

Background and Research

**Marijuana Rescheduling**

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For Oregon Board of Pharmacy  
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During the 2009 Legislative Session, the Oregon State Legislature passed SB 728 into law requiring the Oregon Board of Pharmacy to reschedule Marijuana from a Schedule I controlled substance to a Schedule II through V controlled substance. The law also directs the Oregon Board of Pharmacy to reschedule Methamphetamine from a Schedule II controlled substance to a Schedule I controlled substance. Additionally, the law specifies that anyone illegally manufacturing or delivering a controlled substance in Schedule I as being guilty of a Class A felony, anyone manufacturing or delivering a controlled substance in Schedule II as being guilty of a Class B felony, anyone manufacturing or delivering a controlled substance in a Schedule III as guilty of a Class C felony, anyone manufacturing or delivering a controlled substance in the Schedule IV category as guilty of a Class B misdemeanor and anyone manufacturing or delivering a controlled substance in the Schedule V category as guilty of a Class C misdemeanor.

As directed, staff has collected background research to assist the Oregon Board of Pharmacy in making the determination of which Schedule, II through V, to place Marijuana. Special thanks are noted to the Oregon State Library staff for their assistance.

The extent of the guidance available from the Controlled Substance Act that speaks to scheduling of controlled substances, is included in the following information (Item A). This is followed by a series of articles that represent a sampling of the information available on marijuana in a variety of capacities. According to drug information experts, there is no clear guidance to be found in the literature that speaks to rescheduling of marijuana. Furthermore, because the product is not commercially available but is an herbal entity and therefore of variable strengths, from variable plant sources etc., there is no definitive scientific research to guide the Board's decision. However, the sampling of articles reflects available literature about the medical and therapeutic uses of marijuana and provides several references speaking about the legal and social aspects of marijuana use. The last article includes the recommendations to the Obama administration that illuminate the current administration's approach potentially related to this topic.

Finally, it is noteworthy that the Oregon Board of Pharmacy sent two participants to the National Boards of Pharmacy 2009 Symposium which featured several marijuana topics. Gary Schnabel, Executive Director and Ann Zweber, Board Member attended the symposium and may provide additional background and helpful input. Ann also serves on Representative Maurer's Marijuana- 2011 legislative workgroup.

## ITEM A

### Schedules of Controlled Substances

The drugs and drug products under the jurisdiction of the Controlled Substances Act (CSA) are divided into five schedules. Controlled substances in Schedules II-V have an accepted medical use in the United States, and Schedule I substances do not.  
(see--- <http://www.justice.gov/dea/pubs/csa/812.htm>)

Schedule I: high abuse potential and no accepted medical use in the United States

Schedule II: high abuse potential with severe psychological or physical dependence liability, have an accepted medical use in the United States, and are available by prescription

Schedule III: abuse potential which is less than those in Schedule II, but more than Schedule IV substances

Schedule IV: abuse potential which is less than those in Schedule III, but more than Schedule V substances

Schedule V: abuse potential less than those listed in Schedule IV

In determining into which schedule a drug or other substance should be placed, or whether a substance should be decontrolled or rescheduled, certain factors are required to be considered. Specific findings are not required for each factor. These factors are listed in Section 201 (c), [21 U.S.C. 811 (c)] of the CSA as follows: (see <http://www.justice.gov/dea/pubs/abuse/1-csa.htm>)

1. The drug's actual or relative potential for abuse.
2. Scientific evidence of the drug's pharmacological effects. The state of knowledge with respect to the effects of a specific drug is, of course, a major consideration. For example, it is vital to know whether or not a drug has a hallucinogenic effect if it is to be controlled due to that effect. The best available knowledge of the pharmacological properties of a drug should be considered.
3. The state of current scientific knowledge regarding the substance. Criteria (2) and (3) are closely related. However, (2) is primarily concerned with pharmacological effects and (3) deals with all scientific knowledge with respect to the substance.
4. Its history and current pattern of abuse. To determine whether or not a drug should be controlled, it is important to know the pattern of abuse of that substance, including the socio-economic characteristics of the segments of the population involved in such abuse.
5. The scope, duration, and significance of abuse. In evaluating existing abuse, the DEA Administrator must know not only the pattern of abuse, but whether the abuse is widespread. In reaching a decision, the Administrator should consider the economics of regulation and enforcement attendant to such a decision. In addition, the Administrator 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.
6. What, if any, risk there is to the public health. If a drug creates dangers to the public health, in addition to or because of its abuse potential, then these dangers must also be considered by the Administrator.
7. The drug's psychic or physiological dependence liability. There must be an assessment of the extent to which a drug is physically addictive or psychologically habit forming, if such information is known.
8. Whether the substance is an immediate precursor of a substance already controlled. The CSA allows inclusion of immediate precursors on this basis alone into the appropriate schedule and thus safeguards against possibilities of clandestine manufacture.

## ITEM B—Summary Statements of Example Articles

### Marijuana Therapeutics and Drug Properties

Seamon MJ, Fass JA, Maniscalco-Feichtl M, Abu-Shraie NA. Medical marijuana and the developing role of the pharmacist. *Am J Health-Syst Pharm.* 2007; 64:1037-44.

The term marijuana refers to the plant substance. It contains more than 460 active chemicals and over 60 unique cannabinoids. The inhalation and vaporization routes of administration result in the highest bloodstream levels most quickly. It is used therapeutically for serious, chronic, or debilitating medical conditions, including 1) severe nausea and vomiting, 2) weight loss associated with cancer chemotherapy and HIV infection, 3) spasticity secondary to neurological diseases, 4) pain syndromes, and 5) glaucoma. Marijuana may cause many different adverse effects including psychological dysfunction, cardiac affects, CNS (central nervous system) effects, seizures, and it is considered a gateway drug to other more harmful drug use. Additionally, marijuana smoke contains more carcinogens than cigarette smoke.

Robson P. Therapeutic aspects of cannabis and cannabinoids. *Br J Psychiatry.* 2001; 178:107-15.

The active component of marijuana is  $\Delta^9$  tetrahydrocannabinol (THC). THC affects two specific protein receptors, CB1, which is located in the CNS and CB2, which is located outside of the CNS. The specific mechanism of action is still unknown. A synthetic form of THC (dronabinol) is available in the United States as a controlled substance (schedule II). Nabilone is a synthetic THC analogue and is available as a schedule III drug. Marijuana has been shown to be beneficial in patients with various ailments, including spasticity due to multiple sclerosis, weight loss due to cancer and AIDS, chronic pain, increased intra-ocular pressure, insomnia, anxiety, and depression, epilepsy, and asthma. However, the therapeutic use of marijuana has been substantiated mainly by anecdotal reports, and well-organized clinical trials must be conducted to determine its place in therapy.

Herman RA, Bohling K. Scientific evidence for medical marijuana use. [From —Iowa Drug Information Network]

A collection of 95 studies of marijuana and its use in various disease states are outlined in this article.

Kumar RN, Chambers WA, Pertwee RG. Pharmacological actions and therapeutic uses of cannabis and cannabinoids. *Anaesthesia.* 2001;56:1059-1068.

Drug properties of marijuana are outlined in this article. The pharmacokinetics demonstrate rapid absorption with inhalation as opposed to slower absorption from ingestion. The brain concentration peak is met within 15 minutes as well as the psychological and physiological effects. These effects typically last 2-4 hours. Metabolism to the active metabolite, 11-hydroxy- $\Delta^9$ THC, which is more potent than  $\Delta^9$ THC, occurs in the liver. Chronic use has detrimental effects on several body systems, including the respiratory, immune, and reproductive systems. Dependence may develop in some individuals. Currently, marijuana is typically used for spasticity, pain, as an anti-emetic, for appetite stimulation, epilepsy, glaucoma, bronchial asthma, and mood disorders. An important issue that must be addressed prior to marijuana being introduced in the clinical practice is development of a more standardized formulation.

Hazekamp A. Cannabis Review. Department of Plant Metabolomics, Leiden, The Netherlands. 2008-2009.

Cannabis is one of the oldest known medicinal plants and has been extensively studied. Cannabinoids are considered to be the main biologically active constituents of the Cannabis plant. Most studies have focused on the effects of THC, the main cannabinoid contained in marijuana. Cannabinoid receptors can be found in most parts of the brain. The main problem in discussion about making cannabis or THC medicinally available is that the curative properties of cannabis/THC are mediated by the same receptors that cause its unwanted side effects. Additionally, cannabis is a highly variable product with respect to composition and (microbiological) contamination.

### **Legal and Social Aspects of Marijuana**

Pacula JL, Chriqui JF, Reichmann DA, Terry-McElrath Y. State medical marijuana laws: understanding the laws and their limitations. *ImpacTeen*, Research paper series, no. 13. October 2001.

Many states have laws about medical marijuana. States typically use one of four main ways to grant allowance for its use. Only one of these four is consistent with federal law. The four types of provisions that states allow medical marijuana to be used include therapeutic research programs, rescheduling laws, physician prescription laws, and medical necessity defense laws. There are three main dimensions that influence the nature of the state laws: 1) type of provision 2) illnesses and symptoms 3) supply of marijuana. Policy makers and advocates of marijuana use should note that the two biggest hurdles medical marijuana laws will have to clear are the recognition of a medical necessity defense in state courts and the creation of a legitimate supply mechanism for patients that does not result in increasing the use of recreational marijuana.

Raff L. Marijuana as medicine. *High Desert Pulse*. Summer/Fall 1999.

Obtaining medical marijuana, although allowed by Oregon state law, is difficult for patients due to the many laws and regulations. Some physicians are willing to allow patients access to this unique drug if they think the patient is in need of it. Physicians are aware that marijuana is not regulated and its source is unknown.

Aggarwal SK, Carter GT, Sullivan MD, ZumBrunnen C, et al. Medicinal use of cannabis in the United States: historical perspectives, current trends, and future directions. *J Opioid Manag.* 2009;5:153-168.

Marijuana use is increasing throughout the United States as more patients and providers are learning about the possible benefits. Studies have examined marijuana, however, variable conclusions have resulted. The drug has been shown to be relatively safe, especially compared to other pain medications. The correct method of providing access to this drug is still in debate.

Barthwell A. Marijuana dispensaries and the federal government: recommendations to the Obama administration 2009:

Crude herbal cannabis is not a medication. The Food and Drug Administration (FDA) approves only specific products for marketing and distribution to patients. These do not include pure active pharmaceutical ingredients, nor crude herbal substances. Only a finished dosage form containing a specific type of controlled substance can obtain FDA approval and become a prescription medication. This debate may serve as a step towards a dosage form that may deliver the active ingredients in the form a medication.