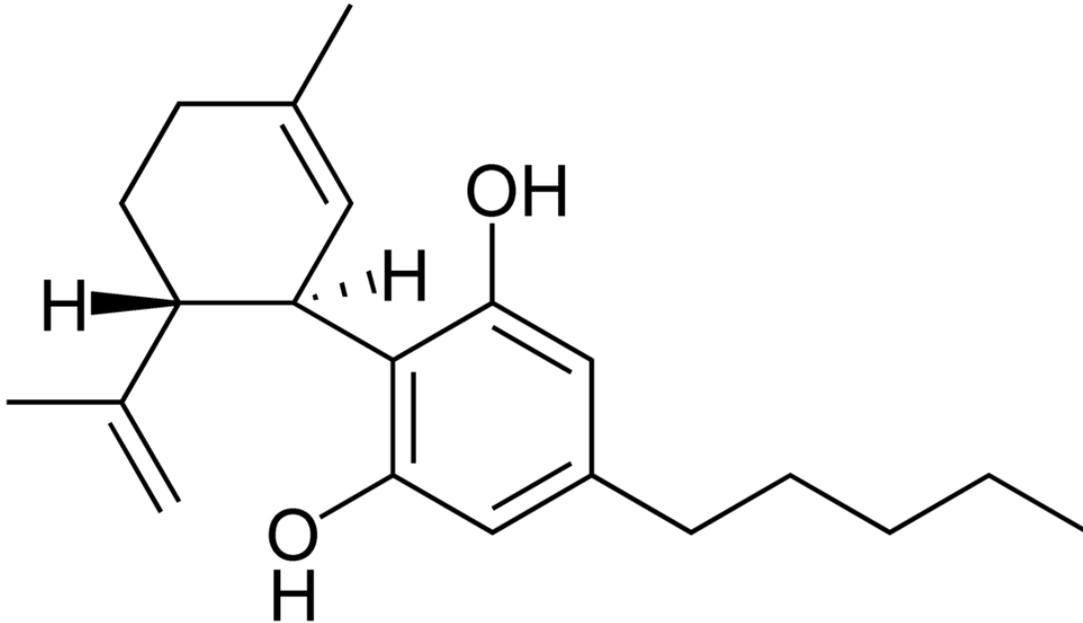


PANACEA or PLACEBO:

The Science behind the Office of Drug Policy's Position on Cannabidiol



State laws permitting the use and sale of marijuana, including high cannabidiol (CBD) low tetrahydrocannabinol (THC) products, contradict federal law. Furthermore, the various renditions of laws that authorize the use, sale, and marketing of artisanal CBD products create public confusion regarding which products are safe, legal, and effective for certain medical conditions. Recent pushes to legalize CBD with anecdotal research, run contrary to the process under which medical methods, treatments, and products are approved in the United States. The Food and Drug Administration (FDA) approval process is rigorous to ensure that medications provide a substantial benefit for the intended treatment that significantly outweighs risks. CBD products should be subject to the same scrupulous methods of FDA approval, resolving the debate regarding artisanal CBD.



CANNABIDIOL AND HEMP

Cannabidiol (CBD), a non-psychoactive substance, was first discovered by Raphael Mechoulam in the 1960's and is one of 60 cannabinoid compounds found in both *Cannabis sativa* and *Cannabis indica*¹. Although trace amounts of cannabinoids are found in all parts of the *Cannabis sativa* and *Cannabis indica* plants, the flower has the largest concentration¹.

Hemp is *Cannabis sativa* or *Cannabis indica*², but has subtle differences to what is generally considered marijuana. According to the fixation index, which measures differentiation in genetic structure, the genetic difference between hemp and marijuana has been described as similar to the difference between Europeans and East Asians². Hemp is a fibrous plant which is primarily male without representing flowering buds at any stage in their life cycle³. Consequently, hemp is limited in cannabinoid production compared to marijuana.

Because marijuana and hemp share the same species, the difference between hemp and marijuana has been largely determined by regulations established in some states and Canada, which only permit hemp cultivating with less than 0.3% THC². For example, West Virginia defines hemp as having less than 1% THC⁴. Thus, it is widely accepted that hemp contains more CBD and less THC than marijuana; however, the designation is relatively arbitrary.

LIMITED SAFETY STANDARDS

Many alleged CBD products contain other cannabinoids, no cannabinoids, or no CBD^{5,6}. Only 31% of CBD products purchased online contain the amount of CBD advertised on the label⁷. Marcel Bonn-Miller, a researcher from the University of Pennsylvania, School of Medicine said, "If the FDA regulated this industry, we would be way better off. They're good at regulating things. When you go and buy a prescription at pharmacy, you know what you're getting... (it's the) same thing for food. When you get a pack of Doritos or a Hershey bar, you know what it is."⁸

PATENT MEDICINE ERA

Until the 20th century, medicines were not regulated in the U.S. Patent medicine was profit-driven and allowed any concoction to be prepared, sold and marketed as relief for any ailment. Due to this practice causing harm, Congress and the FDA developed a process for approving medicine. The FDA ensures that prescription drugs are reliable, pure, and that the benefits of the medication outweigh the risks for the intended population⁹. In the U.S., pharmaceutical companies are not allowed to market their products until the FDA has accepted the proper evidence⁹.

¹ Chandra, S., Lata, H., ElSohly, M. A., Walker, L. A., & Potter, D. (2017). Cannabis cultivation: Methodological issues for obtaining medical-grade product. *Epilepsy & Behavior*, 70, 302-3012. doi: 10.1016/j.yebeh.2016.11.029

² Sawler, J., Stout, J. M., Gardner, K. M., Hudson, D., Vidmar, J., Butler, L., ... & Myles, S. (2015). The genetic structure of marijuana and hemp. *PLoS One*, 10. doi: 10.1371/journal.pone.0133292

³ Kingston, D. (2015). 5 differences between marijuana and hemp. *AZMarijuana.com*. Retrieved from: <https://azmarijuana.com/arizona-medical-marijuana-news/5-differences-between-marijuana-and-hemp/>

⁴ National Conference of State Legislatures (2017). State Industrial Hemp Statutes. Retrieved from: <http://www.ncsl.org/research/agriculture-and-rural-development/state-industrial-hemp-statutes.aspx>

⁵ United States Food and Drug Administration, United States Department of Health and Human Services. 2015 Warning Letters and Test Results for Cannabidiol Related Products. Retrieved from: <https://www.fda.gov/newsevents/publichealthfocus/ucm435591.htm>

⁶ United States Food and Drug Administration, United States Department of Health and Human Services. 2016 Warning Letters and Test Results for Cannabidiol Related Products. Retrieved from: <https://www.fda.gov/newsevents/publichealthfocus/ucm484109.htm>

⁷ Bonn-Miller, M., Loflin, M., Thomas, B., et al (2017) Labeling accuracy of Cannabidiol extracts sold online. *JAMA*, 318(17). Retrieved from <https://jamanetwork.com/journals/jama/article-abstract/2661569?redirect=true>

⁸ Tinker, B. (2017, November 7). Only one-third of marijuana extracts accurately labeled, researchers say. *CNN Health*. Retrieved from <http://www.cnn.com/2017/11/07/health/marijuana-cbd-buy-online-study/index.html>

⁹ Gassman, A. L., Nguyen, C. P., Joffe, H. V. (2017). FDA regulation of prescription drugs. *New England Journal of Medicine*, 376, 674-682. doi: 10.1056/NEJMr1602972

Just as patent medicine promised a panacea for a variety of illnesses, purveyors of medical marijuana, including artisanal CBD products, make claims that their products contain innumerable health benefits. These unsubstantiated claims include benefits such as preventing diabetes, treating fibromyalgia, post-traumatic stress disorder, epilepsy and insomnia, and halting the spread of cancer and mad cow disease. Because of these unsupported claims, the FDA has sent several [warning letters](#), including four sent to firms marketing CBD products who were claiming to prevent, diagnose, treat, or cure cancer without any scientific evidence¹⁰.

Marijuana, including CBD, remains classified as a Schedule I drug. Furthermore, none of the artisanal preparations of marijuana (regardless of THC content) are approved by the FDA for safety or efficacy.

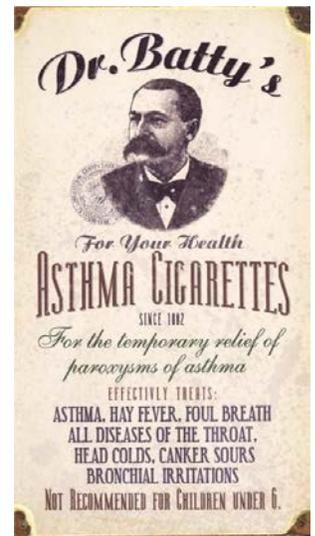
INCREMENTAL LEGALIZATION

No state has passed a retail marijuana law without previously enacting a medical marijuana law¹¹. The path toward marijuana legalization began in the United States in 1996 with medical marijuana in California. Subsequently, 32 states, D.C., Guam, and Puerto Rico have enacted similar laws. Since 2012, ten states have passed laws to allow for retail marijuana use. More recently, some states have turned to low THC, high CBD laws for medical use. Wisconsin was the first state to legalize CBD in 2013. Sixteen other states passed similar laws between 2014-2017¹¹.

A review of states shows that republican controlled states have been likely targeted in high CBD, low THC legalization legislation. Republicans control the governorship and both legislative chambers in 16 of the 18 states in which CBD bills have been introduced^{11,12}. Five states that passed CBD legislation had pending recreational marijuana bills in 2017, including Utah¹¹. Within four years of passing CBD legislation, medical marijuana was legalized in Florida, Missouri, Oklahoma, and Utah¹¹. Additionally, another 7 states have attempted to pass marijuana decriminalization laws since legalizing CBD¹¹.

BACKGROUND OF CBD IN IDAHO

In 2015, CBD was brought to the center of Idaho's legislative session. The bill, S1146a, promised legal relief for parents of children with uncontrolled epilepsy to obtain CBD oil with up to 0.3% THC from across state lines. In addition to ODP, Idaho State Police, Department of Health and Welfare (DHW), the Idaho Prosecuting Attorney's Association, the Fraternal Order of Police, the Idaho Police Chief's Association, the Idaho Sheriff's Association, and the Idaho Criminal Justice Commission opposed S1146a.



¹⁰ United States Food and Drug Administration, United States Department of Health and Human Services. 2017 FDA warns companies marketing unproven products, derived from marijuana, that claim to treat or cure cancer. Retrieved from <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm583295.htm>

¹¹ National Conference of State Legislatures (2018). State Medical Marijuana Laws. Retrieved from: <http://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx#3>

¹² Neely, B. In the States, Republicans Have Never Been so Dominant – Or Vulnerable. *NPR All Things Considered*. Retrieved from: <https://www.npr.org/2017/08/05/541698071/in-the-states-republicans-have-never-been-so-dominant-or-vulnerable>

Concerns about the bill included:

- **Lab testing:** International lab testing standards to discern the level of CBD compared to THC were not present in the legislation. Further, Idaho does not have the capacity to quantify THC in drug testing laboratories and can only determine that THC is present in a sample.
- **Law Enforcement:** Enforcing the law amid CBD legalization is concerning not only because of the inability to quantify THC, but also because products labeled CBD could contain other cannabinoids or a myriad of other illegal drugs. Furthermore, drug sniffing canines are not trained to decipher THC percentages. Consequently, all drug dogs in Idaho would be determined unreliable if legislation similar to SB1146a was passed. According to a report by the Idaho State Police from 2004, police dogs typically cost between \$1,000 and \$10,000 each¹³. Without the capacity to conduct a canine search on all traffic stops or test every product labeled as CBD, officers may face criminals masking drug trafficking operations with the presence of CBD.
- **Product purity:** Marijuana products have been shown to contain contaminants such as mold, fungi, heavy metals and pesticides¹⁴. A small sample of Oregon marijuana products showed contamination in three out of ten samples¹⁵. Oregon has some of the highest standards in marijuana testing, but even so, Andre Ourso the manager of the Oregon Health Authority said, "I don't think it's reasonable for the general public to think that everything is 100 percent clean and safe."¹⁵
- **Product dosing and interactions:** The lack of double-blind, placebo-controlled studies and variability in artisanal CBD products make dosing decisions difficult for prescribers. It is impossible to determine potential interactions with other medications.

The American Epilepsy Society also agreed with the opposition stating, "We are opposed to the use of artisanal preparations of unregulated compounds of cannabis that contain unverified content and are produced by people with no experience in pharmaceutical production."

Despite these concerns, the Idaho legislature passed S1146a. Governor C.L. "Butch" Otter vetoed the measure and, instead, offered a solution by issuing an Executive Order for an Expanded Access Program (EAP). The EAP would provide children with intractable epilepsy access to pharmaceutical grade CBD, Epidiolex, as part of an FDA-approved study. Because families who move to Colorado for oral cannabis extracts are 3 times as likely to report a greater than 50% reduction in seizures as families with established care in Colorado¹⁶, the only way to determine whether positive results can be directly tied to CBD, and not due to other factors, is through rigorous research.

Maintaining drug policy that promotes substance abuse prevention is paramount to the Office of Drug Policy. According to the most recent data available from the National Survey on Drug Use and Health, Idaho ranked 40th among the states and D.C. for the number of individuals aged 12 to 17 reporting marijuana use in the past month. The top 19 states all have either legal retail or medical marijuana.

¹³ Idaho Statistical Analysis Center, Idaho State Police (2004). Canine Drug Program Cost Analysis. Retrieved from: <https://www.isp.idaho.gov/pgr/Research/documents/k9s.pdf>

¹⁴ McLaren, J., Swift, W., Dillon, P., & Allsop, S. (2008). Cannabis potency and contamination: A review of the literature. *Addiction*, 103, 1100-1109. doi: 10.1111/j.1360-0443.2008.02230.x

¹⁵ Crombie, N. (2017). Contaminated marijuana still reaching consumers in Oregon. *The Oregonian*. Retrieved from: http://www.oregonlive.com/marijuana/index.ssf/2017/06/contaminated_marijuana_still_r.html

¹⁶ Press, C., Knupp, K., & Chapman, K. (2014). Parental reporting of response to oral cannabis extract as adjunctive treatment for medically refractory epilepsy. American Epilepsy Society. (Abstract #1.326).

EPIDIOLEX

Epidiolex is a non-synthetic, plant-based medication, containing greater than 98% purified oil-based CBD extract with trace amounts of other cannabinoids. Made by GW Pharmaceuticals (now Greenwich Biosciences in the United States), Epidiolex has been studied in randomized, double-blind, placebo-controlled trials across the U.S.

EAPs allow patients with life-threatening diseases who lack therapeutic alternatives to access investigational drugs outside of a clinical trial¹⁷. EAPs study patients' outcomes while taking investigational drugs, but these programs do not include a placebo group, so all participants receive the medication. The Epidiolex EAP is intended to 1) treat severely ill children not responding to standard medications with a drug that has met FDA requirements for safety in preclinical research while clinical trials take place 2) and gather preliminary information for phased trials that will determine whether Epidiolex can reduce epileptic seizures more effectively than standard medications.

In 2015, Idaho was awarded 25 patient spots for the open-label EAP from the FDA for Epidiolex. In 2016, Idaho was awarded an additional 15 spots, bringing the total available spots to 40. During the course of this study, forty patients were screened to fill all patient spots. During the first cohort, one individual originally withdrew from the study due to intolerability of blood draws but was later readmitted¹⁸ when no other patient was referred to the program before enrollment closed. Because patient slots cannot be filled more than once, a maximum of 39 patients were now eligible for the study. Among these 39 patients, 34 are still enrolled in the study and taking Epidiolex¹⁸. Reasons for withdrawing from the study included no change in seizures (3), worsening seizures (1), and family relocation (1)¹⁸. Although mostly well tolerated, 13 of the 39 patients had adverse events, of which most were resolved when dosing of Epidiolex or other antiepileptic medications were adjusted¹⁸. Regarding efficacy, 25 of the 39 patients had subjective improvement in seizures; however, some families reported seizure improvement, despite seeing no apparent benefit in seizure frequency¹⁸. Of the individuals that reported improvement, 11 reported decreased seizure intensity, six reported decreased seizure frequency, and eight reported decreases in both seizure intensity and frequency¹⁸. Eight reported no change in seizures, and one reported worsening seizures, but opted to continue in the EAP¹⁸.

The FDA accepted the New Drug Application for Epidiolex with Fast Track designation, according to a [press release](#) issued by GW Pharmaceuticals. The FDA approved Epidiolex in June 2018 and the DEA subsequently scheduled Epidiolex as a Schedule V drug. This means Epidiolex is the only legal form of CBD for sale in the state of Idaho. It is also the only federally legal form of CBD oil. Epidiolex is now available with a physician's prescription and will be covered under most Medicaid and insurance plans. Greenwich Biosciences' Patient Assistance Program will provide Epidiolex free of charge to financially eligible patients who cannot afford their medication or don't have sufficient prescription drug coverage.

CONCLUSION

Medical marijuana laws, including high CBD low THC preparations, contradict federal law. These laws create public confusion on what is legal, what is safe, and what is effective. Idaho's Epidiolex EAP complied with both state and federal law, and followed the rigorous testing and production standards of the FDA. Epidiolex is now available for prescription and will be covered by insurance later this year, therefore ODP recommends that

¹⁷ U.S. Food and Drug Administration. Expanded Access (Compassionate Use) (2017). Retrieved from: <https://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm>

¹⁸ Bishop, J.A., Wechsler, R.T., Pape, D.A., Gravett, L.L. (2017, December). *Cannabidiol (CBD, Epidiolex) for Severe, Treatment-Resistant Epilepsy: Continued Experience in Idaho Expanded Access Program*. Poster session presented at the American Epilepsy Society Annual Meeting, Washington, D.C.

lawmakers avoid passing CBD legislation. Additionally, ODP recommends that any legislation related to drugs or pharmaceuticals remain consistent with valid medical and scientific evidence-based practices.