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The legal status of cannabis (marijuana) and cannabidiol (CBD) under U.S. law

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ABSTRACT

In the United States, federal and state laws regarding the medical use of cannabis and cannabinoids are in conflict and have led to confusion among patients, caregivers, and healthcare providers. Currently, cannabis is legal for medical purposes in 50% of the states, and another seventeen states allow products that are high in cannabidiol (CBD) and low in THC (tetrahydrocannabinol) for medical use. Many of these artisanal products are sold in dispensaries or over the internet. However, none of these products has been approved by the Food and Drug Administration (FDA). Understanding how federal laws apply to clinical research and practice can be challenging, and the complexity of these laws has resulted in particular confusion regarding the legal status of CBD. This paper provides an up-to-date overview (as of August 2016) of the legal aspects of cannabis and cannabidiol, including cultivation, manufacture, distribution, and use for medical purposes.

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1. Introduction

Since the 1996 enactment of the first state law allowing the medical use of cannabis, 25 states and the District of Columbia have enacted such laws; another 17 allow products that are high in cannabidiol (CBD) and low in THC (tetrahydrocannabinol). In the past several years, interest has focused on the therapeutic potential of CBD, one of the plant's major cannabinoids. Many cannabis and CBD products are available in dispensaries and over the internet. However, none of these artisanal preparations (irrespective of THC content) has been approved by the Food and Drug Administration (FDA) for safety or efficacy, and state laws requiring quality control are inconsistent and sometimes nonexistent. Controlled clinical trials are underway to investigate the use of CBD as a potential treatment for several types of seizure disorders.

Abbreviations: 8FA, 8-Factor Analysis; CBD, cannabidiol; CFR, Code of Federal Regulation; CSA, Controlled Substances Act; DEA, Drug Enforcement Administration; DHHS, Department of Health and Human Services; DOJ, Department of Justice; DSHEA, Dietary Supplement Health & Education Act; FDA, Food and Drug Administration; FD&C, Food, Drug & Cosmetic (Act); IND, Investigational New Drug; IRB, Institutional Review Board; LSD, D-Lysergic acid diethylamide; NDA, New Drug Application; NIDA, National Institute on Drug Abuse; THC, tetrahydrocannabinol; US, United States.

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2. The Controlled Substances Act

In the United States, the federal Controlled Substances Act (CSA) controls substances that are psychoactive or otherwise have abuse potential. The CSA controls all stages of the manufacturing and supply chain, and all handlers (including "ultimate users," such as patients). The extent or stringency of these controls is largely determined by a substance's classification in one of five schedules for controlled substances. Classification depends on a substance's medical effectiveness and abuse potential (21 USC 812). The general rule is that a substance and products derived from that substance are in the same schedule.

The criteria for substances in Schedule I are no currently accepted medical use in the United States, high potential for abuse, and lack of accepted safety for use of the drug or other substance under medical supervision. These substances include marijuana and its cannabinoid components, THCs, ibogaine, mescaline, psilocybin, peyote, heroin, and D-Lysergic acid diethylamide (LSD).

The criteria for substances in Schedule II are currently accepted medical use in the United States, high potential for abuse, and abuse of the drug or other substances that may lead to severe psychological or physical dependence. Schedule II substances include most opioids (e.g., oxycodone) and stimulants (e.g., methylphenidate). Opium and coca leaves also are listed in Schedule II because approved medications (e.g., morphine) were already on the market in 1970, when the CSA was enacted.

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Like drugs in Schedule II, drugs in Schedules III–V have a currently accepted medical use in the United States. In addition, they have lower abuse potential when compared with drugs in the preceding schedule. The phrase "currently accepted medical use in the United States" is not defined in the CSA or in its implementing regulations. However, the Drug Enforcement Agency (DEA) has developed the following five criteria, all of which must be satisfied: (1) the drug's chemistry must be known and reproducible, (2) there must be adequate safety studies, (3) there must be adequate and well-controlled studies proving efficacy, (4) the drug must be accepted by qualified experts, and (5) the scientific evidence must be widely available.

These criteria have been upheld by federal courts (Alliance for Cannabis Therapeutics v. DEA, 15 F.3d 1131 (D.C.Cir. 1994)). In addition, FDA approval of a product is sufficient to establish its "currently accepted medical use." By contrast, state laws authorizing the use of cannabis for medical purposes and the prevalence of anecdotal reports do not satisfy this statutory standard. [DOJ, DEA, Denial of Petition To Initiate Proceedings To Reschedule Marijuana, 21 C.F.R. 40552 at p. 40567 (July 8, 2011)].

3. Research, manufacture, distribution, and possession of cannabinoids

Schedule I substances like cannabis and cannabinoids cannot be prescribed and can only be lawfully dispensed and possessed as part of a federally approved research program. Investigators seeking to conduct Schedule I research must secure a Schedule I research registration (the CSA term for license); many states also require a state Schedule I research license. These requirements, particularly for those unfamiliar with the steps involved, can be challenging. The research registration is both substance (e.g., cannabis or CBD) and protocol specific. Manufacturers, importers, and distributors also must secure Schedule I, substance-specific registrations.

Currently, investigators interested in conducting research on cannabis plant material must obtain that cannabis through the National Institute on Drug Abuse (NIDA), which has historically contracted only with the University of Mississippi to cultivate different varieties of research-grade cannabis with various THC:CBD ratios. However, the DEA has recently announced that it will register additional sources of cannabis cultivated for research or the development of FDA-approved products [1]. If an investigator is interested in conducting research on a cannabis extract or purified cannabinoid (including one synthesized in a laboratory), the preparation may be obtained through NIDA or from other sources, including importation into the United States.

Schedule II–V substances are subject to less stringent rules. For example, physicians who hold Schedule II–V prescriber registrations, as many do, may conduct research on Schedule II–V substances as a lawful "coincident activity" to their prescriber registration. They need not seek further approvals from the DEA or state controlled drug agencies. Investigators may obtain such substances from any of a number of registered manufacturers. In addition, FDA-approved products containing Schedule II–V substances may be prescribed and dispensed in clinical practice.

That Schedule I substances cannot be dispensed outside of a research program explains why physicians, in states that have authorized the medical use of cannabis, can only "certify" or "recommend" that their patients have a qualifying medical condition and may use cannabis for medical purposes, but cannot actually issue a prescription. Such state laws, which vary significantly from state to state, may permit persons other than patients and/or caregivers to manufacture and distribute cannabis preparations (often through "dispensaries") to patients who have the recommendation of a physician or other healthcare provider. However, such activities remain illegal under federal law.

4. Distinguishing CBD products from other cannabis products

The cannabis plant contains >100 individual cannabinoids [2]. The predominant cannabinoids are THC and CBD. Tetrahydrocanabinol activates the body's endogenous cannabinoid receptors, CB1 and CB2. Activation of CB1 is responsible for THC's psychoactive properties. Cannabidiol does not directly activate those receptors at doses being studied in clinical trials [3] and is considered to be non-psychoactive [4].

There are no standardized definitions of "medical marijuana" and "high-CBD" or "low-THC" products, and media reports commonly use these terms interchangeably. "Medical marijuana" does not refer to a special variety of cannabis, mode of preparation, or dosage form. Rather, cannabis is so classified by the purpose of its use (i.e., for medical rather than recreational use). "Medical marijuana" products may contain a range of cannabinoids, although most are predominantly comprised of THC. "High-CBD" products are commonly higher in CBD content than other "medical marijuana" products, but some of these products may have levels of THC ranging from 0.3% to 5%, depending on the state law.

Similarly, there are no common descriptions of "medical marijuana" or "CBD access" state laws, which vary significantly. Some decriminalize possession by qualified patients or their caregivers, while others authorize the full panoply of manufacturing (including cultivation and manufacturing of various preparations) and distribution/retail sales, to purchase and possession by the ultimate patient users. In all cases, physicians (or in a few states also other healthcare providers) are the "gatekeepers;" that is, a patient cannot become qualified without a physician's recommendation.

5. Transporting CBD, "medical marijuana," and investigational cannabinoid products

The media have reported cases of patients and/or family members who have obtained CBD or "medical marijuana" in another state and brought it back to their state of residence. However, transporting cannabis across states lines may not be lawful under state laws, unless a patient is participating in a clinical trial and has a letter that documents such participation. Even still, the Controlled Substances Act does not permit patients to bring cannabinoid preparations into, or take them out of, the United States, even for medical use. Of course, many patients have purchased CBD artisanal products on the internet, thus far without significant enforcement against either the patients or the vendors. However, Health Canada recently seized a shipment of CBD products being sent from the United States to patients in Canada [5].

6. Legal status of CBD

Cannabidiol is not listed separately in the Code of Federal Regulations (CFR); it is controlled in Schedule I by definition as a "derivative" or "component" of marijuana (21 USC 802). This is also true of other individual cannabinoids. Only THC is listed separately in Schedule I. According to a position statement from the DEA Office of Public Affairs, CBD from any source is a Schedule I substance (DEA, Office of Public Affairs, December 15, 2015, provided upon request to A. Mead).

6.1. Legal status of hemp

The increased interest in CBD has been accompanied by a parallel interest in the cultivation of the hemp variety of cannabis. Typically grown for its fiber or seeds, hemp is generally low in cannabinoid content. In Europe and Canada, specific hemp varieties may be cultivated, and they must have no >0.2% (Europe) [6–8] or 0.3% (Canada) THC [9], as measured in the dried flowering portion of the plant, which is the part of the plant with significant cannabinoid content.

The CSA does not define hemp; it merely exempts certain parts of the cannabis plant – stalk, fiber, and sterilized seeds (and preparations made from them) – from the definition of "marijuana." However, if