

## **Appendix 6.**

# **Marijuana and Health Research Update: Excerpts from Key Reports**

By Jon Gettman, Ph.D.

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The National Research Council published "An Analysis of Marijuana Policy" in 1982. Their policy analysis was based in part on a then recent report on Marijuana and Health by the Institute of Medicine of the National Academy of Sciences, and the appendix of the NRC analysis contains a summary of this 1982 scientific review on the health effects of marijuana use. This appendix contains the complete summary of Marijuana and Health from the 1982 NRC report as well as reports on recent research findings on similar subjects.

**Characteristic Effects of Marijuana (1999)**

The Institute of Medicine reported in 1999 that: "The most commonly reported effects of smoked marijuana are a sense of well-being or euphoria and increased talkativeness and laughter alternating with periods of introspective dreaminess followed by lethargy and sleepiness. . . . A characteristic feature of a marijuana "high" is a distortion in the sense of time associated with deficits in short-term memory and learning. A marijuana smoker typically has a sense of enhanced physical and emotional sensitivity, including a feeling of greater interpersonal closeness. The most obvious behavioral abnormality displayed by someone under the influence of marijuana is difficulty in carrying on an intelligible conversation, perhaps because of an inability to remember what was just said even a few words earlier." [1]

**Marijuana Potency (1973, 1975, 2001)**

In *Ravin v. State of Alaska*, (1975) the Supreme Court of Alaska observed that: "Marijuana is the common term for dried leaves or stalk of the plant *Cannabis sativa* L.

The primary psychoactive ingredient in the plant is delta-9-tetrahydrocannabinol (THC). Most marijuana available in the United States has a THC content of less than one percent. . . However, in smoking marijuana, the usual method of taking it in this country, the user can self-titrate, or control the amount taken in, since the effect builds up gradually." [2]

Higher potency marijuana was available in the United States at this time. In 1973 Gabriel Nahas reports that the THC content of drug-type cannabis ranges from 3.4 to 4.8%. [3] 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. . . has a THC content of 4 to 8 percent." [4]

In 2001 the Department of Health and Human Services reported that: "In the usual mixture of leaves and stems distributed as marijuana, the concentration of delta-9-THC ranges from 0.3 to 4.0 percent by weight. However, specially grown and selected marijuana can contain 15 percent or even more delta-9-THC." [5] In 2001 HHS also reported that: "An experienced marijuana smoker can titrate and regulate the dose to obtain the desired acute psychological effects and to avoid overdose and/or minimize undesired effects." [6]

**Variability of Effects Upon Different Individuals (1975, 2001)**

The *Ravin* Court reported in 1975 that: "Scientific testimony on the physiological and psychological effects of marijuana on humans generally stresses the variability of effects upon different individuals and on any one

individual at different times. The setting and psychological state of the user can affect his responses. Responses also vary with the amount of marijuana one has used in the past. A new user, for instance, often feels no effects at all."

In 2001 HHS reported that: " A smoker's experience is likely an important determinant of the dose that is actually absorbed. Venous blood levels of delta-9-THC or other cannabinoids correlate poorly with intensity of effects and character of intoxication." [7]

#### **Tolerance to Marijuana (1993, 1999)**

In 1993 Miles Herkenham and his team observed that: "[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 . . . tolerance to most psychoactive and physiological effects does occur in humans when high doses are administered daily." [8]

According to the 1999 Institute of Medicine report: "Tolerance to most of the effects of marijuana can develop rapidly after only a few doses, and it also disappears rapidly. Tolerance to large doses has been found to persist in experimental animals for long periods after cessation of drug use. Performance impairment is less among people who use marijuana heavily than it is among those who use marijuana only occasionally." [9]

#### **National Research Council (1982): Description of 1982 IOM Study**

The Institute of Medicine (IOM) of the National Academy of Sciences has conducted a 15-month study of tire health-related effects of marijuana, at the request of the Secretary of Health and Human Services and the

Director of the National Institutes of Health. The IOM appointed a 22-member committee to:

- \* analyze existing scientific evidence bearing on the possible hazards to the health and safety of users of marijuana;
- \* analyze data concerning the possible therapeutic value and health benefits of marijuana;
- \* assess federal research programs in marijuana;
- \* identify promising new research directions, and make suggestions to improve the quality and usefulness of future research; and
- \* draw conclusions from this review that would accurately assess the limits of present knowledge and thereby provide a factual, scientific basis for the development of future government policy.

This assessment of knowledge of the health-related effects of marijuana is important and timely because marijuana is now the most widely used of all the illicit drugs available in the United States. In 1979, more than 50 million persons had tried it at least once. There has been a steep rise in its use during the past decade, particularly among adolescents and young adults, although there has been a leveling-off in its overall use among high school seniors in the past 2 or 3 years and a small decline in the percentage of seniors who use it frequently.

#### **Marijuana Use (2002)**

In 2002 the National Survey on Drug Use and Health reported that 95 million Americans have used marijuana at least once, including 54% of adults age 18 to 25. In 2002 the National Survey on Drug Use reported that 12.2% of past year marijuana users used the drug daily or almost daily, approximately 3.1 million users, or 3.2% of all individuals who have tried marijuana at least once in their lifetime.

### **National Research Council (1982): Concern over Daily Marijuana Use**

Although substantially more high school students have used alcohol than have ever used marijuana, more high school seniors use marijuana on a daily or near-daily basis (9 percent) than alcohol (6 percent).

### **Comparison of Monthly Marijuana Use in 1975 and 2001**

The Ravin Court noted in 1975 that: "The most serious risk to the public health discerned by the [1972] National Commission [on Marijuana and Drug Abuse] is the possibility of an increase in the number of heavy users, who now constitute about 2% (500,000) of those who have used the drug. Within this group certain emotional changes have been observed among "predisposed individuals" as a result of prolonged heavy use. This group seems to carry the highest risk, particularly in view of the risk of retarding social adjustment among adolescents if heavy use should grow."

According to the 1976 Sourcebook of Criminal Justice Statistics 5% of the population in 1975 were current (monthly) marijuana users.<sup>9</sup> According to the National Survey on Drug Use and Health in 2001 monthly marijuana use was reported by 5.4% of the population age 12 to 17.. [11]

### **National Research Council (1982): Reasons for Concern Over Heavy Marijuana Use**

Much of the heavy use of marijuana, unlike alcohol, takes place in school, where effects on behavior, cognition, and psychomotor performance can be particularly disturbing. Unlike alcohol, which is rapidly metabolized and eliminated from the body, the psychoactive components of marijuana

persist in the body for a long time. Similar to alcohol, continued use of marijuana may cause tolerance and dependence. For all these reasons, it is imperative that we have reliable and detailed information about the effects of marijuana use on health, both in the long and short term.

What, then, did we learn from our review of the published scientific literature? Numerous acute effects have been described in animals, in isolated cells and tissues, and in studies of human volunteers; clinical and epidemiological observations also have been reported. This information is briefly summarized in the following paragraphs.

### **National Research Council (1982): Effects On The Nervous System And On Behavior**

We can say with confidence that marijuana produces acute effects on the brain, including chemical and electrophysiological changes. Its most clearly established acute effects are on mental functions and behavior. With a severity directly related to dose, marijuana impairs motor coordination and affects tracking ability and sensory and perceptual functions important for safe driving and the operation of other machines; it also impairs short-term memory and slow learning. Other acute effects include feelings of euphoria and other mood changes, but there also are disturbing mental phenomena, such as brief periods of anxiety, confusion, or psychosis.

### **Marijuana, Driving, and Psychomotor Performance (1998 - 1999)**

Hollister's conclusion in 1998 was that: "Cannabis alone does not contribute substantially to automobile accidents. Alcohol, much more widely used, remains the main culprit. By and large use of cannabis preceding driving should be discouraged. The old admonition, 'If you

drink, don't drive' applies fully to cannabis use." [12]

The Institute of Medicine reported in 1999 that "Marijuana administration has been reported to affect psychomotor performance on a number of tasks. . . Cognitive impairments associated with acutely administered marijuana limit the activities that people would be able to do safely or productively. For example, no one under the influence of marijuana or THC should drive a vehicle or operate potentially dangerous equipment." [13]

The Institute of Medicine reported in 1999 that: "For most people the primary adverse effect of acute marijuana use is diminished psychomotor performance. It is, therefore, inadvisable to operate any vehicle or potentially dangerous equipment while under the influence of marijuana, THC, or any cannabinoid drug with comparable effects. In addition, a minority of marijuana users experience dysphoria, or unpleasant feelings.

#### **Adverse Mood Reactions to Marijuana (1999)**

The Institute of Medicine reported in 1999 that: "Although euphoria is the more common reaction to smoking marijuana, adverse mood reactions can occur. Such reactions occur most frequently in inexperienced users after large doses of smoked or oral marijuana. They usually disappear within hours and respond well to reassurance and a supportive environment. Anxiety and paranoia are the most common acute adverse reactions; others include panic, depression, dysphoria, depersonalization, delusions, illusions, and hallucinations. Of regular marijuana smokers, 17% report that they have experienced at least one of the symptoms, usually early in their use of marijuana. Those observations are

particularly relevant for the use of medical marijuana in people who have not previously used marijuana." [14]

#### **National Research Council (1982): Marijuana Effects on the Brain**

There is not yet any conclusive evidence as to whether prolonged use of marijuana causes permanent changes in the nervous system or sustained impairment of brain function and behavior in human beings. In a few unconfirmed studies in experimental animals, impairment of learning and changes in electrical brain-wave recordings have been observed several months after the cessation of chronic administration of marijuana. In the judgment of the committee, widely cited studies purporting to demonstrate that marijuana affects the gross and microscopic structure of the human or monkey brain are not convincing; much more work is needed to settle this important point.

#### **Marijuana and the Brain (1998, 1999)**

Hollister concluded in 1998 that "the notion of a specific 'cannabis psychosis' has found no support . . . it remains unclear whether chronic use of cannabis might precipitate an episode of schizophrenia in persons predisposed to that disorder." [15]

The Institute of Medicine reported in 1999 that: " A major question remains as to whether marijuana can produce lasting mood disorders or psychotic disorders, such as schizophrenia. . . . Hollister suggests that, because of the varied nature of the psychotic states induced by marijuana, there is no specific "marijuana psychosis." Rather, the marijuana experience might trigger latent psychopathology of many types. More recently, Hall and colleagues concluded that "there is reasonable evidence that heavy cannabis use, and perhaps acute use in sensitive individuals, can produce an acute

psychosis in which confusion, amnesia, delusions, hallucinations, anxiety, agitation and hypomanic symptoms predominate." Regardless of which of those interpretations is correct. . . there is little evidence that marijuana alone produces a psychosis that persists after the period of intoxication." [16]

**National Research Council (1982): Chronic Use, Stepping Stone Hypothesis, and the Amotivational Syndrome.**

Chronic relatively heavy use of marijuana is associated with behavioral dysfunction and mental disorders in human beings, but available evidence does not establish if marijuana use under these circumstances is a cause or a result of the mental condition. There are similar problems in interpreting the evidence linking the use of marijuana to subsequent use of other illicit drugs, such as heroin or cocaine. Association does not prove a causal relation, and the use of marijuana may merely be symptomatic of an underlying disposition to use psychoactive drugs rather than a "stepping stone" to involvement with more dangerous substances. It is also difficult to sort out the relationship between use of marijuana and the complex symptoms known as the amotivational syndrome. Self-selection and effects of the drug are probably both contributing to the motivational problems seen in some chronic users of marijuana.

**Marijuana and Lack of Motivation (1998, 1999)**

Hollister reported in 1998 that "Loss of initiative and motivation have been observed clinically among chronic users of cannabis. It is doubtful that such a syndrome is unique to cannabis rather it might be expected from intoxication with any sedative drug, such as alcohol. Thus it has been difficult to establish that any decrease in motivation among chronic users of cannabis is due to drug use

per se." [17]

The Institute of Medicine reported in 1999 that: " One of the more controversial effects claimed for marijuana is the production of an "amotivational syndrome." This syndrome is not a medical diagnosis, but it has been used to describe young people who drop out of social activities and show little interest in school, work, or other goal-directed activity. When heavy marijuana use accompanies these symptoms, the drug is often cited as the cause, but no convincing data demonstrate a causal relationship between marijuana smoking and these behavioral characteristics. It is not enough to observe that a chronic marijuana user lacks motivation. Instead, relevant personality traits and behavior of subjects must be assessed before and after the subject becomes a heavy marijuana user." [18]

**Marijuana and the Gateway Theory (1999)**

The Institute of Medicine reported in 1999 that: "Many of the data on which the gateway theory is based do not measure dependence; instead, they measure use--even once-only use. Thus, they show only that marijuana users are more likely to use other illicit drugs (even if only once) than are people who never use marijuana, not that they become dependent or even frequent users. The authors of these studies are careful to point out that their data should not be used as evidence of an inexorable causal progression; rather they note that identifying stage-based user groups makes it possible to identify the specific risk factors that predict movement from one stage of drug use to the next--the real issue in the gateway discussion" [19]

"In the sense that marijuana use typically precedes rather than follows initiation into the use of other illicit drugs, it is indeed a gateway drug. However, it does not appear

to be a gateway drug to the extent that it is the cause or even that it is the most significant predictor of serious drug abuse; that is, care must be taken not to attribute cause to association. The most consistent predictors of serious drug use appear to be the intensity of marijuana use and co-occurring psychiatric disorders or a family history of psychopathology (including alcoholism)." [20]

#### **Marijuana and Dependency (1998, 1999)**

Hollister concluded in 1998 that "THC is not self-administered by animals, the usual case with dependence-producing drugs. Some degree of tolerance, dependence, and mild withdrawal symptoms has been reported. On the whole, these alterations are much less prominent than those associated with licit social drugs such as alcohol or nicotine." [21]

The Institute of Medicine reported in 1999 that: "Few marijuana users become dependent on it, but those who do encounter problems similar to those associated with dependence on other drugs. Dependence appears to be less severe among people who use only marijuana than among those who abuse cocaine or those who abuse marijuana with other drugs (including alcohol)." [22]

#### **National Research Council (1982): Conclusions on Marijuana's Long Term Effects**

Thus, the long-term effects of marijuana on the human brain and on human behavior remain to be defined. Although we have no convincing evidence thus far of any effects persisting in human beings after cessation of drug use, there may well be subtle but important physical and psychological consequences that have not been recognized.

#### **National Research Council (1982): Effects**

#### **On The Cardiovascular And Respiratory Systems**

There is good evidence that the smoking of marijuana usually causes acute changes in the heart and circulation that are characteristic of stress, but there' is no evidence to indicate that a permanently deleterious effect on the normal cardiovascular system occurs. There is good evidence to show that marijuana increases the work of the heart, usually by raising heart rate and, in some persons, by raising blood pressure. This rise in workload poses a threat to patients with hypertension, cerebrovascular disease, and coronary atherosclerosis.

Acute exposure to marijuana smoke generally elicits broncho-dilation; chronic heavy smoking of marijuana causes inflammation and pre-neoplastic changes in the airways, similar to those produced by smoking of tobacco. Marijuana smoke is a complex mixture that not only has many chemical components (including carbon monoxide and "tar") and biological effects similar to those of tobacco smoke, but also some unique ingredients. This suggests the strong possibility that prolonged heavy smoking of marijuana, like tobacco, will lead to cancer of the respiratory tract and to serious impairment of lung function. Although there is evidence of impaired lung function in chronic smokers, no direct confirmation of the likelihood of cancer has yet been provided, possibly because marijuana has been widely smoked in this country for only about 20 years, and data have not been collected systematically in other countries with a much longer history of heavy marijuana use.

#### **Chronic Effects of Marijuana (1999)**

The Institute of Medicine reported in 1999 that : "The chronic effects of marijuana

are of greater concern for medical use and fall into two categories: the effects of chronic smoking and the effects of THC. Marijuana smoking is associated with abnormalities of cells lining the human respiratory tract. Marijuana smoke, like tobacco smoke, is associated with increased risk of cancer, lung damage, and poor pregnancy outcomes. Although cellular, genetic, and human studies all suggest that marijuana smoke is an important risk factor for the development of respiratory cancer, proof that habitual marijuana smoking does or does not cause cancer awaits the results of well-designed studies." [23]

#### **National Research Council (1982): Effects On The Reproductive System And On Chromosomes**

Although studies in animals have shown that delta-9-THC (the major psychoactive constituent of marijuana) lowers the concentration in blood serum of pituitary hormones (gonadotropins) that control reproductive functions, it is not known if there is a direct effect on reproductive tissues. Delta-9-THC appears to have a modest reversible suppressive effect on sperm production in men, but there is no proof that it has a deleterious effect on male fertility. Effects on human female hormonal function have been reported, but the evidence is not convincing. However, there is convincing evidence that marijuana interferes with ovulation in female monkeys. No satisfactory studies of the relation between use of marijuana and female fertility and child-bearing have been carried out. Although delta-9-THC is known to cross the placenta readily and to cause birth defects when administered in large doses to experimental animals, no adequate clinical studies have been carried out to determine if marijuana use can harm the human fetus. There is no conclusive evidence of teratogenicity in human offspring, but a slowly developing or

low-level effect might be undetected by the studies done so far. The effects of marijuana on reproductive function and on the fetus are unclear; they may prove to be negligible, but further research to establish or rule out such effects would be of great importance.

Extracts from marijuana smoke particulates ("tar") have been found to produce dose-related mutations in bacteria; however, delta-9-THC, by itself, is not mutagenic. Marijuana and delta-9-THC do not appear to break chromosomes, but marijuana may affect chromosome segregation during cell division, resulting in an abnormal number of chromosomes in daughter cells. Although these results are of concern, their clinical significance is unknown.

#### **Marijuana and Cellular Abnormalities (1998)**

According to a 1998 review by Leo Hollister: "Many older concerns about adverse effects on health (chromosomal damage, cannabinol psychosis, endocrine abnormalities, cardiac events, impaired immunity) no longer seem to elicit much interest. . . it appears that [reported adverse effects] have been limited to somatic cells where the clinical consequences might be quite subtle and not easily detected. . . Chromosomal damage has not been studied further. The aberrations previously noted are common to other widely-used drugs and seem to be of no clinical significance." [24]

#### **National Research Council (1982): The Immune System**

Similar limitations exist in our understanding of the effects of marijuana on other body systems. For example, some studies of the immune system demonstrate a mild, immunosuppressant effect on human beings, but other studies show no effect.



### **Marijuana and the Immune System (1998, 1999)**

Hollister also concludes that "Adverse effects on the immune system have neither accelerated the progress of AIDS nor have they had any other clinical significance." [25] The Institute of Medicine also reported in 1999 that: "Cannabinoids, especially THC, can modulate the function of immune cells in various ways--in some cases enhancing and in others diminishing the immune response . . . . Although the chronic effects of cannabinoids on the immune system have not been studied, based on acute exposure studies in experimental animals it appears that THC concentrations that modulate immunological responses are higher than those required for psycho-activity." [26]

Hollister also reported that "Endocrine abnormalities, both in men and women, were previously reported but not investigated further. Their clinical significance is also questionable." [27] However Hollister also concluded that "Marijuana use during pregnancy results in shorter and smaller offspring, similar to the effects of tobacco smoking." [28] The Institute of Medicine also reported in 1999 that : "THC inhibits reproductive functions. However, studies of men and women who use marijuana regularly have yielded conflicting results and show either depression of reproductive hormones, no effect, or only a short-term effect. . . . In brief, although there are no data on fertility itself, marijuana or THC would probably decrease human fertility--at least in the short term--for both men and women. And it is reasonable to predict that THC can interfere with early pregnancy, particularly with implantation of the embryo. Like tobacco smoke, marijuana smoke is highly likely to be harmful to fetal development and should be avoided by pregnant women and those who might become pregnant in the

near future." [29]

The 1999 IOM report concluded that: "the short-term immunosuppressive effects are not well established but, if they exist, are not likely great enough to preclude a legitimate medical use." [30]

### **National Research Council (1982): Therapeutic Potential Of Marijuana**

The committee also has examined the evidence on the therapeutic effects of marijuana in a variety of medical disorders. Preliminary studies suggest that marijuana and its derivatives or analogues might be useful in the treatment of the raised intraocular pressure of glaucoma. in the control of the severe nausea and vomiting caused by cancer chemotherapy, and in the treatment of asthma. There also is some preliminary evidence that a marijuana constituent (cannabidiol) might be helpful in the treatment of certain types of epileptic seizures. as well as for spastic disorders and other nervous system diseases. But in these and all other conditions much more work is needed. Because marijuana and delta-9-THC often produce troublesome psychotropic or cardiovascular side-effects that limit their therapeutic usefulness, particularly in older patients, the greatest therapeutic potential probably lies in the use of synthetic analogues of marijuana derivatives with higher ratios of therapeutic to undesirable effects.

### **Institute of Medicine (1999): Medical Value of Marijuana**

"The argument against the future of smoked marijuana for treating any condition is not that there is no reason to predict efficacy but that there is risk. . .

"Patients who are currently suffering from debilitating conditions unrelieved by legally

available drugs, and who might find relief with smoked marijuana, will find little comfort in a promise of a better drug 10 years from now . . . This presents a policy issue that must weight - at least temporarily- the needs of individual patients against broader social issues. . .

"Scientific data indicate that the potential therapeutic value of cannabinoid drugs, primarily THC, for pain relief, control of nausea and vomiting, and appetite stimulation; smoked marijuana, however, is a crude THC delivery system that also delivers harmful substances." [31]

#### **National Research Council (1982): The Need For More Research On Marijuana**

The explanation for all of these unanswered questions 'is insufficient research. We need to know much more about the metabolism of the various marijuana chemical compounds and their biologic effects. This will require many more studies in animals, with particular emphasis on subhuman primates. Basic pharmacologic information obtained in animal experiments will ultimately have to be tested in clinical studies on human beings.

Until 10 or 15 years ago, there was virtually no systematic, rigorously controlled research on the human health-related effects of marijuana and its major constituents. Even now, when standardized marijuana and pure synthetic cannabinoids are available for experimental studies, and good qualitative methods exist for the measurement of delta-9-THC and its metabolites in body fluids. Well-designed studies on human beings are relatively few. There are difficulties in studying the clinical effects of marijuana in human beings, particularly the effects of long-term use. And yet, without such studies the debate about the safety or hazard of marijuana will remain unresolved.

Prospective cohort studies, as well as retrospective case-control studies, would be useful in identifying long-term behavioral and biological consequences of marijuana use.

The federal investment in research on the health-related effects of marijuana has been small, both in relation to the expenditure on other illicit drugs and in absolute terms. The committee considers the research particularly inadequate when viewed in light of the extent of marijuana use in this country, especially by young people. We believe there should be a greater investment in research on marijuana, and that investigator-initiated research grants should be the primary vehicle of support.

The committee considers all of the areas of research on marijuana that are supported by the National Institute on Drug Abuse to be important, but we did not judge the appropriateness of the allocation of resources among those areas, other than to conclude that then' should be increased emphasis on studies in human beings 'and other primates. Recommendations for future research are presented at the end of Chapters 1-7 of this report.

#### **National Research Council (1982): Conclusions**

The scientific evidence published to date indicates that marijuana has a broad range of psychological and biological effects, some of which, at least under certain conditions, are harmful to human health. Unfortunately, the available information does not tell us how serious this risk may be.

The major conclusion is that what little we know for certain about the effects of marijuana on human health--and all that we have reason to suspect--justifies serious national concern. Of no less concern is the

extent of our ignorance about many of the most basic and important questions about the drug. Our major recommendation is that there be a greatly intensified and more comprehensive program of research into the effects of marijuana on the health of the American people.

**Notes:**

[1] Institute of Medicine. (1999) Janet E. Joy, Stanley J. Watson, Jr., and John A. Benson, Jr., Editors. Marijuana and Medicine, Assessing the Science Base. Washington, D.C.: National Academy Press. pgs. 83-84. <http://www.nap.edu/>

[2] Ravin v. State of Alaska. 537 P.2d 494 (Alaska, 1975). <http://www.druglibrary.org/schaffer/legal/11970/ravin.htm>

[3] Nahas, G., Marihuana-Deceptive Weed. New York: Raven Press, 1973. pg. 78.

[4] Langer, J. Drugs of Abuse. Drug Enforcement Magazine. Spring, 1975. Vol. 2, No. 2. pg. 8-33. pg. 27.

[5] Department of Health and Human Services. Notice of Denial of Petition. Federal Register Vol. 66. pg 20045. April 18, 2001. <http://www.gpoaccess.gov/fr/index.html>

[6] Department of Health and Human Services. Notice of Denial of Petition. Federal Register Vol. 66. pg 20046. April 18, 2001. <http://www.gpoaccess.gov/fr/index.html>

[7] Department of Health and Human Services. Notice of Denial of Petition. Federal Register Vol. 66. pg 20046. April 18, 2001. <http://www.gpoaccess.gov/fr/index.html>

[8] Oviedo, A., Glowa, J, and Herkenham, M. (1993), "Chronic cannabinoid administration alters cannabinoid receptor binding in rat brain: a quantitative autoradiographic study." Brain Research, 616:293-302. pg 293.

[9] Institute of Medicine (1999) pg 89.

[10] Bureau of Justice Statistics. Sourcebook of Criminal Justice Statistics - 1975. Table 3.3. Pg 166.

[11] Results from the 2002 National Survey on Drug Use and Health: National Findings (Office of Applied Studies [OAS], 2003. <http://www.samhsa.gov/oas/nhsda.htm#NHSDAinfo>

[12] Hollister, L.E. (1998) Health Aspects of Cannabis: Revisited. Int J Neuropsychopharmacol. 1998 Jul;1(1):71-80. pg 77.

[13] Institute of Medicine (1999) pg 107.

[14] Institute of Medicine (1999) pg 84.

[15] Hollister (1998) pg 76.

[16] Institute of Medicine (1999) pgs 105-106.

[17] Hollister (1998) pg 74.

[18] Institute of Medicine (1999) pgs 107-108.

[19] Institute of Medicine (1999) pg 100.

[20] Institute of Medicine (1999) pgs 100-101.

[21] Hollister (1998) pg 77.

[22] Institute of Medicine (1999) pgs 96-97.

[23] Institute of Medicine. (1999) pg 5.

[24] Hollister (1998). Pgs. 71, 76.

[25] Hollister (1998) Pg. 76.

[26] Institute of Medicine (1999) Pg 59.

[27] Hollister (1998) Pg. 76.

[28] Hollister (1998) Pg. 77.

[29] Institute of Medicine (1999) Pg 123.

[30] Institute of Medicine (1999) pg. 5.

[31] Institute of Medicine (1999) pg 178 - 179.