

IN THE WEEDS: NAVIGATING THE SHIFTING FEDERAL REGULATION OF MEDICAL MARIJUANA

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U.S. Food, Drugs, Medical Devices and Cosmetics (FDA) Alert

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The federal government's view of medical marijuana is evolving as the U.S. Food and Drug Administration ("FDA" or "Agency"), on June 25, 2018, approved Epidiolex, the first drug containing cannabidiol ("CBD") [1], a marijuana derivative, and the U.S. Congress considers several bills aimed at relaxing regulatory standards for medical marijuana. In a press release regarding this recent approval, FDA Commissioner Scott Gottlieb reiterated the Agency's commitment to "careful scientific research and development," noting that the "approval serves as a reminder that advancing sound development programs that properly evaluate active ingredients contained in marijuana can lead to important medical therapies." Before Epidiolex can be made available to patients, CBD must be rescheduled by the U.S. Drug Enforcement Administration ("DEA") from its current Schedule I classification under the Controlled Substances Act ("CSA").

This alert provides an overview of the roles of FDA and other federal agencies in regulating the research, development and marketing of medical marijuana, along with a discussion on DEA's rescheduling process for controlled substances and its past actions related to marijuana. This alert also provides information on key proposed congressional legislation focused on relaxing medical marijuana regulations and considerations for stakeholders in light of this shifting regulatory landscape.

FDA'S REGULATION OF MARIJUANA IN DEVELOPMENT AND MARKETING

FDA takes the position that the drug approval process, which it regulates, is the most appropriate manner to determine whether a product derived from marijuana or its derivatives is safe and effective and has an acceptable medical use. Utilizing this pathway, on June 25, 2018, the Agency approved GW Pharmaceuticals' Epidiolex, a CBD oral solution for the treatment of seizures in two rare forms of epilepsy, Dravet syndrome and Lennox-Gastaut syndrome. The drug is approved for such uses in patients 2 years of age and older. Epidiolex will be marketed in the United States by GW Pharmaceuticals' U.S. subsidiary Greenwich Biosciences and is the first FDA-approved drug that contains a drug substance derived from marijuana. [2] FDA's recent approval decision aligns with the FDA Peripheral and Central Nervous System Drugs Advisory Committee's unanimous vote (13–0) in favor of the benefit-risk profile of Epidiolex issued on April 19, 2018. Research and development programs for products containing or derived from marijuana are ongoing for a variety of other diseases and conditions, including pain, substance use disorder, and graft-versus-host disease.

FDA's approval of Epidiolex does not, however, change the Agency's laws and regulations prohibiting the use of marijuana and its derivatives, including products containing CBD and tetrahydrocannabinols (THC), in food, dietary supplements and over-the-counter ("OTC") drug products, such as oil drops, capsules, teas, and topical lotions and creams. Consistent with its previous actions, FDA's enforcement priorities in this area will focus on

marketing of unapproved drugs where firms have made health claims for products containing or derived from marijuana.

DEA SCHEDULING OF MARIJUANA

Currently, marijuana and its derivatives, including CBD, are classified as Schedule I substances by DEA. [3] In accordance with the CSA, DEA classifies substances into five categories based on medical use, potential for abuse, and safety or dependence liability. As a Schedule I drug, marijuana is considered to have a high potential for abuse, have no currently accepted medical use in treatment in the United States, and lack an accepted safety for use under medical supervision. Under federal law, manufacturing and distributing marijuana is illegal and punishable by fines and/or imprisonment.

Before Epidiolex can be made available to patients, DEA will have to reschedule CBD from its current Schedule I classification. As part of this process, FDA will provide a scientific and medical evaluation, through the Secretary of Health and Human Services ("HHS"), and a rescheduling recommendation to DEA. DEA is required to make a rescheduling determination within 90 days. [4]

FEDERAL AGENCIES AND MEDICAL RESEARCH INVOLVING MARIJUANA

Numerous federal agencies currently regulate the clinical research of marijuana and its derivatives. Researchers must submit an Investigational New Drug ("IND") application to FDA's Office of New Drugs within the Center for Drug Evaluation and Research ("CDER") in order to conduct research on marijuana. DEA oversees registration and licensure requirements for researchers and research sites. The National Institute on Drug Abuse ("NIDA"), which is part of the National Institutes of Health ("NIH"), oversees the cultivation of marijuana for medical research and supplies such product to researchers.

For many years, FDA and DEA have been in favor of expanding legitimate research into the medical use of marijuana and its derivatives. In 2003, FDA formed a Botanical Review Team to provide scientific and quality control advice to researchers developing drugs derived from plants, such as marijuana. In December 2016, this team published revised guidance on clinical studies involving botanical drugs and recommendations for quality controls for lot-to-lot consistency. [5] Further, in December 2016, DEA announced a new policy to increase the number of entities under the CSA permitted to grow marijuana for legitimate research purposes. [6] Prior to this policy, DEA relied on a single grower, the University of Mississippi, to produce marijuana for research purposes. The policy allows registrants to grow marijuana not only to supply federally funded and academic researchers, but also the private sector for medical product development. Since then, DEA has received at least 25 applications from entities seeking to grow marijuana for research purposes.

CONGRESSIONAL BILLS ON MEDICAL MARIJUANA

There are currently several bills pending in the U.S. Congress that would impact the regulation of medical marijuana. H.R. 2020, authored by freshman Representative Matt Gaetz (R-FL), would direct DEA to transfer marijuana from Schedule I to Schedule III of the CSA. Representative Bob Goodlatte (R-VA), who chairs the House Judiciary Committee, is one of the bill's co-sponsors. Rep. Goodlatte has long blocked marijuana-related legislation from advancing, so his co-sponsorship signals a shift in Congress.

Another bill seeking to amend the CSA is H.R. 3391, the Medical Marijuana Research Act of 2017, which would establish a new, separate registration process to facilitate research of marijuana for medical purposes. If passed, DEA would register practitioners to conduct medical marijuana research and manufacturers and distributors to supply marijuana for research. Interestingly, this bill is sponsored by Representative Andy Harris (R-MD), who has previously taken actions against marijuana legalization. Rep. Harris indicates that by sponsoring the bill, he expects such research to demonstrate that marijuana is not medically useful.

H.R. 2920/S. 1764, the Compassionate Access, Research Expansion, and Respect States Act of 2017 ("CARERS Act of 2017"), addresses enforcement of the CSA in states in which medical marijuana is legal. The bill would amend the CSA to provide that the administrative, civil, and criminal penalties do not apply to a person who produces, possesses, distributes, dispenses, administers, tests, recommends, or delivers medical marijuana in compliance with state law. This bill was first introduced last session and was re-introduced this session after Attorney General Jeff Sessions sought greater latitude in prosecuting medical marijuana cases. [7]

Moreover, Senators Cory Gardner (R-CO) and Elizabeth Warren (D-MA) recently introduced the Strengthening the Tenth Amendment Through Entrusting States ("STATES") Act (S. 3032), which would amend the CSA so that it would not apply to persons or entities acting in compliance with state laws that allow for the manufacture, production, possession, distribution, and delivery of marijuana for recreational and medical purposes. Representatives David Joyce (R-OH) and Earl Blumenauer (D-OR) introduced a companion bill (H.R. 6043) in the House. Notably, President Trump has signaled that he would support the STATES Act, which is viewed as a compromise with Senator Gardner, who has held up several Department of Justice ("DOJ") nominees since Attorney General Sessions announced that he would rescind the Obama Administration hand-off approach to enforcing federal marijuana laws.

CONCLUSION

The federal regulatory landscape for marijuana will shift depending on DEA's rescheduling determination related to FDA's recent drug approval of Epidiolex. This approval, however, does not change FDA's prohibition on the use of marijuana and its derivatives in food, dietary supplements and OTC drug products. [8]

Further, while FDA has acknowledged that some states have legalized medical marijuana, it has continuously emphasized to states the importance of clinical research regarding the safety and effectiveness of products containing marijuana and its derivatives. Federal agencies have also supported efforts to enhance the generation of valid scientific data regarding marijuana's safety and efficacy for medical use. Such research should demonstrate that products containing marijuana or its derivatives can be delivered in reliable dosages through reproducible delivery routes. Additionally, the regulation of medical marijuana may be relaxed based on pending congressional legislation.

Accordingly, opportunities exist for stakeholders, including growers, manufacturers and researchers, interested in advancing the development of medical marijuana. The K&L Gates FDA and Public Policy and Law practices will continue to monitor and provide updates on future developments in this area. Given our substantive experience in and knowledge of FDA-regulated industries, K&L Gates is well-positioned to facilitate engagement and help you assess risks and opportunities in this area.

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[1] CBD is a chemical component of the Cannabis sativa plant, also known as marijuana.

[2] While, to date, FDA has not approved an NDA for a drug product containing or derived from botanical marijuana, FDA has approved two drug products, Marinol and Syndros, containing dronabinol, a synthetic form of the marijuana derivative delta-9-tetrahydrocannabinol ("THC") as the active ingredient. Marinol is classified as Schedule III, and Syndros is classified as Schedule II. Both Marinol and Syndros are indicated in adults for the treatment of anorexia associated with weight loss in patients with AIDS and nausea and vomiting associated with cancer chemotherapy in patients. In addition, FDA has approved Cesamet, a Schedule II drug that contains a synthetically-derived active ingredient with a chemical structure similar to THC.

[3] THC and marijuana extract are also classified as Schedule I drugs.

[4] DEA has denied all past requests to reschedule marijuana. As recently as 2016, after receiving two requests for rescheduling and subsequently requesting from HHS a medical evaluation and scheduling recommendation, DEA concurred with HHS' recommendation not to reschedule marijuana. While DEA has acknowledged that medical research in this area has progressed over the past years, it takes the position that available evidence has not been sufficient to demonstrate that marijuana and its derivatives have an accepted medical use. Denial of petition to initiate proceedings to reschedule marijuana, 81 Fed. Reg. 53,687 (Aug. 12, 2016); Denial of petition to initiate proceedings to reschedule marijuana, 81 Fed. Reg. 53,767 (Aug. 12, 2016).

[5] Botanical Drug Development, Guidance for Industry,
<https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM458484.pdf>.

[6] Applications To Become Registered Under the Controlled Substances Act To Manufacture Marijuana To Supply Researchers in the United States, 81 Fed. Reg. 53,846 (Aug. 12, 2016).

[7] In January 2018, Attorney General Sessions rescinded the Department of Justice's ("DOJ's") previous hands-off approach, adopted under the Obama Administration, of enforcing federal marijuana laws in those states where marijuana is legal for medical or recreational use, and Session directed all U.S. Attorneys to enforce federal law when pursuing marijuana-related prosecution. <https://www.justice.gov/opa/press-release/file/1022196/download>.

[8] See, e.g., FDA Warning Letter to That's Natural (Oct. 31, 2017),
<https://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2017/ucm583197.htm>.

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