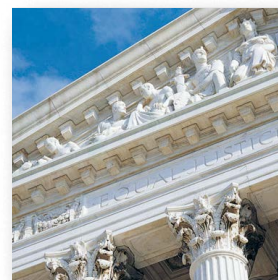


# Regulatory and Legislative Disparities With Cannabis Present Challenges to P&T Committees and Health Care Providers

Rita Marcoux, RPh, MBA; Lauren Holmes, PharmD, MBA, MPH; and F. Randy Vogenberg, BSc Pharm, PhD



## INTRODUCTION

Over the past several years, the legal status of cannabis has been determined by regulatory changes affecting its use, as well as the use of cannabidiol (CBD). Prior to 2018, CBD, along with all forms of marijuana, was considered a Schedule I controlled substance (CI), indicating that these drugs had no medical use



F. Randy Vogenberg

and presented a high potential for abuse. On June 25, 2018, the Food and Drug Administration (FDA) approved Epidiolex (cannabidiol) for the treatment of Lennox-Gastaut and Dravet syndromes.<sup>1</sup> Upon approval, the Drug Enforcement Agency (DEA) added CBD to the list of controlled substances in Schedule V. Previously, the FDA had

**Keywords:** Board of Pharmacy (BOP), cannabidiol (CBD), Controlled Substance Act (CSA), 2018 Farm Bill (FB), Controlled Substance Schedule I (CI), tetrahydrocannabinol (THC), Prescription Drug Monitoring Program (PDMP)

*Ms. Marcoux is a Clinical Professor of Regulations and Managed Care and Director of Pharmacy Outreach Programs at the University of Rhode Island College of Pharmacy in Kingston, Rhode Island. Dr. Holmes is a Post-Doctoral Fellow at Rutgers University's HOPE Center in Piscataway, New Jersey. Dr. Vogenberg is Principal, Institute for Integrated Healthcare in Greenville, South Carolina, and Adjunct Assistant Professor, Pharmacy Administration, Department of Health Economics Research at the University of Illinois College of Pharmacy in Chicago, Illinois.*

**Disclosure:** The authors declare no financial or commercial interest in regard to this article.

approved two products, Marinol<sup>®</sup> CIII and Cesamet<sup>®</sup> CI, which are synthetic analogs to tetrahydrocannabinol (THC), the psychoactive component of marijuana.<sup>2,3</sup>

## Contemporary Legal Landscape

Despite the fact that there are only three FDA-approved marijuana-based products to date, and that marijuana and CBD remain listed as CI substances, medical marijuana continues to gain legal status across the country (see Table 1). In 2018, Vermont became the first state to use the legislative process, as opposed to the ballot initiative, to legalize medicinal marijuana.<sup>4</sup> In addition, the 2018 Farm Bill (FB) legalized the industrial cultivation of hemp that contains less than three-tenths of one percent of THC. The FB has a state–federal regulatory sharing process in regard to the cultivation of hemp. States must submit licensing and regulation plans to the Secretary of the Department of Agriculture (USDA) for approval. The FB removes a hemp-derived product, such as CBD, from its CI status if the CBD product is produced in accordance with all state and federal laws and regulations on hemp. The FB granted oversight authority of hemp cultivation to the USDA but explicitly maintains the FDA's control over marijuana and CBD.<sup>5</sup> Former FDA Commissioner Scott Gottlieb released a statement upon signing the FB stressing that the FDA's continued authority over drug approvals and interstate commerce of medications. He made it clear that CBD and marijuana had both been approved as drugs prior to their use as a food or

dietary supplement. He reiterated that CBD dietary supplements and food labels should not allow information on therapeutic benefit or disease claim unless these products have been approved by the FDA. Gottlieb warned that the agency will take action against violators to protect the public.<sup>6</sup>

Finally, the Consolidated Appropriations Act of 2019, Division C Section 537, contains provisions that prohibit the Department of Justice (DOJ) from using federal funds to prosecute any legal medical-marijuana businesses in states that have passed laws permitting medicinal marijuana.<sup>7</sup>

The shifting attitudes of the public and legislatures, at both the federal and state levels, have resulted in an expanded availability of marijuana and marijuana byproducts. However, for health care entities, leaders, and their organizational committees, the contradictions in laws and/or regulations at the state and federal levels have created a number of employment and health care compliance issues, such as the required submission of dispensing data to the Prescription Drug Monitoring Program (PDMP) and indicating which health care professionals are allowed to certify patients, as shown in Table 1. Other state initiatives can be found in Table 2. These compliance issues must be considered when developing appropriate risk management strategies on the issue of marijuana and CBD, as their current federal CI designation may jeopardize an institution's ability to participate in federally funded programs.

**Table 1 State Practice Requirement(s) Status<sup>4,5,9</sup>**

<b>APRN Approved to Certify Patients</b>	Connecticut, Hawaii, Maine, Massachusetts, Minnesota, New Hampshire, New York, Vermont, Washington
<b>Required Submission of Dispensing Data to PDMP</b>	Connecticut, Illinois, North Dakota, Oklahoma, Utah, Virginia
APRN: Advance Practice Registered Nurse; PDMP: Prescription Drug Monitoring Program	

**Table 2** Abbreviated Summary of States Taking Legal Initiatives<sup>4,5,8,9</sup>

<b>CBD-Only/Low THC</b>	Alabama, Georgia, Indiana, Iowa, Kentucky, Mississippi, North Carolina, South Carolina, Tennessee, Texas, Virginia, Wisconsin, Wyoming
<b>Medical Marijuana</b>	Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, Florida, Hawaii, Illinois, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Missouri, Montana, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, Utah, Vermont, Washington, Washington D.C., West Virginia
<b>Pharmacist/Physician Involvement in Dispensing Required</b>	Arkansas, Connecticut, Minnesota, New York, Pennsylvania
<b>Required Testing</b>	Alaska, Arkansas, California, Colorado, Connecticut, Delaware, Florida, Hawaii, Illinois, Iowa, Kentucky, Maine, Maryland, Massachusetts, Michigan, Minnesota, Missouri, Montana, Nevada, New Hampshire, New Jersey, New Mexico, New York, Ohio, Oregon, Pennsylvania, Utah, Washington

## PATIENTS AND PRESCRIBERS

Currently, 33 states and Washington D.C. have legalized medical marijuana in restricted quantities, with several more states allowing only CBD or products with low THC.<sup>9</sup> Among the states with legalized marijuana, there are varying methods for certification of patients and registry requirements, and various avenues for product acquisition. The states each have their own unique laws addressing what is allowed for possession, cultivation, and caregivers. Each state's program has its own list of diagnoses that qualify a patient, and some may have additional diagnosis-age restrictions. Qualifying diagnosis lists may be limited; Alabama includes only severe, debilitating epileptic conditions, while other states, such as Illinois, New Hampshire, and Connecticut, include a significant list of chronic conditions. No licensed practitioner may prescribe marijuana because of its federal CI status, but those prescribers who wish to certify patients must meet the state's specific program requirements. While most states require the prescriber to be a physician, nine states allow nurse practitioners to certify patients.<sup>9</sup> The state agency tasked with program-management oversight differs between states. The Department of Health remains the predominant oversight agency, but some programs are managed by licensing, consumer protection, law enforcement, or substance abuse agencies.

In most states with medical marijuana, patients receive their marijuana

from dispensaries run by lay personnel, i.e., non-health-care professionals. This results in little comprehensive health care involvement at the dispensing level, with patients receiving limited information on the potential side effects and drug interactions of medical marijuana or CBD. In addition, patients are reluctant to share their marijuana use with licensed health care practitioners, which decreases the value of comprehensive medication reviews within the health care system and at the individual pharmacy level. This challenge is addressed in Connecticut, Minnesota, and New York, which have laws that require pharmacists to dispense and counsel individuals on the use of medical marijuana.<sup>8</sup>

## EMERGING CHALLENGES

Although the regulatory landscape is a quagmire, pharmacists in all states must begin to familiarize themselves with the clinical aspects of, as well as with regulatory mandates on, marijuana and CBD. THC is the chemical in marijuana responsible for the psychotropic behaviors and side effects, which is undesirable for the treatment of medical conditions.<sup>10</sup> Most states require restrictions on the amount of THC that is legally allowed in medical marijuana products as well as in commercial hemp. Although restriction levels are in place, available products may deviate from those limits. A study of marijuana in Colorado found the THC content to be varied and with little-to-zero CBD.<sup>11,12</sup> Health care entities and

providers who are licensed health care practitioners must adhere to their state's Controlled Substances Act (CSA), which may prohibit CBD in their licensed stores. Permitting CBD products in a pharmacy may change as many of the states' boards of pharmacy (BOPs) address their CSA, which lists CBD as a CI drug. Recently, the Alabama and Ohio state BOPs reminded their practitioners that state regulations remain stricter than federal regulations on CBD and that CBD should not be sold in licensed pharmacies.

Another challenge for practitioners is the lack of standardization for the potency of medical marijuana and CBD that patients are taking. Many cultivators are experimenting with marijuana strains and developing hybrid medical-marijuana products to be used in specific disease states or conditions. This increases the complexity of managing patients, as it is difficult to know the exact content of THC and CBD in a product. Anticipating the possible interactions and effects on a patient using these products for their medical condition may be impossible. This is a similar challenge for the different routes of administration for medical marijuana, such as vaping, smoking, and eating. The bioavailability of THC, based on these different administration routes, may lead to different side effects and efficacies in treatment. Smoking or vaping marijuana results in an onset of action within minutes, peak effects within 20 to 30 minutes, and tapering effects within 2 to 3 hours. Infused edible cannabis products (edibles) come in a variety of forms, such as candy, baked goods, lozenges, and drinks. The onset of action for edibles is approximately 30 to 90 minutes, with a peak effect at two to four hours.<sup>13,14</sup> Patient characteristics and habits may impact the onset of edibles' action and duration. In addition, there may be significant batch variation for edibles, as the production process varies for each product and batch. Variability and delayed onset of action for edibles are two factors that have been potentially associated with increased episodes of cannabis intoxication. Cannabis toxicity can result in hyperemesis, behavioral problems—including acute psychosis—or a medical emergency such as bronchospasm as a result of inhalation. Health systems, emergency responders, and pharmacists must consider marijuana as

a possible culprit when treating patients presenting with these symptoms.

Practitioners should be aware of the supply-chain variability with medical marijuana. Many states require testing to ensure the products have the legal/appropriate amounts of CBD and THC, as well as testing for contaminants.<sup>15,12</sup> The accuracy of lab testing for THC has been the subject of debate. In November and December of 2018, Colorado had a recall on marijuana products because of mold. Michigan had a recall on marijuana product in January 2019 for mold, yeast, bacteria, and chemical residue.<sup>15,16</sup> Although marijuana has been labeled as “medical,” patients and health care practitioners must recognize the lack of Current Good Manufacturing Practices (CGMPs) and industry standards that are associated with traditional medications approved by the FDA. Content, various routes of administration, and product purity will continue to challenge professionals under the current system of approving marijuana use for medical conditions.

When considering marijuana’s side-effect and drug-interaction profile, consideration must be given to levels of CBD and THC in the products. Both have the potential to interact with major enzymes of the cytochrome P450 system, specifically 3A4, 2C9, and 2C19.<sup>17</sup> Administering medical marijuana concomitantly with strong inducers or inhibitors of these enzymes may significantly increase or decrease the levels of marijuana, affecting the efficacy and side effects. This is an important consideration as many patients have chronic conditions and may be taking a significant number of medications. Continuous comprehensive medication reviews will be essential to manage patients’ chronic conditions as well as drug interactions and side effects.

## HOSPITALS, HEALTH SYSTEMS, MANAGED CARE, AND P&T COMMITTEES

All health care providers and third-party plan administrators or managed care entities are likely following consumer trends around cannabis use to determine what opportunities or risks they may cause for their organization. Institutions and health care practitioners will need to address marijuana usage from the patient’s perspective as well as

from the employer’s perspective when it comes to the delivery of health care. Traditionally, the health care system has not questioned patients about their consumption of marijuana in any form. With 33 states now allowing the use of medical marijuana, health systems are caring for a significant number of patients who are using marijuana medicinally or recreationally. Although state laws have been passed that permit the use of medical marijuana, these laws continue to be in direct conflict with the CSA, which lists marijuana as a Schedule I drug. The fact that so many states now allow the use of medical marijuana increases the importance of the issue for P&T and medical executive committees, particularly for senior leadership and boards of trustees of health care entities in all states.

The risk-management implications associated with cannabis go beyond mere compliance because of the fast-changing landscape and disparity or contradictions in U.S. laws and regulations. Given what is known to date about marijuana or CBD use along with concomitant medication use, the door is open to reassessing therapies that ensure a rational drug-use policy. Accreditation and litigation matters will drive P&T committees to ensure such a policy is in place.<sup>18</sup> Fortunately, the historical role of P&T committees as medication watchdogs suggests that they will naturally be inclined to prepare for and act upon changes pertaining to access to cannabis products by their patient population.<sup>19</sup>

Avoiding the risk of injury or complication with drug therapy is becoming more complicated with the evolving cannabis landscape in the U.S. It is worth bearing in mind that drug-injury litigation is the second most frequent reason for medical malpractice lawsuits, although injury itself does not establish malpractice or negligence.<sup>20</sup> As a result, it is incumbent on health care entities and practitioners to review their risk-management policies and mitigation strategies related to the changes surrounding cannabis use.

## CONCLUSION

The increase in cannabis access and use has sparked changing attitudes on policy and regulations. The resulting federal and state legislative or regulatory actions have created a plethora of rules that can vary widely from state to

state. In some situations, the rule-making can be contradictory or counterintuitive from the perspective of both health care practitioner and patient. Balancing consumer safety regarding cannabis products with drug-product injury has splintered various agency rule-making and oversight responsibilities, causing further confusion and compromising the ability of practitioners to protect consumers.

A majority of states currently allows for some degree of access and use of cannabis products whereas a relevant minority does not. The states’ lack of coordination in their legal initiatives has led to their hitting the wall of existing federal laws and agency regulations, thwarting an effective approach to addressing consumer dissatisfaction over the use of and access to cannabis products when needed.

For health care practitioners, this rapidly escalating issue necessitates careful decision-making, whether or not cannabis is being used by patients under their care. Similarly, health care entities and their P&T committees will have to do likewise in their deliberations about rational drug use. Acute-care organizations may have an advantage over their managed-care counterparts because of the short-term nature of their treatment and detailed knowledge of patient-care metrics. Nonetheless, all health care entities are likely to be ensnared in the current, complex law and regulatory environment resulting from the rapid race to address cannabis use that is driven by consumer demand in the U.S.

## REFERENCES

1. Food and Drug Administration. FDA approves first drug comprised of an active ingredient derived from marijuana to treat rare, severe forms of epilepsy. June 25, 2018. Available at: <https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm611046.htm> Accessed March 21, 2019.
2. Drug Enforcement Administration. FDA-approved drug Epidiolex placed in schedule V of Controlled Substance Act. September 27, 2018. Available at: <https://www.dea.gov/press-releases/2018/09/27/fda-approved-drug-epidiolex-placed-schedule-v-controlled-substance-act>. Accessed March 21, 2019.
3. Drug Enforcement Administration. Title 21 United States Code (USC) Controlled Substances Act. Available at: <https://www.deadiversion.usdoj.gov/21cfr/21usc/812.htm>. Accessed March 21, 2019.



4. National Conference of State Legislators. Marijuana overview. December 14, 2018. Available at: <http://www.ncsl.org/research/civil-and-criminal-justice/marijuana-overview.aspx>. Accessed March 21, 2019.
5. Romero D. Hemp industry expected to blossom under new farm bill." NBCNews.com. December 16, 2018. [www.nbcnews.com/news/us-news/hemp-industry-expected-blossom-under-new-farm-bill-n947791](http://www.nbcnews.com/news/us-news/hemp-industry-expected-blossom-under-new-farm-bill-n947791). Accessed March 21, 2019.
6. FDA. Statement from FDA Commissioner Scott Gottlieb, M.D., on signing of the agriculture improvement act and the agency's regulation of products containing cannabis and cannabis-derived compounds. Available at: [www.fda.gov/newsevents/newsroom/pressAnnouncements/ucm628988.htm](http://www.fda.gov/newsevents/newsroom/pressAnnouncements/ucm628988.htm). Accessed March 21, 2019.
7. Whitehouse.gov. Statement by the President. February 15, 2019. Available at: [www.whitehouse.gov/briefings-statements/statement-by-the-president-28/](http://www.whitehouse.gov/briefings-statements/statement-by-the-president-28/). Accessed March 21, 2019.
8. Prescription Drug Monitoring Program Training and Technical Assistance Center. 2018 legislation impacting Prescription Drug Monitoring Program. 2018. Available at: [http://www.pdmpassist.org/pdf/2018\\_PDMP\\_Legislative\\_Summary\\_20190201.pdf](http://www.pdmpassist.org/pdf/2018_PDMP_Legislative_Summary_20190201.pdf). Accessed March 21, 2019.
9. NORML (National Organization for the Reform of Marijuana Laws). Medical marijuana. 2019. Available at: <https://norml.org/legal/medical-marijuana-2>. Accessed March 21, 2019.
10. Leung, L. Cannabis and its derivatives: review of medical use. *J Am Board Fam Med* 2011;24(4):452-462. doi: 10.3122/jabfm.2011.04.100280
11. NBCNews.com. Colorado marijuana study finds legal weed contains potent THC levels. March 23, 2015. Available at: [www.nbcnews.com/storyline/legal-pot/legal-weed-surprisingly-strong-dirty-tests-find-n327811](http://www.nbcnews.com/storyline/legal-pot/legal-weed-surprisingly-strong-dirty-tests-find-n327811). Accessed March 21, 2019.
12. GenTech Scientific.com. State regulations for cannabis testing. 2019. Available at: <https://cannabis.gentechscientific.com/cannabis-testing-regulations>. Accessed March 21, 2019.
13. Grotenhermen F. Pharmacokinetics and pharmacodynamics of cannabinoids. *Clin Pharmacokinet* 2003;42(4):327-360. doi: 10.2165/00003088-200342040-00003
14. Turner AR, Agrawal S. Marijuana toxicity. [Updated 2018 Oct 27]. In: *StatPearls*. Treasure Island, Florida: StatPearls Publishing; 2018. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK430823/>. Accessed March 21, 2019.
15. News 10 Digital Team. Homegrown releases statement re. state approved product. WILX.com, [www.wilx.com/content/news/State-issues-warning-recalled-marijuana-products-504212731.html](http://www.wilx.com/content/news/State-issues-warning-recalled-marijuana-products-504212731.html).
16. Mitchell T. Marijuana mold recall hits multiple dispensaries in Colorado. Westword. December 31, 2018. Available at: [www.westword.com/marijuana/marijuana-mold-recall-from-doctors-orders-hits-multiple-dispensaries-in-colorado-11063282](http://www.westword.com/marijuana/marijuana-mold-recall-from-doctors-orders-hits-multiple-dispensaries-in-colorado-11063282). Accessed March 21, 2019.
17. Bridgeman MB, Abazia DT. Medicinal cannabis: history, pharmacology, and implications for the acute care setting. *P T* 2017;42(3):180-188.
18. O'Donnell JT, Vogenberg FR. Focusing on basis, including drug-use policy, remains important for today's P&T committee. *P T* 2017;42(9):577-580. Available at: <https://www.ptcommunity.com/journal/article/full/2017/9/577/focusing-basics-including-drug-use-policy-remains-important-today-s>.
19. Balu S, O'Connor PO, Vogenberg FR. Contemporary issues affecting P&T committees, part 1: the evolution. *P T* 2004;29(11):709-711. Available at: [https://www.ptcommunity.com/system/files/pdf/ptj2911709\\_0.pdf](https://www.ptcommunity.com/system/files/pdf/ptj2911709_0.pdf).
20. O'Donnell JT. Adverse drug reactions: the extent of the problem. In: O'Donnell JT, O'Donnell JJ III, eds. *O'Donnell's Drug Injury*. Tucson, Arizona: Lawyers & Judges Publishing Company, Inc; 2016:132. ■