



Testimony
Before the House Committee on Government Reform
Subcommittee on Criminal Justice, Drug Policy and
Human Resources
United States House of Representatives

**Marijuana and Medicine: The Need for a
Science-Based Approach**

Statement of
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Chairman Souder and Members of the Subcommittee, thank you for inviting the National Institute on Drug Abuse (NIDA), a component of the National Institutes of Health, to participate in this important hearing. As the world's largest supporter of biomedical research on drug abuse and addiction, we have learned much about the behavioral and health effects of marijuana over the past 15 years. Additionally, we have a greater understanding of how marijuana and other drugs of abuse affect the brain. I am pleased to be here with my colleagues to present what the science has taught us about marijuana, the health consequences associated with its use, as well as to briefly describe the role that NIDA and the Department play in supporting research on the potential medical uses for marijuana and its constituents.

MARIJUANA OVERVIEW

I would like to begin this afternoon by providing a quick overview of our Nation's most commonly used illicit drug, marijuana. As we all know, marijuana is not a new drug. It has been around and used for thousands of years. In fact, more than 95 million Americans (40 percent) age 12 and older have tried marijuana at least once, according to the 2002 National Survey on Drug Use and Health (NSDUH). In 2000, among the 1.5 million adult substance abuse treatment admissions (age 18 or older), 154,400 were admitted as primary marijuana abusers.

Marijuana is also not just a single drug—it is a mixture of dried flowering leaves from the hemp plant *cannabis sativa*. It contains more than 400 chemicals. Over 60 of these chemicals are referred to as cannabinoids. Delta-9-tetrahydrocannabinol or (THC) is the main psychoactive cannabinoid or ingredient in marijuana and the one that causes intoxication.

Scientists have learned a great deal about how THC acts in the brain to produce its many effects. When someone smokes marijuana, THC rapidly passes from the lungs into the bloodstream, which carries the chemical to organs throughout the body, including the brain. In the brain, THC connects to specific sites called *cannabinoid receptors* on nerve cells and thereby influences the activity of those cells. Some brain areas have many cannabinoid receptors; others have few or none. Most cannabinoid receptors are found in the parts of the brain that influence pleasure, memory, thought, concentration, sensory and time perception, and coordinated movement. Recently researchers have also found that cannabinoid receptors are found outside the brain. The newly discovered cannabinoid 2 receptors, for example, are found mostly in areas associated with immune function.

HEALTH EFFECTS OF MARIJUANA

There are numerous deleterious health consequences associated with short and long-term marijuana use, including the possibility of becoming addicted. During the period of intoxication, marijuana disrupts short-term memory, attention, judgment, as well as other cognitive functions. In addition, marijuana has also been shown to impair coordination and balance, and can increase an individual's heart rate. Longer lasting cognitive deficits have been reported in heavy marijuana users, although these have been shown to be reversible following a period of sustained abstinence. New research published last year shows that those who engage in a lifetime of heavy marijuana use reported an overall dissatisfaction with their mental and physical health as well as their life achievement.

Recently we have learned that there is in fact a marijuana withdrawal syndrome that can last several days to a week following abstinence. This syndrome is characterized by increased anxiety, increased drug craving, sleep difficulties, and decreased appetite. It is very similar to the withdrawal that many users report after abstaining from nicotine and may explain why quitting marijuana can be difficult for some.

New research is also showing us that marijuana can affect almost every organ in the body, from the central nervous system to the cardiovascular, endocrine, respiratory/pulmonary, and immune systems. Because marijuana is typically rolled into a cigarette or “joint” and smoked, it has been shown to greatly impact the respiratory system and increases the likelihood of some cancers. Marijuana users typically inhale more deeply and hold their breath longer than tobacco smokers do, exposing them to the 50 percent to 70 percent more carcinogenic hydrocarbons than tobacco smoke has. Also, animal studies show us that THC can impair the immune system's ability to fight off infectious diseases thus increasing the likelihood of adverse health consequences. In humans however, the overall effect on the immune system is not clear. One clinical study on short-term exposure (21 day) to marijuana cigarettes in HIV-infected adults who were on a stable antiretroviral regimen did not find an effect of marijuana on the immune system in this population. Whether marijuana exerts significant immune effects when administered over long periods of time has not been studied.

Also, we are finding that early exposure to marijuana is associated with an increased likelihood of a lifetime of subsequent drug problems. A study, published last year in the Journal of the American Medical Association of over 300 fraternal and identical twin pairs, who differed on whether or not they used marijuana before the age of 17, found that those who had used marijuana early had elevated rates of other drug use and drug problems later on, compared to their twin who did not use marijuana before age 17.

Finally, there are also some known subtle effects associated with children born to mothers who used marijuana frequently while pregnant. An ongoing longitudinal study that has been investigating the consequences of prenatal exposure to marijuana, for example, recently published results in this now

adolescent aged population and found that prenatal exposure was associated with worse performance on tasks that required visual memory, analysis, and integration.

**RESEARCH ON MEDICAL USES OF MARIJUANA:
TWO SIGNIFICANT REPORTS BY THE NIH AND IOM**

Marijuana is currently listed as a Schedule I drug. Schedule I under the Controlled Substances Act means that the drug has a high potential for abuse and that there is no current accepted medical use in the United States. However, there continue to be claims about the potential medical uses of marijuana, particularly smoked marijuana. THC, the main active ingredient in marijuana, produces effects that can be useful for treating several medical conditions. Several early studies supported by NIH to examine claims, for example, that marijuana relieved the nausea and vomiting accompanying cancer chemotherapy, have in fact led to the FDA approval of a synthetic form of oral THC for nausea associated with cancer chemotherapy. More recently, the FDA has approved oral THC for treatment of AIDS wasting.

There have been at least two exhaustive and comprehensive reports written in the past decade regarding the medical potential of marijuana by the National Institutes of Health (NIH) and the Institute of Medicine (IOM). In February 1997, the NIH convened a panel of eight non-federal experts in fields such as cancer treatment, infectious diseases, neurology, and ophthalmology for a two-day meeting to examine the extant research on the medical uses of marijuana and its active constituents, primarily THC. In 1999, the Office of National Drug Control Policy commissioned the IOM to do an exhaustive study as well. “Marijuana and Medicine: Assessing the Science Base” was published in 1999.

Both reports found that there are too few scientific studies to determine marijuana’s therapeutic utility, but that research is justified into marijuana’s use for certain conditions or diseases including

pain, neurological and movement disorders, nausea in patients who are undergoing chemotherapy for cancer, and loss of appetite and weight (cachexia) related to AIDS.

The reports noted that there is greater promise in purifying the active constituents of marijuana and developing alternate delivery systems, such as inhalers, rather than studying smoked marijuana. The reports also noted that alternative FDA-approved medications already exist for treatment of the majority of proposed uses of smoked marijuana. For example, synthetic oral forms of THC, the major active ingredient in marijuana, have been approved by the FDA for use by patients undergoing chemotherapy and by patients with AIDS.

FACILITATING RESEARCH ON THE MEDICAL USES OF MARIJUANA

Additional research on the possible medical uses of marijuana and its constituents has continued since these reports were issued. The NIH has continued to accept proposals to investigate potential therapeutic uses of marijuana through its peer review process, and those that are scientifically meritorious have been considered for funding. Since the Reports by the IOM and NIH have been written, there have been two studies that have been supported by the NIH. One study looked at the effects of smoked marijuana on HIV levels and appetite and reducing weight loss associated with HIV-related wasting syndrome. Another ongoing study is looking at the effects of THC (smoked marijuana and oral) in individuals who have the human immunodeficiency virus infection (HIV+) with unintended weight loss (<90 percent body cell mass/height). In addition to studying food intake and body composition, they are also studying mood and physical symptoms (e.g. nausea stomach pain), psychomotor task performance and sleep to determine the specificity of the drug effects on food intake in relation to other behaviors.

In May 1999, the Department announced it would create a new mechanism to provide research-grade marijuana not only for NIH-funded research but also for scientifically valid research that is funded by other sources. A multi-agency Public Health Service (PHS) committee now reviews non-NIH funded studies and assesses them both for scientific quality and the likelihood that they will yield data on possible benefits.

After the PHS committee approves a study, the researcher applies for an Investigational New Drug Application (IND) from the FDA and must also obtain a DEA registration number for Schedule I substances. When these are obtained, NIH provides research-grade marijuana for the project on a reimbursable basis (researchers reimburse NIDA's contractor for the costs of growing and producing the research-grade marijuana). Since NIDA's inception in 1974, it has been the administrator of a contract to grow marijuana for research purposes on behalf of the US government. In this way, NIH is able to produce and supply research-grade marijuana for a variety of clinical studies that would not otherwise be possible.

Most of the research approved by the PHS committee so far is sponsored by the Center for Medicinal Cannabis Research at the University of California in San Diego, a state funded research center. Currently there are 17 pre-clinical or clinical studies that have been approved by HHS for this Center. Topics to be covered include cannabis for spasticity/tremors in multiple sclerosis patients, sleep disorders, CD4 immunity in AIDS, and for neuropathic pain. This represents a substantial increase in scientifically valid research studies involving marijuana.

THE PROMISE OF RESEARCH

Researchers have made much progress in the past 15 years in understanding how marijuana exerts its effects. In fact, the support of basic research on marijuana led to the discovery of the endogenous cannabinoid system. Since 1988, scientists have discovered two major classes of

cannabinoid receptors, one that is mostly found in the brain, “CB1,” and “CB2,” which is not in the central nervous system and is predominantly found on immune system cells. This cannabinoid system is involved in a number of physiological functions, including pain regulation, appetite, movement and motor function, memory, as well as its role in marijuana’s abuse liability and addiction.

These breakthroughs have led to research advances and medicinal developments at a rapid pace. The presence of this newly discovered receptor system in the brain circuitry controlling learning and memory is yielding new insights into how marijuana disrupts memory traces. Additionally, recent research shows that there are connections between the cannabinoid system and the neuronal processes connected with relapse to cocaine abuse, lending further support to the commonality in the brain processes mediating addiction.

The discovery and characterization of the cannabinoid receptors has allowed scientists to begin to develop potential medications to treat a variety of ailments, including obesity, pain, and addictive disorders. In 1994, researchers produced the first CB1-specific cannabinoid receptor antagonist, SR141716, (now called Rimonabant) which is able to block THC’s ability to activate the CB1 receptor. Preclinical and clinical research suggests that Rimonabant blocks the subjective high elicited by marijuana and may also be useful in preventing relapse to other drug use. Two large clinical trials supported by the pharmaceutical industry also have found that Rimonabant may help people lose weight and stop smoking.

Today marijuana-related research continues to yield valuable insights into the effects of THC on critical brain functions, such as cognition and memory, the role of the drug’s receptor system in addiction and relapse, as well as insights into the treatment of marijuana addiction and the potential role of cannabinoid-based medications in treating a variety of medical conditions. Finally, these insights are

leading us to an overall greater understanding of neurobiology, memory, and immunity. They also provide us with proven strategies that can be employed to help us elucidate other systems.

CONCLUSION

Marijuana is not a benign drug. It is illegal and has significant adverse health and social consequences associated with its use. Given the fairly recent discovery of the endogenous cannabinoid system and the tremendous science advances that followed, the development of useful cannabinoid-based medicines is an important area of investigation that should prove fruitful for a variety of health conditions. However, the use of smoked marijuana as a medicine is problematic due to its adverse health consequences and the inherent difficulties with respect to accurate dosing and the purity of the formulation. Approval for the use of marijuana, or perhaps more importantly purified compounds based upon the chemicals found in marijuana, as therapeutic agents must show substantial evidence of effectiveness and show the product is safe under the conditions of use in the proposed labeling. Safe, in this context, means that the benefits of the drug appear to outweigh its risks.

Thank you for allowing me to share this information with you. I will be happy to answer any questions you may have.