary of any relevant medical or scientific evidence known to the petitioner, section 6 of 8 sections.

6. Public Health

The legislative history of the Controlled Substances Act instructs that:

if a drug creates no danger to the public health, it would be inappropriate to control the drug under this bill.379

As discussed above, teenage marijuana use is an indicator of the effectiveness of public policy and law, not an indicator of the harmfulness or abuse potential of marijuana when used by adults for any reason.

The legislative history notes that misuse of a drug in suicides and attempted suicides, as well as injuries resulting from unsupervised use are regarded as indicative of a drug's potential for abuse.380

As discussed in section 4, the DAWN data indicates that rated for each 100,000 people in our population, marijuana use alone produced less emergency room visits than common household painkillers such as Advil, Tylenol, and aspirin or benzodiazepines such as alprazolam (Xanax), diazepam (Valium), or lorazepam. (The Controlled Substances Act regulates drugs by classes, so for useful comparisons, DAWN statistics for marijuana should be compared to other classes of drugs.)

As discussed in section 3 and section 4, marijuana is a non-toxic drug. Cannabinoid receptors do not affect the medullary controls of heart and lung activity. It is virtually impossible to commit suicide with marijuana. The use of marijuana in suicide attempts is a futile exercise, and is an indication of ignorance about the substance's effects more so than an indication of a dangerous abuse potential. Nonetheless, the

DAWN statistics are frequently offered as proof that marijuana use equals marijuana abuse. Like their hypothesis about marijuana potency, the DAWN statistics are used by advocates of schedule I status to give the greater significance to the prevalence of marijuana use as an index of abuse. Such claims lack a scientific and medical basis.

Section four above contains comments by the Secretary of Health and Human Services on data from the Drug Abuse Warning Network (DAWN) and critiques the Secretary's use of the DAWN data. A more concise excerpt of Secretary Shalala's comments are presented below, and are included to support the assertion that current U.S. government policy is based on the mistaken assumption that marijuana users are like all other drug users, and will "eventually' end up in the emergency room begging for assistance.

We must act now to ensure that our young people understand the serious health effects of marijuana and other drugs so they don't end up like so many of the long-term drug users in the DAWN survey -- chronically ill, in need of detoxification, and standing in line in overcrowded hospital emergency rooms.

This isn't hyperbole.

There is a large body of research over the past 20 years that shows that children who use tobacco, alcohol, and particularly marijuana are at increased risk of using other drugs.

That's why these increases in marijuana use are of grave concern.

The more young people know that all drugs -- including marijuana -- are harmful, the less likely they are to engage in the self-destructive behaviors that we see culminating in the DAWN data.381

This section will support the assertion that the connection between teenage marijuana use and other drug use is social, not pharmacological, and is not an indication

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that adult marijuana use represents a threat to public health by increasing use of other addictive drugs.

Section 3 criticized the assertion that marijuana use is related to risk perception. The research cited to support the assertion did no more than provide an affirmation of the consequent of the assertion. A rival hypothesis was presented, which was that if non-use of marijuana was related to risk perception, than use of marijuana would be correlated with the absence of risk perception. An examination of the National Household Survey data suggests that many individuals who do not believe marijuana is risky still do not choose to use the drug. This suggests that health concerns may not have as much influence in drug use as policy makers believe, or as argued in section 3 that many adults simply don't believe the government when it comes to claims about marijuana and health.

There are arguments for both positions. Lloyd Johnston is the project director for the Monitoring the Future Project. In a 1988 paper, Johnston and his colleagues try to explain the decline in school-age marijuana use during the 1980's by testing two theories, 1) lifestyle variables, such as being more conservative, explain the drop, and 2) that risk perception explains the drop in use. They found that lifestyle variables did not explain the drop, but that changing attitudes about marijuana and health did.382

the perceptions of greater risks "got the ball rolling" and provided the basis for increased personal disapproval and decreased (perceived) use by friends and acquaintances with each succeeding class of seniors since 1979.

. . . Early efforts to dissuade students from use of marijuana often made exaggerated claims about harmful effects; meanwhile students could observe readily that friends and acquaintances who used marijuana did not suffer such disastrous consequences. More recently, however, reports about the health consequences have been more balanced, have received better and more extensive media coverage, and have been based on much more extensive research. Similarly, reports about psychological

consequences, such as poor school performance, reduced interest in extracurricular activities, and impaired interpersonal relationships have now acquired the ring of truth: regular use of marijuana (and other drugs) has been widespread for a long enough time to give most students first-hand contact with at least a few classmates who fit the popular description of "burnout". Indeed, we have found that daily marijuana users themselves perceive some such consequences as stemming from their use of the drug. Thus it seems that direct observation, and the resulting vicarious learning, have become consonant in recent years with messages from "the system."  

In 1990 the authors published another study testing the same hypothesis with cocaine use, and they reached the same conclusion that use reduction is correlated with risk perception. If one accepts this assertion, then what is one to make of the recent series of increases in adolescent marijuana use during the early 1990's? Does this mean that the government warnings have not held up to scrutiny, or does it mean that risk perception just isn't as important a factor as first believed?

The exaggerated claims about the danger presented by potent marijuana were discussed in section 4. These claims were an integral part of the anti-marijuana warnings of the mid-1980's Johnston and colleagues praise in the excerpt above. Furthermore, these mid-1980's health warnings were based on "new evidence" of the period which has since been discredited by the recognition that marijuana's effects are receptor-based, not membrane-based as once believed. This is particularly relevant to the proposition that marijuana use leads to "burnout" in some teenage users, a symptom of the amotivation syndrome supposedly created by a desensitization in brain cells. This phenomenon has since been shown not to exist. Since these once-praised findings have since been shown to be faulty, is it a surprise that marijuana use has begun to increase?

Discussion below will concern two issues of great significance to assessing the public health threat, if any, presented by marijuana use. The first issue is whether or not

383 ibid. pg. 108.
use of marijuana is a valid predictor of the use of more dangerous and more addictive
drugs. The second issue is related, whether marijuana use necessarily an indication of
psychological or behavioral problems. Both issues address the same question, does
marijuana use provide the basis for successful predictions about an individual's behavior?
What does marijuana use, alone, tell us about an individual? Advocates of marijuana
prohibition have long argued that marijuana use may not appear harmful to an individual,
but is a marker that the individual is ultimately headed for trouble as a result of their
marijuana use alone.

If marijuana use is a valid predictor of harmful behavior, then, it is argued,
marijuana use is a threat to public health regardless of the effect on the individual.

Social scientists are well aware of the pitfalls of addressing such questions;
correlations do not establish causation. In an example widely used by radio commentator
Rush Limbaugh, many criminals eat carrots, but eating carrots does not cause crime.
Claims that marijuana presents a threat to public health by leading individuals to use and
abuse other drugs can be criticized on both logical and empirical grounds. Let us
examine the literature.

Gabriel Nahas summarizes the evidence supporting the theory connecting
marijuana use to other drug use in the preface to 1990's 5th edition of *Keep Off the Grass* :

> It appears that the biochemical changes induced by marijuana in
the brain results in a drug-seeking, drug taking behavior, which in many
instances will lead the user to experiment with other pleasurable
substances. The risk of progressing from marijuana to cocaine or heroin is
now well documented.

Marijuana users are sixty-six times more likely to use cocaine
subsequently than subjects who have never consumed marijuana. This
1990 survey of PRIDE documents further the fact that marijuana is a
"gateway" drug to more destructive dependency-producing drugs such as
heroin or cocaine. Such a most significant risk of escalating from
marijuana to cocaine was reported by Kandel and colleagues in 1975
Clayton and Voss (U.S. Journal of Drug and Alcohol Dependence, Jan. 1982) confirmed Kandel's observation and reported that the risk for a marijuana user to progress to cocaine consumption is ten times greater than the risk of a heavy tobacco smoker to develop cancer of the lung. Dr. Herbert Kleber (Journal of Clinical Psychiatry, 1988, 48:3) reports that 75% of frequent users of marijuana have used cocaine at least once. It is a fact that the major epidemic of cocaine consumption besetting the country since the mid-eighties was preceded by the marijuana epidemic of the seventies.385

It widely accepted in the scientific community that a correlation does not establish causality.386 Over reliance on correlations in the verification of hypotheses represent an error in reasoning well-known to statistical analysts in the social sciences -- the fallacy of affirming the consequent.387

The 1993 National Household Survey indicates that 79% of regular marijuana users do not use any other illicit drug.388

Denise Kandel, also a professor at Columbia University, and colleagues published a series of articles in the American Journal of Public Health in 1984 on patterns of drug use, updating the data published in 1975 with reports on the same cohort; the 1984 report studies the 1975 cohort, now at age 25. A summary of their findings:

The sequence of involvement into drugs progresses from the use of at least one legal drug, alcohol and/or cigarettes, to marijuana, and from marijuana to other illicit drugs, and/or prescribed psychoactive drugs.389

The Office of Technology Assessment of the U.S. Congress, citing recent work by Clayton, Kandel, and other research, concluded:

385 Nahas (1990) supra. pg. xxiii-xxiv.
388 See section 4 above, or see U.S. Department of Health and Human Services, Public Health Service, Substance Abuse and Mental Health Services Administration (1994) "Advanced Report number 7, Preliminary Estimates From the 1993 National Household Survey on Drug Abuse." Rockville, MD: Office of Applied Studies, July 1994. See Table 4A, pg. 48. To calculate, subtract "any illicit drug other than marijuana" from "any illicit drug" to produce estimate of marijuana users who do not use other illegal drugs. For percentage, divide this number by the number of marijuana users.
While study results vary somewhat, the sequence most often reported is that alcohol and cigarette use come first, followed by marijuana use and then by the use of other illicit substances.\textsuperscript{390}

Neurobiological research has discredited the hypothesis that marijuana and other drugs target the same brain system (the mesocorticolimbic pathway), as will be discussed in section 7 below. Are there other explanations why some marijuana users also use more addictive drugs? One hypothesis is that:

\( (T)\)he criminalization of marijuana may have caused some marijuana users to move on to other illicit substances through contact with the subculture of illicit users.\textsuperscript{391}

Research is beginning to suggest that targeting marijuana as the key battleground for preventing drug abuse is a little like closing the doors after the horses have already left the barn. Marijuana use among adolescents appears to be a symptom of problem behavior, not a cause.

[In one study] delinquency and youthful sexual activity tended to precede the use of marijuana and hard liquor. . . The early use of so-called gateway drugs, such as beer and cigarettes, may contribute to later problem behaviors, while the later use of marijuana, hard liquor, and other illicit substances may be more the result of extended participation in problem behaviors\textsuperscript{392}

Scientific theories are scientific because they are the basis for consistently successful predictions. Gravity is a prediction that when apples leave a tree branch, they fall. Gravity is a scientific theory because things fall, largely without exception. The Office of Technology Assessment does not say that the gateway drug theory is unscientific, but they reach a similar conclusion.

\textsuperscript{391} ibid. pg. 74.
\textsuperscript{392} ibid. pg. 78.
Because many individuals who use substances do not go on to substance abuse, and because one level does not guarantee use at a higher level, these stages are descriptive but not predictive.393

Yamaguchi and Kandel elaborate in their conclusion:

The existence of sequential stages of progression, however, does not necessarily imply causal linkages among different drugs since the observed sequences could simply reflect the association of each class of drugs with different ages of initiation and/or individual attributes rather than the specific effect of the use of one class of drug on the use of another. Furthermore, it is important to keep in mind that although a clear development sequence in drug involvement has been identified, use of a drug at a particular stage does not invariably lead to the use of other drugs higher up in the sequence. Many youths stop at a particular stage and do not progress further.394

In a related article, Yamaguchi and Kandel conclude that "the probability that individuals who never use marijuana will initiate the use of other illicit drugs is very low."395 They conclude that teenagers are especially at risk to drug abuse if they begin to use marijuana. The dangers have less to do with marijuana itself than with use of marijuana by adolescents.

Generally the risk of initiation to the use of any drug rapidly decreases about age 20, although with marijuana there appears to be a residual initiation rate at about age 23 - 24.396 A maturation trend is also apparent in marijuana use, with use stabilizing at age 19 and amount of use decreasing after age 20 even as use continues strongly (50% of males and 33% of females in the cohort) into the mid twenties.

Yamaguchi and Kandel's findings deserve close consideration, and must not be removed from their original context. The authors specifically argue that their findings are

393 ibid. pg. 80.
394 Yamaguchi and Kandel (1984a) pg. 671.
relevant to public policy considerations regarding prevention and educational programs for adolescents.\textsuperscript{397}

This 1984 article by Yamaguchi and Kandel has served as the basis for the 'gateway theory' that asserts that prior use of marijuana is necessary to progress to other drugs. Their specific policy recommendation, though, involves reduction of the use of legal drugs by school aged youth.

The findings in this paper suggests potentially important policy implications for the development of preventive and educational efforts, namely that prevention of early involvement in legal drugs would reduce the use of marijuana, and that prevention of early marijuana use would reduce involvement in other illicit drugs. . . It is important to remember that age effects determine, in part, the sequential patterns observed between the licit drugs and marijuana. . .\textsuperscript{398} (emphasis added)

The focus of attention is on early use, and this is one of the most overlooked aspects of Kandel's gateway theory. It is early use itself, in high school for example, that presents a risk of further drug exposure, not later use of marijuana by adults.

The probabilities of initiating other illicit drug are very much reduced if marijuana is initiated at age 20 or over. . .\textsuperscript{399}

Both current and former users of drugs share the same risk of progression to other drug use, and for this reason Kandel advocates making prevention of early use the fundamental priority of public policy.

In 1992 Kandel and Yamaguchi published another follow-up study on the same cohort, now followed from age 15 to age 35.\textsuperscript{400} They reiterate the importance of early use of drugs to later use of dangerous drugs.

\textsuperscript{397} Yamaguchi, K., Kandel, D. (1984b)
\textsuperscript{398} Yamaguchi And Kandel (1984b) pg. 679-680.
\textsuperscript{399} ibid. pg. 677.
Two characteristics of an individual's drug history are especially important predictors of progression from a lower to a higher stage of drug use: age of initiation into use of a drug class and extent of use of the drug.401

Here is how they update their description of the stages:

While the patterns described during adolescence hold for the transitional period into adulthood, the use of prescribed psychoactive drugs, first identified in the mid-twenties for the cohort, had been confirmed as a further step in the sequence by the mid-thirties. The last stage, involving prescribed drugs, however, is the least strong in the sequence: it accounts for two-thirds of those who have ever used these drugs compared with 80% for stages involving legal and illegal drugs. The potential existence of problem drinking as an intervening stage between the use of marijuana and other illicit drugs (Donovan and Jessor, 1983)402 could not be investigated with the data available in this study.403

The authors repeat that their gateway theory of stages does not mean that drug users "invariably" use stronger drugs; many youths stop at a particular stage. They elaborate on their 1984 comments:

The notion of stages in drug behavior does not imply that these stages are either obligatory or universal such that all adolescents must progress through each in turn, as has been proposed by Piaget or Kohlberg for stages in moral development. The use of a particular drug does not invariably lead to the use of other drugs higher up in the sequence. The model is not meant to be a variant of the controversial "stepping stone" theory of drug addiction in which the use of marijuana was assumed to lead inexorably to the use of other illicit "hard" drugs, especially heroin. Rather the phases in drug behavior are facilitative. Entry into a particular stage is a common and perhaps even a necessary although not a sufficient prerequisite for entry into the next higher stage . . . [I]t is because all drug users come from a common pool of young people, who all started using the same drug classes, that they share certain factors in common.404 (emphasis added.)

401 ibid. pg. 451.
404 ibid., pg. 453-4.
The policy recommendation advanced by Kandel and her colleagues is that the optimum public health policy is to delay the age of onset of use of drugs. Once again they conclude that:

Early intervention would not only prevent participation in behaviors, such as smoking cigarettes, that have been detrimental consequences of their own but would also probably deter and/or reduce progression to other forms of drug use. 405

A 1993 paper by Kandel and Yamaguchi on the sequence from beer to crack illustrates the importance of delaying onset of first use. In the sample for this study, adolescents who use cocaine or crack began use of gateway drugs (alcohol, tobacco, or marijuana) two years earlier than those adolescents who do not use cocaine or crack, despite their use of gateway drugs. Age of first use at a lower stage is a strong predictor of further progression. 406

In 1995 Chen and Kandel published "The Natural History of Drug Use from Adolescence to the Mid-Thirties in a General Population Sample" in the American Journal of Public Health. 407 Summarizing their previous findings, the conclusion of their abstract reads simply that "cigarettes are the most persistent of any drug used. Drug-focuses intervention must target adolescents and young adults." 408

The natural history of marijuana use is that it begins in adolescence after the use of cigarettes and/or alcohol; consumption quantities and frequency of use increase to age 19, and then stabilizes until age 23-24, after which marijuana use declines. Like alcohol, there is an apparent maturation trend with the highest use of marijuana between ages 19 and 22. The daily consumption of marijuana drops as individuals reach their thirties.

405 ibid., pg. 454.
408 ibid. pg. 41.
An interesting aspect of these findings is that they lend support to an earlier hypothesis of Johnston and colleagues. In 1984, O'Malley, Bachman and Johnston published a paper on "Period, Age and Cohort Effects on Substance Use Among American Youth, 1976-82."\textsuperscript{409} The purpose of this study was to develop a hypothesis with a close fit to the longitudinal data of the Monitoring the Future Project. One theory developed is that "transitions" mediate drug use as adolescents grow older. This lends credence to the notion that teens take drugs because they are available and interesting, and that most of them grow out of it.

Age effects also encompass a very broad range of possible underlying causes. For example, many behaviors are age-regulated (voting, driving, marrying, purchasing alcohol), and thus age per se ought to have an effect on such behaviors. There are also consistent biological changes associated with aging, as well as some important transitions in social roles and environments. The latter are especially important for the age span under study here, with all the major transitions that occur between adolescence and adulthood. One important social transition is graduation from high school, and we see a clear effect of this transition on the frequency of cigarette use. Other important transitions which typically occur during the years after high school graduation include becoming a full-time worker, moving out of the parental home (possibly to go to college, to enter military service, or to marry and set up an independent living situation), and becoming a parent. Some of these transitions would be expected to lead to a decrease in drug use.\textsuperscript{410}

Throughout the discussions conducted by Kandel, Johnston, and their colleagues social rather than biological factors dominate the analysis. The connection between marijuana use and other drug use is a function of set and setting, not a function of the pharmacological properties of the drug. As Brady pointed out in section 5, if you want to influence decisions about the use of some drugs, circumstances can be arranged. The paramount issue is whether or not the pharmacological properties of the drug outweigh the influence of set and setting. This is certainly not the case with marijuana, and this


\textsuperscript{410} ibid. pg. 687-688.
will be discussed in more detail in section 7. The addictive qualities of nicotine, by contrast, are a factor that outweighs or at least rivals the influence of set and setting -- note the persistence of cigarette use found in Chen and Kandel's 1995 report.

It is important to distinguish between the policy recommendations of Kandel's team about teenage marijuana use and the implications their work has for the ramifications of adult marijuana use.

It would be a horrible misrepresentation of their findings to argue that Kandel and Yamaguchi support the use of criminal sanctions for adult marijuana use because their findings indicate that adult marijuana users are likely to move on to the use of cocaine and/or heroin.

On the other hand, Gabriel Nahas has unequivocally stated for the record that, in his opinion, scientific evidence supports "stricter enforcement of drug laws including those aimed at discouraging the use of marihuana . . ."411 (emphasis added).

Social science, in fact, is based on percentage plays and probability. Justice in the United States, however, is not. We do not engage in preventive detention in this country; we do not hold people in prison because we believe they are likely to commit some crime in the future, nor should we criminalize adult marijuana users because a small percentage of them are at risk or susceptible to the use of dangerous drugs. It becomes an even further stretch of logic to suggest that the criminalization of adult marijuana use is an acceptable educational and prevention tool in discouraging teenage use of any drug, an especially ironic policy considering the complete prohibition of marijuana creates an illegal market which virtually guarantees teenage availability.

Many contemporary defenses of existing U.S. marijuana policy rest on the assumption that marijuana use is always symptomatic of other psychological, emotional,

or behavioral problems, that is that use is always abuse. However there has never been sufficient evidence to support such a generalization, nor is there today.

The question for analysis is whether acute or chronic use of marijuana produces behavioral problems that pose a threat to public, as contrasted with individual, health. The relation of marijuana use to other drug use has been discussed above. As discussed in section 4 above, there is a considerable population of 'marijuana only' drug users in the United States. Has research provided any basis for generalizing about this group?

Usually this question is only half-answered. Samples of marijuana users are studied by different researchers, and reports of similar findings appear to validate the generalization that marijuana use has some negative, apparently harmful effect on all individual users. For example, a study was conducted in 1983 - 84 on the "Demographic and Health Characteristics of Heavy Marijuana Smokers in Los Angeles County" as part of Tashkin's ongoing research on the respiratory and pulmonary effects of marijuana use (discussed in section 2). The abstract reports their findings that:

The demographic, life-style, and self-reported health characteristics of a convenience sample of 207 male and 70 female non-Hispanic White, heavy marijuana users in Los Angeles County were compared with those of more representative county and national samples. Consistent with other researchers' findings, heavy marijuana users were found to differ significantly in living arrangements, job stability, and income. Heavy marijuana users did not differ in completed education, self-reported physical health, or use of alcohol and cigarettes. Heavy marijuana users were less likely to be married than nonusers, but reported the same number of close friends with whom they interacted more frequently than same-aged comparison groups. Our findings suggest that heavy marijuana uses are not homogeneous, and that female users differ significantly from male users.412 (emphasis added)

Advocates could quote selectively from this abstract to support fundamentally different assertions, that heavy marijuana use is connected with job and income difficulties, or that there are no universal traits that can be associated with heavy

marijuana use. Subjects for the study responded to advertisements. Perhaps heavy marijuana users with stable jobs and high incomes found it "inconvenient" to respond? Certainly the authors of the study took such a possibility into consideration, but reviews seldom include such technical qualifications or nuances.

It is relatively easy to mis-cite or misquote scientific research, and one of the first clarification's to be ignored involve the limitations of the data and the theoretical construct which provides whatever meaning the data might have. Scientific reasoning requires the testing of predictive hypotheses to validate or reject assertions.

Can marijuana use be explained by some predisposition, allowing some predictor of marijuana use to be determined?

Howard Becker approached this issue in 1953 in an article on "Becoming a Marihuana User" in the *American Journal of Sociology*. Here is the abstract.

An individual will be able to use marihuana for pleasure only when he (1) learns to smoke it in a way that will produce real effects; (2) learns to recognize the effects and connect them with drug use; and (3) learns to enjoy the sensations he perceives. This proposition based on an analysis of fifty interviews with marihuana users, calls into question theories which ascribe behavior to antecedent predispositions and suggests the utility of explaining behavior in terms of the emergence of motives and dispositions in the course of experience.413

One of the topics Becker discussed with subjects was when users "didn't get high the first time." Becker is part of the sociological tradition which influenced Zinberg's *Drug Set and Setting*, which also discusses drug use as learned behavior. Becker observes that a user must learn to smoke marijuana properly, and "must learn to enjoy the effects he has just learned to experience."414

414 ibid. pg. 239.
In his concluding remarks, Becker criticizes predictive theories regarding marijuana use. This criticism still holds today, as research reported below will demonstrate.

In comparing this theory with those which ascribe marihuana use to motives or predispositions rooted deep in individual behavior, the evidence makes it clear that marihuana use for pleasure can occur only when the process described above is undergone and cannot occur without it. This is apparently so without reference to the nature of the individual's personality makeup or psychic problems. Such theories assume that people have stable modes of response which predetermine the way they will act in relation to any particular situation or object and that, when they come in contact with the given object or situation, they act in the way in which their makeup predisposes them.415

Considerable studies have been conducted in search of variables which will explain drug abuse, and present markers of individuals especially at risk to drug dependency. The purpose of these studies is to identify variables that have high correlations with drug use. This process eliminates variables with low statistical correlations and identifies the few variables that are likely to explain drug use in a particular statistical sample. Several thousand of these correlations between various independent variables and school-age drug use have been quantified in hundreds of different social science research projects.

A review and summary of these thousands of correlations would be extremely valuable to analysts converting such basic research into policy or scheduling decisions. In the early 1990's the Congressional Office of Technology Assessment contracted with a professor at the Bowman Gray School of Medicine at Wake Forest University for this sort of report on "Drug Abuse in Schools: Contributing Factors and Preventive Interventions."416 The report is described by OTA in a 1994 publication:

415 ibid. pg. 242.
OTA commissioned a review of the survey research literature on school-aged substance use that compiled, classified, and examined 9,930 statistical analyses from 242 separate studies. This is by far the most extensive systematic examination of this body of research conducted so far. Most of the studies dealt with school-based populations, but some focused on school-age army recruits, dropouts, children of alcoholics, and individuals involved in clinics. The studies reported statistical relationships between substance use and its postulated causes. Statistical findings from the study reports were sorted into 11 major categories and 50 subcategories, and then analyzed to identify strong, moderate, and weak statistical relationships, as well as those that had been insufficiently studied.417

Use of tobacco, alcohol, and marijuana accounted for 82 percent of the analyses in the report, prepared by William B. Hansen.

In part, the focus on use rather than abuse reflects much of the philosophy that has guided research and educational funding. Namely, for youth, any use of illegal substances (including alcohol and tobacco) has been considered abuse by some. Use has received the most extensive attention perhaps in part because use among youth is easier to define than abuse but there are also multiple methods for defining use. These include any use versus no use definitions as well as intensity, frequency, quantity and problematic measures. The point at which use becomes abusive escapes definition.

At a minimum, use is a precursor to abuse although abuse does not necessarily follow from use . . . Nearly half of the youth who experiment with cigarettes go on to develop long-term smoking habits. The use of alcohol and marijuana by youth who use but have no definable chronic problems contribute to the highway death toll, violence, and crime. The public costs of these alone support the study and prevention of even low levels of use.

This report addresses the causes of school-aged substance use as examined through the use of survey research methods418

As described by OTA the analyses were sorted into 50 subcategories, and the average correlations in each sub category were determined.

Four categories of evaluation were established. First, the most important variables are those with a relatively strong statistical relationship, and these should be used in explanatory models regarding experimentation and progression of use behaviors. The next category includes variables with moderate relationships, and these variables provide secondary explanations. The third category is variables with weak relationships. These are variables with no empirical support for playing a causal role in the onset of substance use or transition from experimentation to abuse.419

Finally, there are some variables that have not been sufficiently studied.

How will the correlations of variables in different studies be compared?

The average magnitude of correlations for each category will be examined. Previous research has suggested that correlations with absolute values above .300 have clear meaning and contribute important information to understanding the nature of such behaviors as substance use. On the other hand, correlations of less than .200 have minimal importance. Correlational values in between are of moderate importance.420

Meta-analyses are difficult to interpret because of the possible variations in the manner individual studies define and measure their variables.421 This paper reports unweighted mean correlation coefficients, and most of the variables produced consistent measures in the meta-analysis (standard deviations, for example).422

For the Hansen meta-analysis, primary correlations were defined as over .30, secondary correlations were between .20 and .30, and correlations under .20 were considered tertiary and of minimal importance.

The four variables that dominate as correlates of and possible contributors to substance use are: 1) prior and concurrent use of substances, 2) substance use by peers and friends, 3) perceived peer

419 ibid. pg. 16.
420 ibid. pg. 16-17.
421 Hansen, W. Personal Communication, 6/30/95.
422 ibid.
attitudes about substance use, and 4) offers to use substances. *The prominence of prior and concurrent use is consistent with the reinforcing nature of substance use itself.* The prominence of the other three variables emphasizes the importance of the social environment in contributing to and reinforcing substance use among school-age youth. (emphasis added)423

Section one above discusses contemporary standards for evaluating the reinforcing nature of a substance, which are based on self-administration of the drug in animal models. The evidence in this petition asserts that marijuana does not have a significant dependence liability. The Hansen report supports the assertion that it is not the drug, but the set and setting, which have the greatest influence on school-age use of marijuana. Consequently, negative effects of marijuana on adolescents can not be an indication or predictor of the substance's effects on adult users.

The first variable clearly speaks to the behavioral and neuropharmacological nature of substance use, suggesting that substance use is patterned behavior that is highly influenced by neurological reinforcement. *The remaining three variables all suggest that a major cause of substance use among school-age youth is the social environment.* That is, theories of substance use and abuse must include social processes as central explanations of the onset and development of patterns of consumption. Social norms (including issues about prevalence and acceptability), the process of social development, the ready availability of substances in the social environment, and the structure of social groups must all be considered as central elements for explaining substance use.424 (emphasis added)

The role of risk perception, for example, is integral to the social environment; it is a component of the "set" in drug, set, and setting. However as an explanatory variable for marijuana use, it is secondary to prior use of alcohol and tobacco.

Here is a summary of the variables that have secondary explanatory value, many of which can be considered corollaries of the primary correlates above.

An additional fifteen variables were judged to be of secondary importance. These included (a) self-efficacy (assertiveness, resistance

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424 ibid. pg. 53.
skills and susceptibility to peer pressure), (b) deviance, (c) attitudes toward drug use, (d) beliefs about psychological consequences of substance use, (e) age and grade, (f) beliefs about social consequences of substance use, (g) intimacy, (h) intentions, (i) school bondedness, (j) others' attitudes about drug use, (k) independence, (l) achievement values, (m) parental attitudes about drug use, (n) non-structured activities, and (o) peer group characteristics.425

One of the great contributions of the Hansen meta-analysis is the following list of variables which can be considered somewhat irrelevant to explaining substance use among school-age youths.

This analysis leaves 38 variables with minor or no justifiable role in causing substance use onset or development. Among these are variables that have been extensively examined in research projects, including (a) substance use by parents, (b) personality traits, (c) intelligence (d) social personality traits, (e) parental relations, (f) affect, (g) participation in structured activities, and (j) self-esteem. Based on the observations that each of these variables were included in at least 100 correlational analyses, the popularity of these issues can be judged to be high. Each contribute in only a minor way to understanding substance use. The practical value of including these in theories of substance use is minimal and, without compelling empirical findings that support strong theoretical arguments, should be removed from theories of substance use onset and development.

Ten of the remaining tertiary variables had 50 or more analyses reported, suggesting that researchers considered them of relative importance. Included in this list were (k) general values, (l) school performance, (m) stress management skills, (n) non-peer, non-family attitudes about drug use, (o) church attendance, (p) availability, (q) academic expectations, (r) drug use by extended relatives, (s) drug use by siblings, and (t) socioeconomic status. Given the frequency with which these variables have been examined, these variables also seem to play little or no role in explaining substance use onset or development.426

The variables with insufficient study to draw conclusions from were religious affiliation, motivation to comply, self-management skills, exposure to moral codes, media influences, and values specific to substance use. It is interesting to note that when called upon to explain recent increases in teenage marijuana use, both Donna Shalala and Lloyd

425 ibid. pg. 53.
426 ibid. pg. 55.
Johnston attributed the rise to the media influences of grunge, rap and rock music stars (see section 4).

Hansen did several confirmatory analyses, and one specific to marijuana shows that regardless of the factors that shape them, peer attitudes have an overwhelming influence on the decision to use marijuana. The top seven variables with the highest mean correlations with marijuana use are (a) Peer attitudes about Drug Use (.677); (b) Drug Use by Peers (.381); (c) Offers (.377); (d) Deviance (.344); (e) Previous Drug Use (.335); (f) Beliefs about social consequences (.314); and (g) attitude toward drug use (.291).427

The .677 correlation coefficient between marijuana use and peer attitudes is inconsistent with the other measures. According to Dr. Hansen, this particular variable was "unusual" because it only relied on 18 correlation coefficients from 5 studies. Over half the correlations came from one study. A reanalysis based on equally weighted studies (compensation for differing study sizes) produced a mean correlation coefficient of .53 with a standard deviation of .21, still higher than all the others.428 The high standard deviation suggests "that in some cases, the particular method of measurement differed or the sample was unusual."429 In this case, the .67 figure is an anomaly, a piece of data that sticks out of the distribution. It is easy to pluck this figure out of context and claim that peer attitudes explain more about teenage marijuana use than any other variable, especially since this would confirm the NIDA hypothesis that risk perception is the key to discouraging teen marijuana use. A closer examination of the data suggests that the some odd data has skewed the distribution in this particular sub-category distribution.

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427 ibid. pg. 59.
428 Hansen, W. Personal Communication 6/30/95.
429 ibid.
Hansen's paper is an early but valuable attempt to provide a statistically-based review of quantified social science data regarding the use of drugs by school-aged youths. Future reviews will refine Hansen's analytical techniques and build on his findings. The meta-analysis discussed above was only one aspect of the paper OTA requested from Hansen; future reviews of this material will have a closer focus on the material than the scope of OTA's request allowed in this review.

Forty years after Becker's paper in the *American Journal of Sociology*, the report prepared for OTA by confirms his criticisms of theories based on deeply rooted motives or predispositions. Availability, and the prior use it contributes to, explain school aged drug use better than any other variables. The purpose of the Controlled Substances Act is to create a closed system of regulation and distribution that would, in part, reduce the access of school-aged youth to all drugs. There is nothing in the pharmacological profile of marijuana that makes it any more of a public health threat than alcohol, tobacco, or benzodiazepines; social science research on the relationship between marijuana and other drug use provides further support for this assertion.

The Hansen report also comments on the use of theory in the research it reviewed, and as such evaluates the scientific foundation and context of emerging research in the area of school-age drug use.

It is evident that well thought out assumptions did play an important role in most studies. Nearly all articles referenced prior findings. Investigators made inferences from the literature that were theory-like in nature. They often related in the discussion sections of their papers what the implications of their findings were in theory-like terms. Thus, while the field has, for the most part, been loosely theoretical in terms of grounded theory, a solid rationale has evolved that has connected empirical facts with logic and philosophy. . . there is sufficient evidence to suggest that the social influences model represents an emergent model that represents a body of yet-to-be-codified explanations which generally guide the field.431

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430 ibid.
Hansen's conclusions address the need for the field to move beyond theory generating to theory testing. They echo the comments of natural science researchers about the wide latitude for speculation which has previously dominated their field of study.

There are two conclusions to be drawn from this. First, general theories and eclectic aggregations of theory have advanced the field to date but must be used more explicitly in driving the construction of hypotheses and experiments. Theories should be reexamined critically and abandoned if they do not meet the explanatory criteria needed by both epidemiologists and interventionists.

Second, as a field, school-based substance abuse researchers have been more interested in public health than science. The concerns have been primarily practical - solving the nation's problem. This has led to modest achievements so far. However, before further progress can be expected, theory development and testing must become an integral characteristic of all research. The empirical information is plentiful and offers a ready opportunity for theory development.432

These comments lend support to assertions that social science findings used as the basis for prior scheduling decisions were not based on rigorous scientific grounds, as the field itself had yet to enter the theory testing and abandonment stage of scientific development. The abandonment of old theories in response to new natural and social science findings forms the basis of this petition.

The research by Kandel, Zinberg, Becker, and Hansen cited above support the assertion that public policy would best serve the young people of this country by successful actions to delay the age of first drug use by school age youth.

In each case, though, it is the recent neurobiological findings about marijuana that have provided the bridge between social and natural science. As always, Leo Hollister has something enlightening to add to the discussion. In his acceptance of the Oscar B. Hunter Award from the American Society for Clinical Pharmacology and Therapeutics in

432 ibid. pg. 90.
1988, Hollister addressed the topic of "Psychopharmacology: The bridge between psychiatry and biology."\textsuperscript{433}

Two separate psychopharmacologic developments heralded this return of psychiatry to the biologic sciences. The most important was the discovery of drugs such as reserpine and chlorpromazine, which were truly effective for treating major psychiatric disorders. The second was the discovery of LSD, which indicated that extremely small amounts of an aberrant chemical could have profound mental effects. In somewhat more than three decades, psychiatric thinking has changed profoundly. No longer does one speak of schizophrenic, manic, or depressive "reactions" (the latter term implying that these abnormal mental states were reactions to life events), but rather these disorders are thought of as malfunctions of the brain determined by a genetic predisposition and mediated by biologic mechanisms involving neurotransmitters, receptors, and metabolic alterations.\textsuperscript{434}

Some conditions are reactions to life events, and others are not. Hollister's bridge enables contemporary science to distinguish the two. Both Hollister and Kandel refer to instances where marijuana use may be explained by self-medication for depression or other psychopharmacological deficits, and in the some cases of therapeutic use of marijuana correction of neurochemical deficits in the cannabinoid receptor system may also have explanatory value. The preeminent value of the bridge between social science and biology is in its explanatory value, which reveals to us which aspects of behavior are more strongly influenced by biological variables than individual characteristics or the social environment. Hollister's bridge connects drugs to sets and settings, and allows scientists to view their work from both sides of the river of life.

Lee Robins of the Department of Psychiatry at the Washington University School of Medicine published an editorial in the January 1995 issue of the American Journal of Public Health based on Kandel's work; the editorial's title is "The Natural History of


\textsuperscript{434} ibid. pg. 124.
One interesting possibility might be to simultaneously ban tobacco and legalize marijuana, as antithetical as these two acts appear at first. Such an action might result in cigarettes' and marijuana's swapping position in adolescents' progression from one drug to another. If tobacco is banned without legalizing marijuana, there is a greater risk that alcohol's domination of the drug scene will increase further, with known risks to drinkers' livers, hearts, memories, and offspring. Even if it did not achieve a diminution of alcohol's role, such a transposition of the legal status's of tobacco and marijuana should bring the public perception of which drug's are "soft" (i.e., relatively safe) and which are "hard" (i.e. relatively risky) closer to matching what we know about their relative physiological effects and addictive properties.436

Section 7 will return to the biological evidence that marijuana does not have sufficient enough of a dependence liability to justify schedule I status.

436 ibid. pg. 13.
Exhibit C.

A summary of any relevant medical or scientific evidence known to the petitioner, section 7 of 8 sections.

7) Psychic or physiological dependence liability.

As with many of the topics discussed in prior sections, the evaluation of the psychic or physiological liability presented by marijuana use depends on the standards applied to the issue.

According to the legislative history,

There must be an assessment of the extent to which a drug is physically addictive or psychologically habit forming, if such information is known.437

The key word here is "extent."

At the time Congress created the Controlled Substances Act the United States public was debating reconsideration of criminal penalties for marijuana use and sales.

The extent to which marihuana should be controlled is a subject upon which opinions diverge widely. There are some who not only advocate its legalization but would encourage its use; at the other extreme there are some States which have established the death penalty for distribution of marihuana to minors. During the hearings, Dr. Stanley F. Yolles, who was the Director of the National Institute of Mental Health, submitted a chart of fable and fact concerning marihuana . . .[Among the facts are the following statements.]

Marihuana does not cause physical addiction, since tolerance to its effects and symptoms on sudden withdrawals does not occur. It can produce habituation (psychological dependence) . . .

We know nothing in the nature of marihuana that predisposes to heroin abuse. . .

Marihuana use has increased enormously in spite of the most severely punitive laws.438

The Congress asked the Department of Health, Education and Welfare for their recommendation where marijuana should be placed in the Controlled Substances Act.

The response, by letter of 8/14/70, of the Assistant Secretary for Health and Scientific Affairs is as follows:

Dear Mr. Chairman: In a prior communication, comments requested by your committee on the scientific aspects of the drug classification scheme incorporated in H.R. 18583 were provided. This communication is concerned with the proposed classification of marihuana.

It is presently classed in schedule I(C) along with its active constituents, the tetrahydrocannabinols and other psychotropic drugs.

Some question has been raised whether the use of the plant itself produces "severe psychological or physical dependence" as required by a schedule I or even schedule II criterion. Since there is still a considerable void in our knowledge of the plant and effects of the active drug contained in it, our recommendation is that marihuana be retained within schedule I at least until the completion of certain studies now underway to resolve the issue. If those studies make it appropriate for the Attorney General to change the placement of marihuana to a different schedule, he may do so in accordance with the authority provided under section 201 of the bill.

We are advised by the Office of Management and Budget that there is no objection to the presentation of this report from the standpoint of the administration's program.

Sincerely yours, (signed) Roger O. Egeberg, M.D.439

The Controlled Substances Act states explicitly that:

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 [schedule I and II substances include] (A) the drug or other substance has a high potential for abuse.440

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438 ibid. pg. 4578.
439 ibid. pg. 4630.
440 21 USC §812(b)
The statute allows for exceptions to be made in accordance with international treaty obligations. However, 1) no treaty obligation can require the U.S. government to deny due process and/or equal protection under the law to any of its citizens and 2) the U.S. Court of Appeals has ruled that regardless of treaty obligations rulemaking petitions must first be evaluated on merit.441

The Court of Appeals also ruled in 1977 that they believed that the U.S. treaty obligations limited the scheduling of marijuana to schedule's I or II. The Court did not rule on the responsibilities of the United States as a signatory of the Single Convention Treaty when faced with clear evidence that marijuana is not only mis-scheduled domestically (in the CSA), but internationally as well (in the Single Convention Treaty.)

Most importantly, the Court clarified the important issue of legislative intent in regards to interpretation of 21 USC §812(b); Congress intended the abuse potential of a drug to determine the severity of its regulation.

If, as respondent (DEA) contends, a determination that the substance has no accepted medical use ends the inquiry, then presumably Congress would have spelled that out in its procedural guidelines. Its failure to do so indicates an intent to reserve to HEW a finely tuned balancing process involving several medical and scientific considerations.

Admittedly, Section 202(b), 21 U. S.C. § 812(b), which sets forth the criteria for placement in each of the five CSA schedules, established medical use as the factor that distinguishes substances in Schedule I from those in Schedule I. However, placement in Schedule I does not appear to flow inevitably from lack of a currently accepted medical use. Like that of Section 201(c), the structure of Section 202(b) contemplates balancing of medical usefulness along with several other considerations, including potential for abuse and danger of dependence. To treat medical use as the controlling factor in classification decisions is to render irrelevant the other "findings" required by Section 202(b). The legislative history of the CSA indicates that medical use is but one factor to be considered, and by no means the most important one.442

441 NORML v. DEA, 559 F.2d 735 (1977)
442 NORML v. DEA, 559 F.2d 735, 748. (1977)
As the court cites in a footnote, the legislative history is clear that:

    A key criterion for controlling a substance, and the one which will be used most often, is the substances potential for abuse. . .Final Control by the Attorney General will also be based on his findings as to the substance's potential for abuse.443

While the legislative history contains a definition of potential for abuse, courts have acknowledged that legal doctrine must adjust to technological innovation.444

The history is plain. Marijuana was placed in schedule I on the presumption of a finding, rather than on the basis of a finding. Legally, this is a congressional prerogative. However the scheduling of marijuana was challenged in the 1980's and while DEA rejected the proposed rule to remove marijuana from schedule I, it did so on its own authority. Marijuana is now a schedule I drug on account of executive rather than legislative action. Unlike the legislative branch, the executive branch does not have the constitutional prerogative to schedule marijuana on the basis of a presumed finding.

The present scheduling of marijuana is based on a presumptive finding by the Food and Drug Administration.

    FDA also concluded that abuse of the plant material may lead to severe psychological dependence in some individuals but that the information available was insufficient to determine with certainty whether the plant material produce physical dependence.445

As cited above, the law states that a finding "must be made" to place a substance in any of the schedules. The legislative history clearly indicates that a finding on the dependence liability is essential to a drugs scheduling status. The record clearly shows that such a finding does not exist.

These are Hollister's conclusions on marijuana dependency in 1986:

444 See, for example, Katz v. U.S., 389 U.S. 347, 88 S.Ct. 507, 19 L.Ed.2d 576 (1967)
445 51 FR 22947 (1986)
Brain damage has not been proven. Physical dependence is rarely encountered in the usual pattern of social use, despite some degree of tolerance that may develop.446

These are Abood and Martin's comments on dependence in 1992:

It is well established that chronic heavy use of cannabis does not result in a withdrawal syndrome with severe symptomatology. However, the occurrence of some form of psychological dependency or craving is more probable than physical dependence . . . There are few reports in which an abrupt interruption in marijuana use has led to incapacitation of the individual using the substance. The number of people who have difficulty in controlling their abuse of cannabis to the extent that they require professional treatment is relatively small.447

The only rationale defense for basing marijuana's scheduling on a presumptive finding is that at the time no scientific knowledge was available regarding marijuana's mechanism of action in the brain that allowed a comparative assessment of the abuse potential of marijuana and other drugs. The discovery of the cannabinoid receptor system has finally provided the means to mark the "extent' to which marijuana has a dependence liability.

Early research into brain functions centered on the role of electrical impulses in creating pleasure and pain. Dr. Gabriel Nahas praises Robert Heath's work in this field, and includes a commentary by Heath on the relationship between his work and public policy in a 1981 text on Drug Abuse in the Modern World.448

Dr. Heath's research also suggested that marijuana use caused irreversible brain damage, however this conclusion has rejected by reviewers for various reasons including excessive doses and lack of replication.449 Given his own conclusions about marijuana, Heath eloquently describes what he believes to be the problem at hand:

446 Hollister, 1986 pg. 17.
447 Abood and Martin, 1992 pg. 204.
449 See, for example, Institute of Medicine, Marihuana and Health (Washington, D.C., National Academy Press, 1982.) pg. 80 - 93.
In short, the initial use of marihuana produces a provocative phenomenon: the person smoking the joint can, at will, activate his brain's pleasure system . . . What is wrong with this? . . . The deleterious effects to both the individual and society have been repeatedly and consistently demonstrated. . . The fate of cultures in which drug use has been extensive serves to substantiate the consequences of inducing pleasure dissociated from utility and survival. In our own culture . . . when the pleasure a person gains from taking a drug replaces reward for a job well done, we have shoddy workmanship. When puffs from a joint replace the pleasure of a good golf game or a swim on a warm afternoon, we have apathy and physical deterioration. When the anxiety before an examination is eliminated by the instant pleasure of a drug, the student does not prepare and fails the examination. When ingestion of a chemical substitute replaces the pleasant arousal of solving a problem or designing a new engine, what are the implications for the future of our society -- or even our survival as a nation?450

More recent research also associates addiction with the pleasure/reward system in the brain. Unlike Heath, who associated activity in various regions of the brain as pleasure-oriented, modern theory is based on activation of the pleasure/reward system by the neurotransmitter dopamine. Izenwasser and Kornetsky discuss the discovery by Olds and Milner in 1954 that animals would work to receive electrical stimulation to brain regions, and the modern "evidence about the neurochemical bases underlying drug reinforcement [that] suggests that dopamine plays a major role."451 The role of dopamine in the brain pleasure/reward system is now well established in the pharmacological literature.452

According to Izenwasser and Kornetsky:

450 Heath (1981) pg. 5-6.
Using *in vivo* microdialysis, Di Chiara and Imperato\(^{453}\) (in 1988) showed that many drugs abused by humans (opiates, ethanol, nicotine, amphetamine, and cocaine) increased extracellular dopamine in the nucleus accumbens, whereas drugs that are dysphoric . . . reduce dopamine release. Drugs such as diphenhydramine (an antihistamine), imipramine (an antidepressant), and atropine (a muscarinic cholinergic agonist), which are not abused by humans, have no effect on the concentration of synaptic dopamine in the nucleus accumbens.\(^{454}\)

Microdialysis in freely moving rats is a new technology that allows researchers to implant measuring devices in the rat brain. The device extrudes from the live rat's skull. When the rat recovers from the surgery, researchers are able to use the microdialysis device to measure changes in dopamine levels in a living, "freely moving" specimen. Izenwasser and Kornetsky have used these and other experimental data to correlate brain wave data with neurobiological processes, as have others. Technological innovation allows modern researchers access to more accurate data than was available to their predecessors.

In 1992 the National Institute on Drug Abuse published a monograph on *Neurobiological Approaches to Brain-Behavior Interaction*.\(^{455}\) This monograph presents several papers on the various technologies being applied to brain-behavior research. A paper on microdialysis provides extensive citations on the role of dopamine in reinforcement. These citations will not be repeated in the excerpt below, but are available in the NIDA monograph.

The mesolimbic DA [Dopamine] system has attracted the most attention in the study of the neural circuitry underlying drug abuse. Its importance is undeniable. If the mesolimbic system is blocked or almost completely depleted of DA, animals refuse to work for food, self stimulation, or self-injection. . . . Not only is the DA system necessary, its functions are sufficient to motivate and reward behavior. Rats will work


to stimulate certain DA cell regions electrically or chemically. For example, they will electrically self-stimulate the mesolimbic DA cell body region in the ventral tegmental area (VTA).456

Many drugs of abuse given systematically increase extracellular DA. Similarly, when AMPH, cocaine, PCP, or nicotine was injected locally into the nucleus accumbens or infused through the microdialysis probe itself, this local treatment increased levels of extracellular DA in a manner similar to an intraperitoneal injection.457

The Office of Technology Assessment cites several pharmacological studies in support of the following summary.

A key part of this drug reward pathway appears to be the mesocorticolimbic pathway (MCLP) . . .

These structures and pathways are thought to play a role in the reinforcing properties of many drugs of abuse, although the precise mechanisms involved in all drugs of abuse lack a thorough description. The mesocorticolimbic dopamine pathway appears to be critical in the rewarding properties of stimulant drugs such as cocaine and amphetamines. Also, both the ventral tegmental area and the nucleus accumbens appear to be important for opiate reward, while these same structures and their connections to other limbic areas, like the amygdala, may play a role in the rewarding properties of barbiturates and alcohol.458

As recent as 1992 many believed marijuana had an effect on dopamine levels in the brain. Izenwasser and Kornetsky cite research on self-stimulation by Lewis rats in support of the notion that marijuana shares this quality with other drugs.459 They also note that this quality is only observable in the Lewis Rat strain. Martin also notes that this finding is confined to "one strain of rat" and its application "to human abuse is

457 Ibid. pg. 11.
tentative at best."460 This conclusion is also reported by the Office of Technology Assessment, which attributes the finding to an in-bred quality specific to Lewis Rats.461

In 1992 Herkenham, using a lesion-technique, established that there are no cannabinoid receptors in the dopamine producing areas of the human brain.462 This confirms a 1991 microdialysis study indicating that THC does not affect striatal dopamine release in freely moving rats.463

Dopaminergic qualities are now a widely acknowledged biological marker of a drug's dependence producing qualities. The brain is evolutionarily conditioned to adjust behavior to increase dopamine production. Usually, this neurotransmitter activity rewards essential activities related to eating, reproduction, and physical fitness that contribute to the perpetuation of the species. Dopamine release provides a reinforcing effect that encourages repetition of the source activity.

Addressing interest in dopamine release in the brain, Herkenham and his colleagues noted in his breakthrough 1990 report that:

The presence of cannabinoid receptors in the ventromedial striatum suggests an association with dopamine circuits thought to mediate reward. However, reinforcing properties of cannabinoids have been difficult to demonstrate in animals. Moreover, cannabinoid receptors in the basal ganglia are not localized on dopamine neurons.464

Herkenham's 1992 review of the literature concludes that:

The effects of cannabinoids on dopamine circuits thought to be common mediators of reward are indirect and different from those drugs such as cocaine and morphine which directly affect extracellular dopamine levels and produce craving and powerful drug-seeking behavior.465

462 Herkenham (1992)
465 Herkenham (1992) pg. 29.
Marijuana does not stimulate the pleasure/reward center of the brain and is categorically different from popular drugs of abuse.

This information explains why marijuana does not produce self-administration in animals, and why evidence of a damaging dependence liability in humans has not emerged in the 25 years since the creation of the Controlled Substances Act.

Popular drugs of abuse, such as heroin, cocaine, and amphetamines, produce reinforcing self-administration in animal models, and all have effects on the production of the neurotransmitter dopamine, explaining the biological basis for their respective dependence liabilities. Marijuana does not produce reinforcing self-administration in animal models, and does not have an effect on the production of dopamine, explaining the biological basis for its lack of a significant dependence liability.

Consequently, marijuana does not have a sufficient dependence liability for schedule I or II status.
Exhibit C.

A summary of any relevant medical or scientific evidence known to the petitioner, section 8 of 8 sections.

8) Related or Precursor Chemicals

This factor is included in the Controlled Substances Act to allow the control of chemicals (like lysergic acid) and substances (like poppy straw) that are involved in the manufacture of controlled substances. The relationship of marijuana and its constituent parts is analogous to that of precursor chemicals. This is a good context for a discussion of the relationship of marijuana to its constituent parts.

The DEA maintains that studies involving THC or other cannabinoids are not a valid basis for scientific assertions about marijuana. The topic has been discussed above in section 2 on the pharmacology of marijuana. This section addresses this issue within the context of the practices and traditions of the scientific community, particularly in a historical context.

The National Institute on Drug Abuse has funded a marijuana "Potency Monitoring Project" at the school of Pharmacy at the University of Mississippi that has tracked important cannabinoid levels in confiscated marijuana since 1975. One indicator of generally accepted standards in any research field is the type of data deemed significant for researchers to study. In terms of analysis, this refers to the study of correspondence rules. Research analyzes indicators, variables x, y, and so on, and these indicators are assumed to correspond to the object of the scientist's study. The flaws in research designs can be found in an examination of whether the indicators really represent the phenomena being studied. This section asserts that scientists studying marijuana accept a correspondence rule which asserts that the constituent parts of marijuana, particularly $\Delta^9$-THC, provide valid indicators for the marijuana itself. The Potency Monitoring Project provides an implicit example of this: it tracks and reports
historical data for just four cannabinoids -- $\Delta^9$-THC, Cannabidiol (CBD), Cannabichromene (CBC), and Cannabinol (CBN).466

The inability to make reliable assertions about marijuana based on research on its constituent parts is a recurring theme in DEA's rejection of an Administrative Law Judge recommendation that marijuana has accepted medical use in the United States. Here are eight examples.

Although delta-9-THC is an active ingredient in the marijuana plant material, marijuana contains over 400 other chemicals. At least 61 of these chemicals are cannabinoids. All these chemicals could have some effect on the human body. Since THC is only one of many active ingredients in marijuana, THC studies are of very limited value in evaluating the therapeutic utility of marijuana.467

THC is only one constituent among hundreds found in marijuana. Therefore, the consequences of an individual ingesting pure THC as compared to smoking marijuana are vastly different.468

Twenty-one (21) cannabinoids have been clinically evaluated. Most of this testing centered on the psychotropic effects of the compounds, and only eight or nine of the cannabinoids have been tested for therapeutic utility. These studies have only been cursory except for the testing of synthetic THC. Cannabigerol (CBG) cannabinoids show antibacterial activity against gram positive bacteria, and have been shown to effect basic cell metabolism. Cannabinol (CBN) type compounds have exhibited anticonvulsant, anti-inflammatory, immunological, and behavioral effects. CBN has also exhibited possible potentiation of THC effects in man. Cannabidiol (CBD) has exhibited anticonvulsant activity.469

As well as significant variations in naturally occurring substances in natural cannabis, there are variations in the active substances based on conditions under which the plant material has been maintained or stored. THC is labile (sic) to air oxidation forming cannabiol (CBN).

Cannabidiol (CBD), in the presence of oxygen and light and upon heating, is converted to cannabielsoic acids.\textsuperscript{470}

Although THC is usually a constituent present in marijuana, since marijuana also contains at least 60 other active cannabinoids in varying quantities, the results of antiemetic trials using THC cannot be extrapolated in evaluating marijuana's antiemetic properties. For example, cannabidiol, a constituent present in marijuana, can potentiate some effects of THC, while suppressing other effects, including the antiemetic effect.\textsuperscript{471}

Most pharmacological research with cannabis or its constituents has actually been conducted with orally ingested THC, rather than smoked marijuana. Although the pharmacologic effects are presumed to be similar, the studies with oral THC do not provide a complete picture of marijuana's effects. Few of the other cannabinoids have been pharmacologically evaluated. The health consequences from smoking marijuana are likely to be quite different than those of orally ingested THC. Yet most of the chronic animal studies have been conducted with oral or intravenous THC.\textsuperscript{472}

The effect of taking a drug in combination with other chemicals is seldom the same as taking just the pure drug.\textsuperscript{473}

\textquote{M}arijuana's chemistry is neither fully known, nor reproducible. Thus far, over 400 different chemicals have been identified in the plant. The proportions and concentrations differ from plant to plant, depending on growing conditions, age of the plant, harvesting and storage factors. THC levels can vary from less than 0.2% to over 10%. It is not known how smoking or burning the plant material affects the composition of all these chemicals. It is not possible to reproduce the drug in dosages which can be considered standardized by any currently accepted scientific criteria.\textsuperscript{474}

The DEA has approved synthetic THC for schedule II status.\textsuperscript{475} This has created the interesting situation in which a chemical derivative from a naturally occurring substance has been deemed safer for use than its source. Usually the opposite is true. In

\textsuperscript{470} 54 Fed. Reg. 53,774 (1989)
\textsuperscript{473} 57 Fed. Reg. 10,499 (1992)
\textsuperscript{474} 57 Fed. Reg. 10,499 (1992)
\textsuperscript{475} 51 Fed. Reg. 17,476 (1986)
1973 Gabriel Nahas believed this would be the case for THC as well. Nonetheless, in the passage below Nahas recognizes and describes the value of using THC in marijuana-related research. Nahas recognizes the THC research will provide validity for assertions about marijuana itself. The following is the conclusion from the chapter on chemistry from Nahas' 1973 edition of *Marihuana--Deceptive Weed*.

> It has taken all the refinements of modern technology to isolate and define the elusive psychoactive substance which has led man to use Cannabis as an intoxicant. Now that this substance is available, the pharmacologist and biochemist will be able to assess quantitatively its mechanism of action, and some advances in understanding basic biological processes are to be expected.

> However, the chemical identification of delta-9-THC will not solve in any way the social problem of Cannabis use or abuse by man. Indeed, the history of the past 100 years indicates that when morphine and heroin were isolated from the poppy and cocaine from coca leaves, these alkaloids were rapidly abused in preference to the less potent natural substances from which they were derived. The same holds true for the Mexican peyote cactus and its alkaloid, mescaline. If there is any continuity in history, one might therefore expect delta-9-THC to be increasingly used by man as a euphoriant and mind-altering drug in preference to the deceptive Cannabis of fluctuating potency. Furthermore, it is very simple to synthesize delta-9-THC from olivetol, a basic chemical available commercially in the United States.476

As discussion in sections 1 and 7 demonstrate, marijuana does not share essential characteristics of drugs with significant potentials for abuse. Not surprisingly, use of synthetic THC has not produced any evidence of abuse. For example, this excerpt on Dronabinol from a 1995 reference guide for health care professionals published by the United States Pharmacopeial Convention:

> Although chronic abuse of cannabis has been associated with decreases in motivation, cognition, judgement, and perception, no such decrements in psychological, social, or neurological status have been associated with the administration of dronabinol for therapeutic purposes. In an open-label study in patients with AIDS who received dronabinol for up to 5 months, no abuse, diversion, or systematic change in personality or

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social functioning was observed, even in those patients with a history of drug abuse.477

This petition asserts that evaluating the validity of data for the purposes of scientific reasoning is not the prerogative of the Attorney General or her representative. The DEA is on record as recognizing that this limitation of their discretion is based in statute, not executive policy.

Clearly, the Controlled Substances Act does not authorize the Attorney General, nor by delegation the DEA Administrator, to make the ultimate medical and policy decision as to whether a drug should be used as medicine. Instead, he is limited to determining whether others accept a drug for medical use.478

When a drug lacks NDA approval and is not accepted by a consensus of experts outside FDA, it cannot be found by the Attorney General or his delegate to have a currently accepted medical use. To do so would require the Attorney General to resolve complex scientific and medical disputes among experts, to decide the ultimate medical policy question, rather than merely determine whether the drug is accepted by others.479

This petition asserts that the validity of assertions about marijuana that are based on the study of its constituent parts is not only a matter of consensus in scientific and medical circles, but also one recognized in U.S. policy.

A historical context will provide the basis for understanding how scientists develop and change their standards for evaluating the significance of scientific data. The standards are provided by paradigms that guide scientific research. This issue concerns the paradigm that guides research on marijuana and its constituent parts. The U.S. government can not recognize this paradigm's validity in a scientific context, such as the awarding of grants by the National Institute on Drug Abuse, and reject the paradigm's validity in an administrative rule-making procedure.

Here is DEA's description of the historical background of the paradigm they are using to evaluate scientific data about marijuana.

In 1901, Congress intervened with the passage of the Food, Drug and Cosmetic Act (FDCA). A shift began away from anecdotal evidence to objectively conducted scientific research, away from uninformed opinions of lay persons and local doctors to expert opinions of specialists trained to evaluate the safety and effectiveness of drugs, and away from totally democratic decision-making to oversight by the Federal Government.480

DEA maintains that the paradigms developed to evaluate manufactured pharmaceutical substances indicate that marijuana is too unstable for medical use.

Modern drug-research is based on the use of well-defined preparations of pure compounds which, when administered to patients, allow reproducible results. The problems associated with using natural substances as drugs include the inability to regulate the doses of active constituents, and the interaction of the active constituents with other potentially active compounds in the natural substance. The presence of active constituents with other potentially active compounds in the natural substance. The presence of active constituents in most natural drugs may vary based on genetic factors, county of origin and growing conditions. As a result, most natural drugs cannot meet established quality control standards in the United States. Before a drug substance may be used in the practice of medicine, it must have a composition of active ingredients that has been established and accepted as standard. Such standardization, which includes identity, purity, potency, and quality, is specified in either a New Drug Application (NDA) or an official compendium such as The United States Pharmacopeia or National Formulary.481

The purpose of research, though, is to obtain scientifically valid assertions. Paradigms, like judicial doctrine, changes in the hands of its practitioners. While one paradigm that utilizes pure compounds can not provide valid assertions about marijuana, surely others can. In terms of evaluating dependence, the development of new testing paradigms is one of the functions of the College on the Problems of Drug Dependency (CPDD).

This petition has reviewed several other new paradigms now in use to evaluate the significance of data about marijuana's effects on health and behavior. The relation of dopamine to addictive behavior has provided a new paradigm for understanding the biological basis for substance abuse. New technologies such as autoradiographic assay techniques, microdialysis, and the development of non-classical cannabinoid isomers produced new research paradigms for studying the human brain. The resultant knowledge created a new paradigm for understanding the significance of experimental research on the effects of cannabinoids in that data can now be evaluated in the context on a known mechanism of action for the substance. Social science is producing new paradigms to understand the abuse and addiction, whether it be the refinement of the gateway theory to incorporate Jessor's observation that heavy drinking is an intermediate step between marijuana and hard drug use, or further application of Zinberg's theories of drug, set and setting. The use of data on marijuana's constituent parts, however, as the basis for making scientifically valid generalizations about marijuana has been a scientific convention since Mechoulam and Gaoni discovered the structure of $\Delta^9$-THC in 1963.

A 1982 report from the Institute of Medicine provides a benchmark and context for understanding the nature of modern understanding of the chemistry and pharmacology of marijuana.

Although the behavioral and psychological effects were well described in literature of the nineteenth century, the complex chemistry and pharmacology of the cannabis plant discouraged extensive investigation until 15 years ago.

The most prominent effects of cannabis are on psychological phenomena and behavior. Psychopharmacology and behavioral pharmacology have developed as divisions of scientific inquiry only over the past 25 years; therefore, the older cannabis literature, no matter how valuable for observations on other matters, does not provide a basis for quantitative pharmacological analysis and evaluation.

Early pharmacologists could work only with crude extracts of the plant. Although the general structure of the cannabinoids was known by
the turn of the century, the particular cannabinoids that were identified early and were available as pure substances were largely devoid of the characteristic psychoactive effects of cannabis. Synthetic cannabinoids with cannabis-like activity became available in the 1930's. It was not until 1964 that an active ingredient of cannabis was identified as Δ9-tetrahydrocannabinol (THC) and synthesized. In the 1960's, the isolation and synthesis of the main psychoactive component of cannabis and related cannabinoids, together with a rapid increase in the use of marijuana by middle class North American students, stimulated scientific activity . .

Cannabis, the crude material from the plant Cannabis sativa, contains hundreds of chemicals. Most of these are found in other plants, but 61, termed cannabinoids, are unique to the cannabis plant . . . A single cannabinoid, Δ-9-THC, produces almost all the characteristic specific pharmacological effects of the complex, crude cannabis mixtures. A number of synthetic cannabinoids have pharmacological effects similar to Δ-9-THC. Other cannabinoids in the plant, for example, cannabiol, are almost inactive pharmacologically or may interact with Δ-9-THC to modify its actions. One cannabinoid, cannabidiol (CBD), can influence the metabolism of another, Δ-9-THC. A few cannabinoids have effects quite different from Δ-9-THC. For example, cannabidiol has relatively little psychoactive and cardiovascular effect but is an active anticonvulsant.

Investigators have chemically altered the Δ-9-THC molecule in an attempt to determine which of its structural elements are required to produce behavioral and other effects. Studies of the structure-activity relationships indicate that, to produce effects on behavior, a pyran ring must be part of the three-ring system, a free phenolic hydroxyl on the aromatic ring at C-1, and a lipophilic side chain (C5H11) at C-3. Understanding chemical structure-effect relationships is important to guide the synthesis of cannabinoids with differing pharmacological effects. Different effects of Δ-9-THC activity by chemical design will require further syntheses and pharmacological study of a large number of cannabinoids.

Even at this relatively early date (1982) scientists have established that the key to unlocking the pharmacological secrets of the marijuana plant lies in an understanding of the active ingredients as a chemically distinct family of interrelated molecules.

There are 61 known cannabinoids, however they can be further subdivided into 12 categorical types.

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1. Cannabigerol (CBG) type: 6 known
2. Cannabichomene (CBC) type: 4 known
3. Cannabidiol (CBD) type: 7 known
4. Δ-9-Tetrahydrocannabinol (Δ-9-THC) type: 9 known
5. Δ-8-Tetrahydrocannabinol (Δ-8-THC) type: 2 known
6. Cannabicycol (CBL) type: 3 known
7. Cannabiolsin (CBE) type: 3 known
8. Cannabinol (CBN) type: 2 known
9. Cannabinodiol (CBND) type: 2 known
10. Cannabitriol (CBT) type: 6 known
11. Miscellaneous types: 9 known
12. Other cannabinoids: 4 known

Raz Razdan published an extensive review on "Structure-Activity Relationships in Cannabinoids" in 1986. Razdan emphasizes that:

the potential exists for development of novel analgesics from this field, as cannabinoids act at different receptors than the opiates (analgesic action is not antagonized by naloxone), do not have the physical dependence liability and respiratory depression properties of the strong opiates, and are orally active with a long duration of action.\textsuperscript{484}

Certainly, as Razdan wrote before the receptor breakthrough in 1988 - 1993, much more scientific research was required to develop therapeutic, pharmacologically pure drugs from cannabinoids. This does not mean, in the mid-1980's or in the mid 1990's, that the pharmacological activity of cannabinoids was unknown to scientists. Razdan, for example, lists seven characteristics of the Structure Activity Relationship of cannabinoids in man\textsuperscript{485}, and presents extensive tables documenting what was then known about the SAR of cannabinoids in animals.\textsuperscript{486}

Despite the extensive knowledge about the pharmacological actions of cannabinoids, the two most promising therapeutic areas of Δ\textsuperscript{9}-THC, i.e., antiemetic and antiglaucoma activities, were discovered serendipitiously without any preclinical pharmacology. This emphasizes the importance of early studies in humans and the difficulties encountered.

\textsuperscript{483} Institute of Medicine (1982) pg. 14.
\textsuperscript{484} Razdan, R. (1986) pg. 77.
\textsuperscript{485} ibid. pg. 82.
\textsuperscript{486} ibid. pg. 84 - 146.
in correlating animal activity with activity in man for this class of compounds.487

It is widely recognized and accepted that valid scientific theories and assertions regarding marijuana can be based on general or specific cannabinoid research. In the language of contemporary research, 'cannabinoids' has become the precise scientific term for 'the unique chemicals in marijuana' and is used as a widely recognized and accepted synonym.

The U.S. Department of Health and Human Services is required by law to publish a report on "Drug Abuse and Drug Abuse Research" every three years. The Second Triennial Report to Congress was written in 1986 and published in 1987. The title of the chapter on marijuana research is "Marijuana and the Cannabinoids."488 In discussing research on "Marijuana and Reproduction" the report describes current theories and data on "the effects of cannabinoids on the hormones that modulate the reproductive process,"489 "regular marijuana use"490, and "effects caused by the chronic treatment of animals with THC."491 The review of research on "Effects Upon Fetal Development" refers to "marijuana's effects", "marijuana use", "exposure to THC, cannabinol, and cannabidiol," "cannabinoid administration", and plasma "cannabinoid levels."492 A review of research on "Immune Status" reviews research on "THC", and "marijuana smokers."493 Discussion of "Psychomotor Functioning" makes reference to correlations between "marijuana intoxication" and "THC or its acid metabolite", and "blood levels of THC".494 "High Priority Research Questions" include research on "heavy use of current

487 ibid. pg. 146.
489 ibid. pg. 78.
490 ibid. pg. 79.
491 ibid. pg. 79.
492 ibid. pg. 80.
493 ibid. pg. 82-83.
494 ibid. pg. 85-86.
higher potency marijuana", "significance of the cumulation of cannabinoids", and "the retention of THC." 495

The same pattern of use is present in the Third triennial report. 496 The relationship between the individual effects of cannabinoids and their sum total effect in marijuana is not the objective of modern research, but its fundamental foundation. Certainly scientists will learn more about marijuana by learning more about the interrelationships of cannabinoid effects, but lack of knowledge about these relationships neither inhibits the production of valid theories about marijuana nor does it dominate discussion of the effects of marijuana on the human body. The family relationship among cannabinoids is viewed by scientists as an asset, not a liability, in their work to better understand the effects of human, non-therapeutic use of marijuana.

The rapid increase in the use of marijuana that occurred in the late 1960s and early 1970s resulted in an intensive research effort to identify the effects of cannabinoids on normal physiological function. There has been particular interest in the effects of cannabinoids on the brain in an effort to better understand their behavioral effects. Although much information has been gathered on the biochemistry of cannabinoids in the brain, it is unclear whether biochemical effects are responsible for the behavioral alterations caused by marijuana use. It is reasonable to ask why answers to this question have not been forthcoming. Part of the answer may be found by comparing cannabinoid research with that which has led to the much better understanding of opioid actions in the brain. Certainly opioids have been researched much more intensely for a much longer period of time. Two major factors that led to the elucidation of the opioid receptors and the subsequent identification of the endogenous opioids were the availability of structural analogs with widely varying agonist potencies and specific antagonist. Although progress in cannabinoid research lags behind that of opioids, recent evidence suggests that these same tools are becoming available to cannabinoid researchers.

495 ibid. pg. 88.
Considerable effort has been expended in synthesizing cannabinoid analogs largely because of the need to develop new therapeutic agents.\textsuperscript{497} These synthetic analogs have also been extensively used to characterize cannabinoid actions . . .

For the past several years, other synthetic analogs have been emerging that are both highly potent and highly stereoselective.\textsuperscript{498} It is these properties of the analogs which suggest very specific mechanisms in the central nervous system that are involved in the behavioral effects of the cannabinoids.\textsuperscript{499}

The use of highly potent, stereoselective synthetic cannabinoid analogs made the discovery and characterization of the endogenous cannabinoid receptor system between 1988 and 1993 possible. As discussed throughout the petition above, all recent advances in understanding about the effects of marijuana have been based on the discovery of the common mechanism of action for cannabinoids, including $\Delta^9$-THC, which provide the pharmacological basis for the effects of marijuana.

A review of the conclusions of Herkenham's team's findings on tolerance reiterates this important point:

The magnitude of the present effect, like the striking behavioral tolerance, may stem in part that, unlike other psychoactive agonist drugs, cannabinoids can be administered in very high doses. It is ironic that the magnitude of both tolerance (complete disappearance of the inhibitory motor effect) and receptor down-regulation (78\% loss . . .) is so large, whereas cannabinoid dependence and withdrawal phenomena are minimal. This supports the claim\textsuperscript{500} that tolerance and dependence are independently mediated in the brain.\textsuperscript{501}

\textsuperscript{499} HHS (1991) pg. 138-139.
\textsuperscript{501} Oviedo, et al. (1993) pg. 300.
WIN 55,212 is another experimental cannabinoid which produces the same effects as $\Delta^9$-THC and CP-55,940, however there are some differences in the effects of each of the three. A 1994 study demonstrated cross-tolerance between these three cannabinoids. The authors hypothesize that $\Delta^9$-THC and WIN-55,212 are partial agonists whereas CP 55,940 is a complete agonist, explaining some of the minor differences between these cannabinoids. Cross tolerance among certain psychoactive cannabinoids has been well documented.

Valid assertions about the relative abuse potential and relative dependence liability of marijuana can now be made by scientists on the basis of the known existence of a cannabinoid receptor system in the human body. Valid assertions about the relative abuse potential and relative dependence liability of all cannabinoids can be made on the same scientific basis.

The psychoactive qualities of marijuana are produced by one constituent chemical, $\Delta^9$-THC. Conclusive evidence exists that marijuana does not have a dependence liability greater than that of $\Delta^9$-THC alone, and that no other cannabinoid has psychoactive properties. Conclusive evidence exists that the pharmacological properties of individual natural cannabinoids have less pharmacological action than either marijuana or $\Delta^9$-THC alone, and that their dependence liabilities (if any) and potential for abuse is less than that of marijuana and $\Delta^9$-THC.

Experimental cannabinoids may have greater potencies, and may present qualities which warrant stricter controls than necessary for natural cannabinoids or synthetic copies of naturally occurring cannabinoids, such as synthetic THC.

There is no scientific basis for an assertion that marijuana had a greater dependence liability than $\Delta^9$-THC. There is no scientific basis for an assertion that any

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503 ibid. pg. 1387.
cannabinoid compound has a greater dependence liability than $\Delta^9$-THC. Consequently, there is no basis for distinguishing between the scheduling of marijuana, cannabinoids, and $\Delta^9$-THC on the basis of dependence liability or potential for abuse.

As discussed in sections 1 and 7 above, neither marijuana, cannabinoids, or $\Delta^9$-THC have sufficient potential for abuse for inclusion in schedule I or II of the Controlled Substances Act.

On the basis of the chemical similarities between marijuana, cannabinoids, and specifically $\Delta^9$-THC, their common endogenous receptor system, the lack of self-administration of cannabinoids in animals, the lack of cannabinoid receptor activity in dopamine producing areas of the brain, and the additional scientific and medical evidence discussed above, this petition calls for the repeal of the administrative rules placing marijuana and cannabinoids in schedule I and placing $\Delta^9$-THC in schedule II.