Issue

The American Pharmacists Association (APhA) Board of Trustees has directed the 2014–2015 Policy Committee to recommend policy to the APhA House of Delegates related to the sale of cannabis in pharmacies. Specifically, the Board asked the committee to comment on the increasing availability of inhaled cannabis for both medical and recreational use and the pharmacist’s role in the care of patients who use inhaled cannabis.

Currently, more than 23 states and Washington, DC, have laws and regulations regarding the use of medical marijuana. Two of those states, Colorado and Washington, have written legislation to legalize the recreational use of medical marijuana. Although various states have allowed the use of inhaled cannabis for medical purposes, federal statutes still classify inhaled cannabis as a Schedule I substance. The Controlled Substances Act was signed into law in 1970 by President Richard Nixon, and the legislation defined different classes based on physical dependence, abuse potential, and appropriate medical use. Schedule I substances are defined as substances that have a high potential for abuse, no current medical use in the United States, and a lack of accepted safety when used under medical supervision. According to federal statute, inhaled cannabis shall not be used for medical reasons in the United States, despite changes in state laws. In terms of compliance with both state and federal statutes, pharmacists must comply with the law that is most stringent, in this case recognizing inhaled cannabis as a Schedule I substance. Violation of federal statutes can result in fines, imprisonment, and/or the revocation of the pharmacy’s Drug Enforcement Agency (DEA) registration, preventing the dispensing of controlled substances.

Despite not being able to legally dispense or stock inhaled cannabis according to federal law, clinical issues have been raised by pharmacists in managing patients who use inhaled cannabis. The concerns that have been raised include the use of inhaled cannabis in disease states in which efficacy and safety have not been evaluated, restrictions on patients who are able to access inhaled cannabis, and the effect of inhaled cannabis on patient decision-making skills as well as their medication regimen. With few credible large-scale trials on inhaled cannabis, coupled with the potential legal ramifications on pharmacist involvement with a patient’s inhaled cannabis regimen and lack of guidance by the Food and Drug Administration (FDA), pharmacists are hesitant to jeopardize their careers by dispensing inhaled cannabis, and they are concerned about their inability to make clinically sound decisions to assess its appropriateness in therapy. Current APhA policy (adopted in 1980 and last reviewed in 2011) on medical marijuana supports research on its use but not the circumvention of federal law involving marijuana.
Summary of Key Concepts

- There is very limited peer-reviewed, published literature on the therapeutic use of inhaled cannabis, but the research that does exist supports its efficacy. However, a litany of identified potential adverse effects from the use of inhaled cannabis raises issues of safety for the patient.
- Currently, more than 20 states have legalized medical marijuana use, with two of them legalizing marijuana for recreational use as well. At this time, federal law still states that marijuana is a Schedule I drug, without a purpose for medical use.
- Distribution and regulation remain a concern for pharmacists; if they were to dispense inhaled cannabis, they would want to ensure that they have a product with consistent quality and purity falling under the same regulations as other FDA-approved medications.
- Safety concerns for pharmacists and other personnel working in pharmacies stocking inhaled cannabis involve being at risk for burglaries and robberies and diversion by pharmacy staff.
- Currently, Connecticut is the only state in which a pharmacist dispenses inhaled cannabis for medical use. Connecticut could be viewed as a model for other states in evaluating the role of pharmacists in dispensing inhaled cannabis for medical purposes. Other states, like Minnesota, are considering legislation that gives pharmacists a consultative role within the manufacturing and dispensing process.

Background

*What is inhaled cannabis and why is it a concern for pharmacists?*

Inhaled cannabis, also known as “smoked marijuana,” has been in existence since the third century A.D. It was first utilized for medical purposes in the mid-nineteenth century by Dr. O’Shaugnessy, who used cannabis for a wide array of medical conditions. The major psychoactive component of *cannabis sativa* was identified as ∆9-tetrahydrocannabinol (THC). THC has been shown to increase pulse rate, decrease blood pressure, cause muscle weakening, increase appetite, cause euphoria, and decrease memory recollection, among other symptoms. Research showed that the body has two different types of cannabinoid receptors, both of which are from the G-protein-coupled receptor family. The brain has a high concentration of CB1 receptors, which have a GABAergic effect on the body. Likewise, cannabis has a dopaminergic effect on the body via stimulation of the nucleus accumbens. The CB2 receptor is found in the periphery of the body, most notably in the spleen, macrophages, kidneys, lungs, and other internal organs. The CB1 receptor has been shown to increase appetite, provide analgesia, impair cognition, and relax muscles, whereas the CB2 receptors are immunosuppressive and decrease inflammation. In terms of how cannabis affects the human body for medical purposes, studies have shown cannabis to have a significant antiemetic effect. Other medical uses include stimulating appetite and treating associated protein wasting of patients with advanced human immunodeficiency virus (HIV), as well as providing a potent analgesic compared with codeine.

Smoking cannabis has been shown to provide a rapid and efficient delivery of THC to the brain and can be detected in the plasma immediately. Peak plasma concentrations can be seen within 10 minutes and then decrease to 20% within 30 minutes of the peak. In comparison, the oral synthetic THC (dronabinol, Marinol®) and THC analogs (nabilone, Cesamet®) have a different pharmacologic profile because absorption of THC from the gut is slower and exhibits a delayed peak plasma concentration compared
with the inhaled formulation. The oral formulation has a bioavailability of 5% to 20% of the dose compared with the inhaled formulation. In short, inhaled cannabis has a better pharmacologic profile and its “rapid on-set and predictable decay means that self-titration of dosing is attainable.”

**What is the efficacy of inhaled cannabis in primary literature? The safety profile?**

A number of small-scale studies have been conducted to show the efficacy of inhaled cannabis for the treatment of various medical conditions. In a study conducted by Ware et al., inhaled cannabis was shown to improve neuropathic pain \( (p = 0.023) \) and provide a better quality sleep \( (p < 0.05) \). In a study conducted by Wilsey et al., inhaled cannabis decreased neuropathic pain and allowed for a greater perceived degree of relief \( (p < 0.05) \). Other studies assessing the efficacy of inhaled cannabis include the following: fibromyalgia (improvement in pain and stiffness \( [p < 0.001] \), enhancement of relaxation and increased somnolence \( [p < 0.05] \) and feeling of well-being \( [p < 0.001] \), posttraumatic or postsurgical neuropathic pain \( (p = 0.023 \text{ for pain intensity being lowered}) \), and neuropathic pain associated with HIV \( (p < 0.016) \). A decrease in nausea and increase in appetite were also reported in various studies in cancer patients. While it is noted that most studies of this nature use the oral formulation, the pharmacokinetics of cannabis once again show that inhaled cannabis has a more predictable and therapeutic peak plasma concentration compared with the oral formulation.

In contrast with the medical benefits of inhaled cannabis, research has revealed a litany of adverse effects with its use. In a meta-analysis conducted by Crane et al., a list of acute adverse effects was noted with cannabis use in clinical trials. The adverse effects include decreased episodic memory; decreased attention, concentration, and working memory; decreased decision-making capabilities; increased risk-taking; decreased inhibitory control; and decreased psychomotor control. Long-term effects were also seen in the previously listed domains in chronic users of cannabis. Similarly, Pavisian et al. showed the adverse effect of cannabis on cognition in patients with multiple sclerosis. The performance of the cannabis group fell below that of the non-cannabis group on the Paced Auditory Serial Addition Test tasks \( (p < 0.02) \) and the 10/36 Spatial Recall Test \( (p < 0.03) \). The cannabis users also had more diffuse cerebral activation compared with nonusers in the domain of working memory.

**The legality of inhaled cannabis in the United States**

Currently, the Controlled Substances Act lists marijuana as a Schedule I substance. This statute states that marijuana has no medical use and is deemed illegal. Contrary to federal legislation, 23 states and the District of Columbia have allowed the use of medical marijuana. Two of those states, Colorado and Washington, allow the recreational use of marijuana. Conflicting federal and state law creates a scenario in which pharmacists can be acting lawfully under state law while simultaneously being at risk of federal prosecution. For this reason, pharmacists have been reluctant to be involved with medical marijuana; federal prosecution could result in severe consequences such as fines and imprisonment. Another concern is that the pharmacy could lose its DEA registration, leading to the inability to dispense controlled substances. Table 1 shows a list of the states that permit the use of medical marijuana and whether the user has to use a compassion center (defined as a place allowed to dispense marijuana), has the ability to home cultivate, or must use a pharmacy. A list of medically approved uses for marijuana can be found in each state’s statutes and regulations.
Table 1: States With Approved Use of Medical Marijuana

<table>
<thead>
<tr>
<th>States</th>
<th>How to Obtain Medical Marijuana</th>
</tr>
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<tbody>
<tr>
<td>Alaska</td>
<td>Individual caregiver* or home cultivation</td>
</tr>
<tr>
<td>Arizona</td>
<td>Individual caregiver, compassion center, or home cultivation</td>
</tr>
<tr>
<td>California</td>
<td>Individual caregiver or compassion center</td>
</tr>
<tr>
<td>Colorado</td>
<td>Individual caregiver or dispensary</td>
</tr>
<tr>
<td>Connecticut</td>
<td>Individual caregiver or dispensary. Once regulations are in place, the only area to obtain medical marijuana will be a pharmacy run by a pharmacist.</td>
</tr>
<tr>
<td>Delaware</td>
<td>Individual caregiver or compassion center</td>
</tr>
<tr>
<td>District of Columbia</td>
<td>Individual caregiver or dispensary</td>
</tr>
<tr>
<td>Hawaii</td>
<td>Individual caregiver</td>
</tr>
<tr>
<td>Maine</td>
<td>Individual caregiver or compassion center</td>
</tr>
<tr>
<td>Massachusetts</td>
<td>Compassion center</td>
</tr>
<tr>
<td>Michigan</td>
<td>Individual caregiver or home cultivation</td>
</tr>
<tr>
<td>Montana</td>
<td>Individual caregiver or home cultivation</td>
</tr>
<tr>
<td>Nevada</td>
<td>Individual caregiver or home cultivation</td>
</tr>
<tr>
<td>New Jersey</td>
<td>Compassion center</td>
</tr>
<tr>
<td>New Mexico</td>
<td>Individual caregiver or home cultivation</td>
</tr>
<tr>
<td>Oregon</td>
<td>Individual caregiver or home cultivation</td>
</tr>
<tr>
<td>Rhode Island</td>
<td>Individual caregiver, compassion center, or home cultivation</td>
</tr>
<tr>
<td>Vermont</td>
<td>Individual caregiver, compassion center, or home cultivation</td>
</tr>
<tr>
<td>Washington</td>
<td>Individual caregiver or home cultivation</td>
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*The definition of “individual caregiver” varies by state.*

As noted in Table 1, Connecticut is the only state with direct pharmacist involvement. Although the process is still being formulated, the Connecticut Department of Consumer Protection has issued six dispensary licenses for pharmacists. Before being dispensed, the marijuana must be deemed “pharmaceutical grade” by a state-appointed laboratory. The pharmacist will then hold a consultation session with the patient about the use of marijuana and its effects.16-18 Because Connecticut is the only state to utilize a pharmacist in the continuum of care for patients using inhaled medical cannabis, it may be used as a model if marijuana becomes rescheduled by the federal government. How an assessment of a patient’s use of cannabis will be incorporated and documented within the pharmacist’s patient care process is still to be determined.

It is important to note that in 2009, U.S. Attorney General Eric Holder stated that it was not a priority for him to prosecute people who used marijuana for medical purposes, but people using it illicitly would be prosecuted. In 2011, a petition was raised to the DEA to reschedule marijuana, but it was denied with the statement that marijuana still has no scientific or medical evidence for its use. In June 2014, FDA announced that it intends to conduct an 8-factor test to determine whether cannabis should be rescheduled. On July 28, 2014, a bill, HR 5226, was introduced by co-sponsors Scott Perry (R-PA), Paul Broun (R-GA), Steve Cohen (D-TN), and Dana Rohrabacher (R-CA) to amend the definition of marijuana and to exclude medical marijuana from controlled substance lists.19
Because of increased reports of employment termination and arrests when traveling into states that have not legalized the use of marijuana, patient awareness of marijuana screening and zero-tolerance policy must be addressed.

**The Role of the Pharmacist in the Use of Inhaled Cannabis for Medical Purposes**

As with any substance used for medical purposes, pharmacists are expected to assess patients’ medication and health status and counsel them on the medical use and adverse effects associated with the use of inhaled cannabis. This expectation will grow if pharmacists are involved in the dispensing of inhaled cannabis, akin to the model currently being utilized in Connecticut. During counseling, pharmacists may discuss the effects of inhaled cannabis on cognition; the risks associated with inhaled carcinogens, which may lead to certain types of cancers; respiratory ailments such as chronic obstructive pulmonary disease; and risks to the reproductive system, such as impaired sperm production, disruption of ovulatory cycle, and decreased birth weight.20 Other adverse effects include psychological dysfunction and cardiac effects (palpitations, syncope, hypotension, stroke, paroxysmal atrial fibrillation). Likewise, the pharmacist must assess drug-drug interactions with other medications such as opioids, barbiturates, central nervous system depressants, protease inhibitors, selective serotonin reuptake inhibitors, sildenafil, theophylline, tricyclic antidepressants, anticholinergics, alpha-agonists, naltrexone, disulfiram, lithium, neuroleptic antipsychotics, and anesthetic agents.21

**Pharmacist Concerns Regarding Dispensing Marijuana in a Pharmacy**

Pharmacists raised various concerns in a focus group when questioned about dispensing marijuana in a pharmacy. The biggest concern was the potential for federal prosecution of pharmacists for dispensing marijuana. Another concern was how the pharmacy staff would treat marijuana once it reached the pharmacy. The pharmacists feared diversion within the pharmacy by technicians, pharmacists, and other staff. The personal safety of pharmacists and technicians was also a concern. If marijuana were to be stored in a pharmacy, the risk of burglary could potentially increase. In terms of patient safety, pharmacists did not feel confident about counseling patients and dispensing marijuana to them. With the increase in fake prescriptions, pharmacists worry about procedures involving the receipt of valid prescriptions. Another issue concerning the pharmaceutical distribution of inhaled cannabis is the purity of the marijuana dispensed as well as how the product would be distributed to the pharmacy. Finally, some pharmacists expressed concern with a pharmacy selling medical marijuana along with tobacco and cigarettes. Some pharmacists feel that the potential revenue stream associated with dispensing medical marijuana could be similar to the way in which cigarettes are sold—in contradiction to the purpose of a pharmacy as a health care facility.

**Unanswered Questions**

One area that has not been addressed but is certainly in the forefront of the discussion is the ability to bill for inhaled cannabis. At present, these products are purchased with cash because of current interpretations of the statutes and financial transaction regulations; these sales are illegal drug sales per federal law. In addition, the cost of purchasing these products is increasing with market demand and a desire to obtain state tax revenue. At some point in time, with these products classified for medical use, the public will request coverage by health care benefit programs. If inhaled cannabis is transitioned from Schedule I to another schedule, will health care benefit programs in the public and private sector cover a non-FDA
approved medication? Thus far, no health plan has stated that it would be willing to cover medical marijuana as a potential therapy. Another question involves who qualifies for medical marijuana. Each state has its own individual criterion by which patients are determined to be eligible for medical marijuana therapy. One would think that if federally approved, legislation would include criteria for patient eligibility for prescribed medical marijuana. Another question for further evaluation involves the safety profile of marijuana compared with other currently available therapies. Although the data point to the therapeutic effectiveness of inhaled cannabis, the research presents many safety concerns. It is also important to note that a study published in the Journal of the American Medical Association concluded that “States with medical cannabis laws had a 24.8% lower mean annual opioid overdose mortality rate compared with states without medical cannabis laws.” A final question involves the way in which the media will portray the use of medical marijuana. The media may sensationalize its use and thereby cause an increase in public demand.

**Conclusion**

Inhaled cannabis for medical purposes has been a hot topic in the medical community over the past decade. Although the federal statute still lists marijuana as a Schedule I substance, state governments have allowed for its use medically and, in some cases, decriminalized marijuana entirely. Connecticut is the first state to utilize the pharmacist as the person dispensing medical marijuana, which raises some concerns regarding the role of the pharmacist related to access to and use of medical marijuana. Pharmacists have expressed their concerns about punitive retaliation for breaking federal law and about marijuana’s safety profile; however, pharmacists could play a unique role in fostering the safe and effective use of medical marijuana. Pharmacists should become educated on the therapeutic use of inhaled cannabis as well as the safety issues that arise with chronic inhaled cannabis use. Since the American Pharmacists Association is one of the major leaders in the pharmacy and medical community, it is important to reevaluate APHA’s policy on medical marijuana.
References


Related APhA Policy

1980 Medicinal Use of Marijuana
1. APhA supports research by properly qualified investigators operating under the investigational new drug (IND) process to explore fully the potential medicinal uses of marijuana and its constituents or derivatives.
2. APhA opposes state by state, marijuana specific, or other drug specific legislation intended to circumvent the federal laws and regulations pertaining to (a) marketing approval of new drugs based on demonstrated safety and efficacy, or; (b) control restrictions relating to those substances having a recognized hazard of abuse.


2003, 1983 The Use of Controlled Substances in the Treatment of Intractable Pain
1. APhA supports the continued classification of heroin as a Schedule I controlled substance.
2. APhA supports research by qualified investigators under the Investigational New Drug (IND) process to explore the potential medicinal uses of Schedule I controlled substances and their analogues.
3. APhA supports comprehensive education to maximize the proper use of approved analgesic drugs for treating patients with chronic pain.
4. APhA recognizes that pharmacists receiving controlled substance prescription orders used for analgesia have a responsibility to ensure that the medication has been prescribed for a legitimate medical use and that patients achieve the intended therapeutic outcomes.
5. APhA advocates that pharmacists play an important role on the patient care team providing pain control and management.


2012 Controlled Substances Regulation and Patient Care
1. APhA encourages the Drug Enforcement Administration (DEA) and other regulatory agencies to recognize pharmacists as partners that are committed to ensuring that patients in legitimate need of controlled substances are able to receive the medications.
2. APhA supports efforts to modernize and harmonize state and federal controlled substance laws.
3. APhA urges DEA and other regulatory agencies to balance patient care and regulatory issues when developing, interpreting, and enforcing laws and regulations.
4. APhA encourages DEA and other regulatory agencies to recognize the changes occurring in health care delivery and to establish a transparent and inclusive process for the timely updating of laws and regulations.
5. APhA encourages the U.S. Department of Justice to collaborate with professional organizations to identify and reduce:
   a. the burdens on health care providers,
   b. the cost of health care delivery, and
   c. the barriers to patient care in the establishment and enforcement of controlled substance laws.

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2014 Controlled Substances and Other Medications with the Potential for Abuse and Use of Opioid Reversal Agents

1. APhA supports education for pharmacists and student pharmacists to address issues of pain management, palliative care, the appropriate use of opioid reversal agents in overdose and of drug diversion and substance–related and addictive disorders.

2. APhA supports recognition of pharmacists as the health care providers who must exercise professional judgment in the assessment of a patient’s conditions to fulfill corresponding responsibility for the use of controlled substances and other medications with the potential for misuse, abuse, and/or diversion.

3. APhA supports pharmacists’ access to and use of prescription monitoring programs to identify and prevent drug misuse, abuse and/or diversion.

4. APhA supports the development and implementation of state and federal laws and regulations that permit pharmacists to furnish opioid reversal agents to prevent opioid related deaths due to overdose.

5. APhA supports the pharmacist's role in selecting appropriate therapy, dosing, initiating and providing education about the proper use of opioid reversal agents to prevent opioid related deaths due to overdose.

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