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CANNABINOID CONUNDRUM::

A STUDY OF MARIJUANA AND HEMP LEGALITY IN THE UNITED STATES¹

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Abstract

Marijuana is the most commonly used, cultivated, and trafficked illicit drug worldwide. In the United States, the use and acceptance of marijuana is evolving rapidly as indicated by the volume of new state cannabis legislation. However, marijuana is still a Schedule I drug under the federal Controlled Substances Act (CSA). Further complicating the matter, the 2018 Farm Bill removed hemp from the list of controlled substances under the CSA, resulting in a market flooded with cannabidiol (CBD) products that have not been approved by the Food and Drug Administration (FDA). Many of the changes in state laws have occurred without significant input from medical or scientific communities. The status of marijuana and, until recently, hemp as Schedule I drugs under the CSA creates numerous restrictions which ultimately impact the industry as a whole. The central issues facing marijuana legality in the U.S. are: convoluted state and federal law, adverse

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health effects of cannabis use, research restrictions that produce knowledge gaps, and inconsistency between the U.S. Food and Drug Administration (FDA) and the U.S. Environmental Protection Agency (EPA) regulations. Marijuana policy must evolve to protect and inform both the general public and individuals involved in the cannabis industry. Potential reform options include: federal exemptions following state compliance, rescheduling marijuana, or complete removal from the CSA. The most vital step in the federal legalization process needs to be less restrictive research opportunities for marijuana.

I. Introduction

As a Schedule I controlled substance under the Controlled Substances Act (CSA), controversies surrounding legal, ethical, and societal implications associated with the use of marijuana are compounded by its adverse health effects, limited clinical data for therapeutic indications, and safe administration/packaging/dispensing regulations. The fragmented transition of marijuana from a vilified substance to one with legitimate therapeutic merit has been convoluted and controversial.

Cannabis is the most commonly cultivated, trafficked, and abused drug worldwide, with an annual usage by approximately 147 million individuals, which equates to 2.5% of the global population.⁵ The social attitudes and cultural norms surrounding marijuana use are shifting in a positive direction, as shown by the rapidly evolving cannabis policy at the state level. State cannabis laws are widespread and highly variable—which leads to some ambiguity and concern.⁶ As state legal restrictions have eased, marijuana use has increased.⁷ In states where it is legal, sales topped \$8 billion in 2017, and they are projected to grow to \$24 billion by 2025.⁸ State marijuana legalization and industry growth show no signs of slowing.⁹

This paper will outline the central issues within marijuana legality, provide potential legislative solutions, and pose several core questions that must be answered before significant changes occur at the federal level. The central issues regarding marijuana legality include: convoluted state and federal laws, adverse health effects of cannabis use, research restrictions that produce knowledge gaps, and inconsistency with Food and Drug Administration (FDA) and Environmental Protection Agency (EPA) regulations.

In order to resolve the conflict, it is imperative to stress the importance of science in this policy debate. The changes in state laws have occurred largely without significant input from the medical, scientific, or policy research communities.¹⁰ Updating marijuana policy on the federal level is a desirable goal, but we must seek to minimize any adverse consequences in

⁵ Cannabis, WORLD HEALTH ORG., https://www.who.int/substance_abuse/facts/cannabis/en/ (last visited Apr. 19, 2019).

⁶ Mary Barna Bridgeman & Daniel T. Abazia, *Medicinal Cannabis: History, Pharmacology, And Implications for the Acute Care Setting*, 42 PHARMACOLOGY & THERAPEUTICS 180 (2017).

⁷ Cannabis, *supra* note 5.

⁸ Rebecca L. Haffajee, Robert J. MacCoun & Michelle M. Mello, *Behind Schedule — Reconciling Federal and State Marijuana Policy*, 379 NEW ENGLAND J. OF MED. 501 (2018).

⁹ Barna Bridgeman & Abazia, *supra* note 6.

¹⁰ Susan R.B. Weiss, Katia D. Howlett & Ruben D. Baler, *Building smart cannabis policy from the science up*, 42 INT'L J. OF DRUG POL'Y 39 (2017).

the form of social and public health costs. Scientific research must be at the heart of all legislative decisions.

II. History

Cannabis is a botanical product with medicinal origins dating back to ancient times.¹¹ In the 19th and early 20th centuries, cannabis was widely used throughout the United States as a medicinal drug and could easily be purchased in pharmacies and general stores.¹² In 1850, it was described in the *United States Pharmacopedia* for the first time as “Extractum Cannabis.”¹³ Cannabis was listed as a treatment for various conditions like neuralgia, tetanus, cholera, opiate addiction, and convulsive disorders.¹⁴ Federal restriction on cannabis use/sale first occurred with the passage of the Marihuana Tax Act of 1937 (“the Act”).¹⁵ The Act imposed registration requirements and a tax on growers, sellers, and buyers of marijuana.¹⁶ It did not outright prohibit marijuana, but its effect was very similar. Prescriptions of the drug greatly decreased after passage of the Act because doctors generally concluded that it was easier to not prescribe marijuana than to contend with the extra work imposed by this law.¹⁷ Subsequent to the Act, cannabis was dropped from the *United States Pharmacopedia* in 1942, which caused the drug to lose its remaining therapeutic legitimacy.¹⁸

In 1970, Congress passed the CSA, which established a single system of control for both narcotic and psychotropic drugs for the first time in U.S. history.¹⁹ The extent of control exercised by the U.S. Drug Enforcement Agency (DEA) is determined by a substance’s classification in one of five schedules for controlled substances. Marijuana was, and still is, classified as Schedule I in the United States, meaning there is no currently accepted medical use, high potential for abuse, and lack of accepted safety for use of the drug or other substance under medical supervision.²⁰ The reasoning behind this classification was mainly due to lack of solid research about the plant and the active substances contained within it.²¹

In 1996, California became the first state to permit legal access to and use of botanical cannabis for medical purposes under physician supervision in accordance with the Compassionate Use Act of 1996.²² Additionally, Section 538 of the Consolidated and Further Continuing Appropriations Act of 2015 (the Rohrabacher-Farr Amendment) prohibits the U.S. Department of Justice from using federal funds to supersede state law in those states that have legalized the use of medical marijuana.²³ As of September 2019, 33

¹¹Barna Bridgeman & Abazia, *supra* note 6.

¹²*Id.*

¹³*Id.*

¹⁴*Id.*

¹⁵*Id.*

¹⁶*Id.*

¹⁷Rosalie Liccardo Pacula et. al., *State Medical Marijuana Laws: Understanding the Laws and Their Limitations*, 23 J. OF PUB. HEALTH POL’Y 413 (2002).

¹⁸Barna Bridgeman & Abazia, *supra* note 6.

¹⁹DRUG ENF’T AGENCY, *Drug Scheduling*, <https://www.dea.gov/druginfo/ds.shtml> (last visited Apr 19, 2019).

²⁰Alice Mead, *The legal status of cannabis (marijuana) and cannabidiol (CBD) under U.S. law*, 70 EPILEPSY & BEHAV. 288 (2017).

²¹NAT’L ACAD. OF SCI., THE HEALTH EFFECTS OF CANNABIS AND CANNABINOIDS: THE CURRENT STATE OF EVIDENCE AND RECOMMENDATIONS FOR RESEARCH (2017).

²²Barna Bridgeman & Abazia, *supra* note 6, at 4.

²³Consolidated and Further Continuing Appropriations Act of 2015, Pub. L. 113–235, sec. 538, 128 Stat. 2130 (2014).

states and the District of Columbia have passed laws broadly legalizing marijuana in some form.²⁴ The District of Columbia and 11 states have legalized marijuana for recreational use.²⁵

The most recent legislative progress in the realm of marijuana was the Hemp Farming Act of 2018, which was included in the 2018 Farm Bill.²⁶ This law removed hemp, a less potent cultivar of marijuana, from the list of controlled substances.²⁷ The 2018 Hemp Bill defines hemp as all parts of the *Cannabis sativa* plant that do not exceed 0.3% THC (.9-tetrahydrocannabinol) by dry weight, including “derivatives,” “extracts,” and “cannabinoids.”²⁸ Prior to the passage of this bill, cultivated hemp was only federally lawful under certain state-sanctioned pilot programs.

III. Central Issues

The status of cannabis as a Schedule I substance under the CSA creates numerous restrictions which ultimately impact the industry. The attitudes and cultural norms surrounding marijuana are shifting in a positive direction as shown by the rapidly evolving cannabis policy on the state level. Although most states have broadly legalized marijuana in some form, significant controversies and issues remain regarding the legal, ethical, and societal implications of cannabis use.

A. Convolved Law

Federal and state laws regarding the medical use of cannabis and cannabinoids are in conflict and have led to severe confusion among patients and healthcare providers. As stated, marijuana and its cannabinoid derivatives are classified as Schedule I drugs that have no currently accepted medical use, high potential for abuse, and lack of accepted safety for use of the drug or other substance under medical supervision. This places marijuana on the same level as drugs like mescaline, psilocybin, heroin, and lysergic acid diethylamide (LSD).²⁹ Schedule I substances cannot be prescribed, only “recommended” as treatment by a health care provider.³⁰ In contrast, state laws are commonly divided into four groups: medical use, High-CBD/Low-THC only, decriminalization, and recreational legalization for adults 21 years old and up.

The cannabis plant contains over 100 individual cannabinoids, most abundantly: THC and CBD (cannabidiol).³¹ There are no standardized definitions of “medical marijuana” and “high-CBD” or “low-THC” products as mainstream media commonly uses these terms interchangeably.³² The term “medical marijuana” does not explicitly refer to a special strain

²⁴State Marijuana Laws in 2019 Map, GOVERNING, <https://www.governing.com/gov-data/safety-justice/state-marijuana-laws-map-medical-recreational.html> (last visited Dec. 20, 2019).

²⁵Id.

²⁶Agricultural Improvement Act of 2018, Pub. L. No. 115–334, 132 Stat. 4490 (2018).

²⁷Id.

²⁸Jamie Corroon & Rod Knight, *Regulatory Status of Cannabidiol in the United States: A Perspective*, 3 CANNABIS AND CANNABINOID RES. 190 (2018); §6, 132 Stat. 4490.

²⁹Drug Scheduling, *supra* note 19.

³⁰Barna Bridgeman & Abazia, *supra* note 6.

³¹Christelle M. Adre, Jean-Francois Hausman & Gea Guerriero, Cannabis sativa: *The Plant of the Thousand and One Molecules*, 7 FRONTIERS IN PLANT SCI. 19 (2016).

³²Mead, *supra* note 20, at 5.

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of cannabis, mode of preparation, or dosage method. “Medical marijuana” products contain a wide range of cannabinoids with varying concentrations of active ingredients. Overall, there is a lack of common descriptions for “medical marijuana” or even “CBD-access only” laws, which vary significantly from state to state.³³ Some laws decriminalize possession by qualified patients or their caregivers, while others authorize full panoply of manufacturing and distribution/retail sales.³⁴

CBD is considered the non-psychoactive component of marijuana and has become the center of the legality confusion, especially after the FDA approval of Epidiolex (CBD-based epilepsy drug). In September 2018, the DEA scheduled Epidiolex and any future drug products containing CBD derived from marijuana with no more than 0.1% THC as Schedule V of the CSA.³⁵ This is a huge stepping-stone in the journey of cannabis legalization. A Schedule V substance is considered to have a low potential for abuse and consists of primarily limited quantities of certain narcotics.³⁶

Despite the approval of Epidiolex and growing popularity of CBD, its legality is perplexing. The source of CBD is critically important in determining its legal status.³⁷ The most common source is the plant *Cannabis sativa*, which encompasses both cannabis and hemp. While they are the same chemical compound, marijuana (cannabis)-derived CBD and hemp-derived CBD each have their own unique regulatory status and legal implications. There are various methods for differentiating marijuana and hemp--i.e. genotype, phenotype, etc.³⁸ From a regulatory standpoint, the differences between the two is in their respective concentrations of THC.³⁹ Hemp is legally defined as a cultivar of *Cannabis sativa* with low concentrations of THC, which cannot exceed 0.3%.⁴⁰ Despite clear differences in traits, marijuana and hemp appear to readily interbreed making it difficult to differentiate the species.⁴¹ CBD from marijuana is still considered a Schedule I controlled substance.⁴² While the scheduling of Epidiolex as a Schedule V substance greatly increased access to the drug, it did not change the regulatory status of CBD itself. To date, the FDA has not approved a marketing application for cannabis for the treatment of any disease or condition, and thus has not determined that cannabis is safe and effective for any disease or condition.⁴³

To further complicate regulation issues, with the approval of Epidiolex, the FDA ruled that any CBD product cannot be included or listed as a dietary supplement.⁴⁴ This ruling now brings a level of uncertainty to the future of online or over-the-counter sales of CBD

³³Id.

³⁴Id.

³⁵Corroon & Knight, *supra* note 28, at 6; 21 C.F.R. § 1308 (2019); 21 C.F.R. § 1312 (2019).

³⁶Drug Scheduling, *supra* note 19.

³⁷Corroon & Knight, *supra* note 28.

³⁸Jason Sawler et al., *The Genetic Structure of Marijuana and Hemp*, 10 PLOS ONE 8 (2015), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4550350/>.

³⁹Id.

⁴⁰Id.; Agricultural Improvement Act of 2018, Pub. L. No. 115–334, 132 Stat. 4490 (2018).

⁴¹Leah N. Sandler et al., *Cannabis as conundrum*, 117 CROP PROT. 37 (2019).

⁴²Drug Scheduling, *supra* note 19.

⁴³U.S. FOOD & Drug Admin., *FDA Regulation of Cannabis and Cannabis-Derived Products: Questions and Answers*, <https://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-questions-and-answers#approved> (last visited Sept. 10, 2019).

⁴⁴Id.

products. The Federal Food, Drug, and Cosmetic Act (FDCA) defines a dietary supplement as a product taken by mouth that contains a “dietary ingredient,” which may include vitamins, minerals, amino acids, and herbs.⁴⁵ According to the FDCA, if a controlled substance (such as CBD) is an active ingredient in an approved drug, then products containing that substance fall outside the definition of a dietary supplement.⁴⁶ Thus, CBD products cannot be marketed, labeled, or produced as dietary supplements.

To add another layer of complexity, the approval of the 2018 Hemp Farming Act removed hemp from the list of controlled substances.⁴⁷ The Hemp Farming Act redefined hemp as all parts of the *Cannabis sativa* plant that do not exceed 0.3% THC by dry weight—including derivatives, extracts, and cannabinoids.⁴⁸ Thus, the bill explicitly removed hemp derived CBD from regulation under the CSA. In addition to domestically cultivated hemp, CBD may also be legal if it is derived from “non-psychoactive hemp” imported into the U.S. from Canada and Europe.⁴⁹ Hemp-derived CBD products can currently be purchased both online and over the counter throughout the country, as if they were dietary supplements.⁵⁰ Marijuana-derived CBD products can only be purchased by qualifying patients in states with medical-marijuana laws.⁵¹

Regardless of rulings that have provided greater access to CBD, marijuana and marijuana-derived CBD are still considered to be illegal on the federal level under the CSA.⁵² The removal of hemp from the controlled substance list is very encouraging progress for the future of marijuana legality. In October of 2009, the Obama Administration sent a memo to federal prosecutors encouraging them not to prosecute people who distribute marijuana for medical purposes in accordance with state law.⁵³ This guidance lead to the approval of the 2013 Cole Memorandum, which deprioritized marijuana prosecutions in states where use was legal.⁵⁴ The Rohrabacher-Farr Amendment adopted by Congress in 2014 prohibits the use of federal funds to prosecute medical marijuana activities.⁵⁵ This Amendment must be renewed each year, and was most recently renewed through December 2019.⁵⁶ More recently, in January of 2018, the Cole Memorandum, which allows federal prosecutors to decide how to prioritize enforcement of federal marijuana policy, was revoked by Attorney General Sessions by the issuance of a Marijuana Enforcement Memorandum.⁵⁷ Sessions noted that the purpose of his memorandum was to “direct all U.S. attorneys to use previously established prosecutorial principles that provide them all necessary tools to disrupt criminal organizations, tackle the drug crisis, and thwart violent crime.”⁵⁸ The most significant

⁴⁵21 U.S.C. § 321 (ff) (2018).

⁴⁶Id.

⁴⁷Agricultural Improvement Act of 2018, Pub. L. No. 115–334, 132 Stat. 4490 (2018).

⁴⁸Corroon & Knight, *supra* note 28; §6, 132 Stat. 4490.

⁴⁹Corroon & Knight, *supra* note 28.

⁵⁰Id.

⁵¹Id.

⁵²*Drug Scheduling*, *supra* note 19.

⁵³Memorandum from James M. Cole, Deputy Attorney Gen., to all U.S. Attorneys (Aug. 29, 2013), <https://www.justice.gov/iso/opa/resources/3052013829132756857467.pdf>.

⁵⁴Haffajee, Maccoun & Mello, *supra* note 8.

⁵⁵Id.

⁵⁶Jacob Pramuk, *Trump signs spending bill into law, dodging a government shutdown for another month*, CNBC (Nov. 21, 2019,

⁵⁷56PM) <https://www.cnbc.com/2019/11/21/trump-signs-spending-bill-avoiding-government-shutdown.html>.

⁵⁷Memorandum from Jefferson B. Sessions, Attorney Gen., to all U.S. Attorneys (Jan. 4, 2018), <https://www.justice.gov/opa/press-release/file/1022196/download>.

policy decisions now relate to how and when the federal government will update marijuana legislation to create a comprehensive, safe, and effective system.

B. Adverse Effects of Cannabis Use

Most of the knowledge regarding the adverse effects of medical cannabis comes from the limited clinical trial data and anecdotal studies of recreational users of marijuana.⁵⁹ The effects associated with acute use are well known: relaxation, appetite stimulation, heightened sensation, increased heart rate, impairment of short-term learning/memory, and possible paranoia or psychosis.⁶⁰ Chronic use of cannabis—especially in individuals who begin using at a young age—has led to altered brain development, cognitive impairment, chronic bronchitis, and increased risk of psychosis health disorders, like schizophrenia and depression.⁶¹ Vascular conditions, including heart attack and stroke, have also been associated with cannabis use.⁶² A recent advisory given by the United States Surgeon General argued against the use of marijuana for its adverse effects on the developing brain, during adolescence and pregnancy.⁶³

Understanding of the consequences of chronic cannabis use with regard to their permanence and causality is inadequate and inconsistent. This is largely due to cannabis and its constituents continued Schedule I status and preclusion of randomized controlled exposures (for ethical reasons).⁶⁴ Controlled exposures to the drug could possibly rule out pre-existing differences, and the common use of multiple substances (i.e. tobacco and alcohol) at the same time as cannabis, especially in adolescent users.⁶⁵

Compounding the debate, metabolic and pharmacokinetic interactions exist between medical cannabis and other pharmaceuticals. Cytochrome 450 (CYP450) and isoenzymes 2C9/3A4 and 2C19/3A4, are responsible for the metabolism of THC and CBD, respectively.⁶⁶ Products that contain both THC and CBD will have drug interactions with all three enzymes.⁶⁷ On a broader scale, the CYP450's constitute the major enzyme family capable of metabolizing most drugs.⁶⁸ Smoking THC is associated with CYP1A2 induction; so theoretically, THC can decrease serum concentrations of clozapine, duloxetine, naproxen, and haloperidol because their metabolic breakdown is CYP1A2-mediated.⁶⁹ These drugs are from various classes, including antidepressants, antipsychotics, anti-inflammatories, and

⁵⁸Press Release, U.S. Dep’t of Justice, Justice Department Issues Memo on Marijuana Enforcement (Jan. 4, 2018), <https://www.justice.gov/opa/press-release/file/1022196/download>.

⁵⁹Barna Bridgeman & Abazia, *supra* note 6.

⁶⁰Weiss, Howlett & Baler, *supra* note 10.

⁶¹*Id.*

⁶²Barna Bridgeman & Abazia, *supra* note 6.

⁶³U.S. DEP’T OF HEALTH & HUMAN SERVICES, U.S. SURGEON GENERAL’S ADVISORY: MARIJUANA USE AND THE DEVELOPING BRAIN, <https://www.hhs.gov/surgeongeneral/reports-and-publications/addiction-and-substance-misuse/advisory-on-marijuana-use-and-developing-brain/index.html> (last visited Sept. 10, 2019).

⁶⁴Weiss, Howlett & Baler, *supra* note 10.

⁶⁵*Id.*

⁶⁶Adriane Fugh-Berman et al., *Medical Cannabis: Adverse Effects and Drug Interactions*, D.C. DEP’T OF HEALTH (2019), https://dchealth.dc.gov/sites/default/files/dc/sites/doh/publication/attachments/Medical%20Cannabis%20Adverse%20Effects%20and%20Drug%20Interactions_0.pdf.

⁶⁷*Id.*

⁶⁸Ulrich M. Zanger & Matthias Schwab, *Cytochrome P450 enzymes in drug metabolism: Regulation of gene expression, enzyme activities, and impact of genetic variation*, 138 PHARMACOLOGY & THERAPEUTICS 103 (2013).

⁶⁹Flockhart Table ™ - Drug Interactions, IND. UNIV. SCH. OF MED., <https://drug-interactions.medicine.iu.edu/Main-Table.aspx> (last visited Apr 19, 2019).

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sedatives.⁷⁰ CYP3A4 metabolizes about a quarter of all drugs, including CBD.⁷¹ Therefore, if CBD is co-administered with a CYP3A4-inhibitor (e.g. ketoconazole) it can increase the serum concentrations of CBD or benzodiazepines, antihistamines, and some statins.⁷² CBD-mediated inhibition of CYP2D6 may also increase serum concentrations of selective serotonin reuptake inhibitors (SSRI's) and antipsychotics.⁷³ It is imperative for patients seeking medical marijuana treatment to consult with their health care provider to learn about and avoid potentially adverse drug interactions.

Truly chronic studies with CBD are still scarce, especially toxicological evaluations of genotoxicity and effects on hormones.⁷⁴ Therefore, more toxicological studies that explore CBD side-effects after chronic administration must be conducted. This research is crucial because currently, the majority of patients being prescribed CBD in the form of Epidiolex are children under ten years of age.⁷⁵ In a 2017 review of CBD clinical studies, the most common side- effects reported were elevated liver enzymes, tiredness, diarrhea, and changes of appetite/weight.⁷⁶ In comparison with other prescription drugs studied in these trials, CBD had a better side-effect profile. Nonetheless, much more research is needed in large-scale human trials to determine CBD's toxicological safety/efficacy.

C. Research Restrictions and Knowledge Gaps

The Schedule I listing of cannabis under the CSA has led to difficulties in access for research purposes. Researchers conducting clinical research on biological products such as cannabis must submit an investigational new drug (IND) application to the FDA.⁷⁷ Next, the investigator must obtain an administrative letter of authorization (LOA) from the National Institute of Drug Abuse (NIDA).⁷⁸ The LOA describes the investigators' facilities and the specifics about the cannabis product they desire to obtain.⁷⁹ To safeguard against the acquisition of cannabis or cannabinoids for non-research purposes, investigators must also apply for a DEA registration and site licensure before conducting any studies involving cannabis or cannabinoid constituents.⁸⁰ Finally, the investigator must submit the IND and the LOA to the FDA and the DEA for further review and approval.⁸¹

Currently, investigators interested in conducting federally-supported research on cannabis must obtain that cannabis, or constituents thereof, through the NIDA Drug Supply Program. Historically, NIDA has only contracted with the University of Mississippi to cultivate different varieties of research-grade cannabis with various THC:CBD ratios.⁸² All

⁷⁰Fugh-Berman et al., *supra* note 66.

⁷¹Id.

⁷²Id.

⁷³Kerstin Iflland & Franjo Grotenhermen, *An Update on Safety and Side Effects of Cannabidiol: A Review of Clinical Data and Relevant Animal Studies*, 2 CANNABIS & CANNABINOID RES. 139 (2017).

⁷⁴Id.

⁷⁵Press Release, Food & Drug Admin., FDA approves first drug comprised of an active ingredient derived from marijuana to treat rare, severe forms of epilepsy (Jun. 25, 2018), <https://www.fda.gov/news-events/press-announcements/fda-approves-first-drug-comprised-active-ingredient-derived-marijuana-treat-rare-severe-forms>.

⁷⁶Zanger & Schwab, *supra* note 68.

⁷⁷THE NAT'L ACAD. OF SCI., *supra* note 21.

⁷⁸Id.

⁷⁹Id.

⁸⁰IND. UNIV. SCH. OF MED., *supra* note 69.

⁸¹THE NAT'L ACAD. OF SCI., *supra* note 21.

⁸²Mead, *supra* note 20.

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researchers, regardless of their institutional affiliation, that plan to use cannabis products from the NIDA Drug Supply Program have to complete the IND and LOA process as mentioned previously, undergo NIH review, and file a “Marijuana Request Package.”⁸³ This package includes cover letter, research protocol, researchers’ curriculum vitae, and several DEA forms.⁸⁴ In 2017, the DEA announced that it will register additional sources of cannabis cultivated for research on the development of FDA-approved products.⁸⁵ Since this announcement, however, no other institution has been authorized/contracted by NIDA to cultivate cannabis.⁸⁶ Recently, the DEA has been sued by researchers in Arizona who were frustrated by the lack of other institutions being approved to cultivate cannabis.⁸⁷ In response, the DEA has stated that it will begin to process the pending applications of other institutions.⁸⁸

In contrast to the issues posed by marijuana’s legal status, drugs that fall under Schedule II-V are subject to less stringent rules. FDA-approved products that contain a Schedule II-V substance may be prescribed and dispensed within a clinical practice.⁸⁹ In contrast, Schedule I substances cannot be legally prescribed by a physician, only “certified” or “recommended.”⁹⁰ Additionally, a Schedule I substance cannot be dispensed outside of a research program;⁹¹ patients must obtain cannabis products from a dispensary, not directly from their health care provider or a pharmacy.⁹² Physicians who hold Schedule II-V prescriber registrations may conduct research on a Schedule II-V substance lawfully.⁹³ They do not need to seek further DEA or state-controlled drug agency approval, and they can obtain the substances from a wide number of registered manufacturers.⁹⁴

Funding for cannabis research is another restrictive process. Without adequate financial support, cannabis research will be unable to inform health care or public health practice, or keep pace with changes in cannabis policy and patterns of cannabis use.⁹⁵ The National Institute of Health (NIH) is responsible for funding research across a number of health domains, and NIDA is a member institute of NIH. In the fiscal year of 2017, NIH spent almost \$140 million on cannabis research.⁹⁶ In 2017, studies supported by NIDA accounted for 60% of all NIH spending on cannabinoid research.⁹⁷ There has been a push recently for

⁸³DRUG SUPPLY PROGRAM CATALOG 21–22 (Nat'l Inst. on Drug Abuse ed., 2016), https://d14rmgrwzf5a.cloudfront.net/sites/default/files/ndsp_catalog_25th_v3_2016.pdf (last visited Sept. 10, 2019).

⁸⁴Id.

⁸⁵Press Release, Drug Enf’t Admin., DEA announces steps necessary to improve access to marijuana research (Aug. 26, 2019), DRUG SUPPLY PROGRAM CATALOG 21–22 (Nat'l Inst. on Drug Abuse ed., 2016), https://d14rmgrwzf5a.cloudfront.net/sites/default/files/ndsp_catalog_25th_v3_2016.pdf (last visited Sept. 10, 2019).

⁸⁶Sara Brittany Somerset, *DEA Responds to Medical Marijuana Research Expansion Lawsuit*, FORBES (Sept. 2, 2019), <https://www.forbes.com/sites/sarabrittanyset/2019/09/02/dea-responds-to-medical-marijuana-research-expansion-lawsuit/#2cdc059b6259>.

⁸⁷Id.

⁸⁸Id.

⁸⁹Barna Bridgeman & Abazia, *supra* note 6.

⁹⁰Id.

⁹¹U.S. DRUG ENF’T ADMIN., PRACTITIONER’S MANUAL: AN INFORMATIONAL OUTLINE OF THE CONTROLLED SUBSTANCES ACT (2006), https://d14rmgrwzf5a.cloudfront.net/sites/default/files/ndsp_catalog_25th_v3_2016.pdf.

⁹²Id.

⁹³DRUG SUPPLY PROGRAM CATALOG 21–22, *supra* note 83.

⁹⁴Id.

⁹⁵IND. UNIV. SCH. OF MED., *supra* note 69.

⁹⁶NIH Research on Marijuana and Cannabinoids, NAT'L INST. ON DRUG ABUSE, <https://www.drugabuse.gov/drugs-abuse/marijuana/nih-research-marijuana-cannabinoids> (last updated May 2018).

⁹⁷IND. UNIV. SCH. OF MED., *supra* note 69.

more experimental therapeutic research with cannabis for a range of conditions including cardiovascular disease, obesity, and Alzheimer's disease.⁹⁸ These conditions are usually administered by other branches and institutes of NIH. It is unrealistic to expect NIDA to have the resources or interest to fund a broader therapeutic research agenda for cannabinoid products. If the legal status of cannabis were to change to allow for broader research access, this will assuredly have an impact on treatments and conditions studied by institutes other than NIDA. In order to support investigation for a broader class of therapeutic conditions, the federal government could allow less stringent regulations if states were to fund such research with a percentage of their marijuana tax revenue. This could be similar to how revenue from federal gas taxes is placed in a trust fund that pays for infrastructure like roads and bridges.⁹⁹

Due to numerous research and funding restrictions, there are inherent knowledge gaps associated with cannabis use that must be addressed. There is insufficient high-quality data regarding the efficacy, dose-dependent (adverse) effect curves, drug interactions, and safety of commercially available medical cannabis products.¹⁰⁰ The dose-dependent curve of a drug is a graphical representation of the response the drug elicits in comparison to the exposure concentration. There is a further lack of sufficient knowledge regarding the exact content and purity of various medical cannabis derivatives. These gaps impair physicians' and patients' ability to reach a fully informed decision regarding the recommendation and use of medical cannabis as a pharmaceutical because many issues of the substance's pharmacokinetics are still unclear. Pharmacokinetics refers to the absorption, metabolism, and excretion-time-course of an ingested drug. There are no clear guidelines of when to "recommend" medical cannabis for a patient.¹⁰¹ The vague indications and relatively high availability of the product may lead to overuse and misuse by patients.¹⁰²

D. FDA/EPA Regulation Inconsistency

As a Schedule I substance, cannabis is effectively barred from obtaining further regulatory policies in terms of differentiation of application, pesticide regulation, and product safety development. Inconsistency within the two regulatory agencies of the FDA and EPA has led to further confusion and risks associated with the medical cannabis industry as a whole.

The FDA states that their top priority is to protect public health.¹⁰³ However, inconsistent regulation by the FDA is disconcerting given the widespread and ever-growing use of cannabis products all over the country.¹⁰⁴ The FDA exercises control over approved cannabis drugs like Epidiolex and Marinol, but it does not regulate most of the medical marijuana products sold online or in dispensary stores.¹⁰⁵ The role of the FDA in the drug

⁹⁸NAT'L ACAD. OF SCI., *supra* note 21.

⁹⁹Richard F. Weingroff, *Federal-Aid Highway Act of 1956: Creating The Interstate System*, 60 PUBLIC ROADS (1996), <https://www.fhwa.dot.gov/publications/publicroads/96summer/p96su10.cfm>.

¹⁰⁰Iftach Sagiv et al., *Ethical issues in medical cannabis use*, 49 EUR. J. OF INT'L MED. 20 (2018).

¹⁰¹Id.

¹⁰²Id.

¹⁰³What You Need to Know (And What We're Working to Find Out) About Products Containing Cannabis or Cannabis-derived Compounds, Including CBD, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/consumers/consumer-updates/what-you-need-know-and-what-were-working-find-out-about-products-containing-cannabis-or-cannabis> (last visited Sept. 10, 2019).

¹⁰⁴Cannabis, *supra* note 5.

¹⁰⁵U.S. FOOD & DRUG ADMIN., *supra* note 43.

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approval and review process is designed to ensure that new medicines, including those derived from botanicals, are appropriately evaluated for safety, effectiveness, and are cultivated/manufactured under safe conditions for human consumption.¹⁰⁶ Changes in state law and the 2018 Farm Bill have led to a substantial increase in availability of unapproved CBD products.¹⁰⁷ These products have had no evaluation regarding their safety, disease treatment efficacy, proper dosage, drug interactions, and dangerous side effects.¹⁰⁸

Consequently, many patients are using cannabis products or extracts that: (1) have not undergone rigorous clinical trials, (2) are not regulated for consistency or quality, and (3) are indicated for medical conditions without sufficient evidence to support their claimed effectiveness³. Without the FDA offering a comprehensive and universal regulation plan for medical marijuana products, state governments are left to make decisions for themselves. Irregularity in marijuana regulation from state to state can allow inappropriate marketing, formulation and packaging practices to persist—making THC/CBD content across samples unpredictable and potentially dangerous.¹⁰⁹

Independent research, separate from the FDA, has confirmed that the CBD content in almost 70% of products available online could be mislabeled (43% of products were under-labeled and 26% over-labeled for actual CBD concentrations).¹¹⁰ In another study conducted by the FDA in 2016, the results showed that most of the online marijuana products contained little-to-no CBD, and other products contained much higher levels of THC than listed on the label.¹¹¹ Without FDA approval and regulation, health care providers and patients are left with a lack of knowledge about the efficacy, dosing, adverse effects, and accessibility to safe marijuana products. If all marijuana products were subjected to FDA approval, access to such products would be hindered initially while intensive efficacy and safety research is conducted, but FDA regulation would ultimately foster a complete and robust system for the improvement of product safety and consistency within the medical cannabis industry.

The EPA has oversight of pesticide registration, safe use, and enforcement over botanical products.¹¹² Unfortunately, there is limited information available about cannabis pests, and there are no pesticides specifically labeled for marijuana cultivation.¹¹³ Status as a Schedule I compound directly impacts whether or not conventional pesticides can be legally used to manage pests associated with cannabis.¹¹⁴ The EPA does not allow registration of pesticides on cannabis because federal law categorizes the plants as illegal.¹¹⁵ Without this registration, conventional pesticides cannot be used legally for marijuana cultivation in the U.S.

¹⁰⁶Weiss, Howlett & Baler, *supra* note 10.

¹⁰⁷U.S. FOOD & DRUG ADMIN., *supra* note 43.

¹⁰⁸*Id.*

¹⁰⁹Haffajee, Maccoun & Mello, *supra* note 8.

¹¹⁰Corroon & Kight, *supra* note 28.

¹¹¹Mead, *supra* note 20.

¹¹²*Our Mission and What We Do*, U.S. ENVTL. PROT. AGENCY, <https://www.epa.gov/aboutepa/our-mission-and-what-we-do> (last visited Dec. 19, 2019).

¹¹³Sandler et al., *supra* note 41.

¹¹⁴*Id.*

¹¹⁵*Id.*

The EPA also establishes pesticide tolerance levels for crops and botanical products.¹¹⁶ The EPA sets a maximum residue level acceptable for each specific crop called a pesticide tolerance.¹¹⁷ The pesticide tolerance information is required before the EPA can officially register pesticides for crops.¹¹⁸ Consequently, as long as cannabis remains a Schedule I drug, the EPA cannot recognize it as a legal crop, thereby preventing the establishment of pesticide tolerances.

Cannabis growers have an economic incentive to improve the quantity and quality of their crops through the use of registered pesticides available for other agricultural crops.¹¹⁹ Cannabis crops are agronomic and have similar pests to other greenhouse crops.¹²⁰ However, pesticides used on other EPA regulated crops cannot be legally used on cannabis. Under federal and state laws, using a pesticide on a crop that is not listed on a product's label is considered illegal, which subjects the grower to crop confiscation, fines, and imprisonment.¹²¹

The EPA has failed to examine potential health effects of pesticide compounds on cannabis by not offering a standardized risk assessment at the federal level. This makes it difficult to determine how serious the exposure to certain pesticides may be to potential consumers. A 2013 study found that 69.5% of tested common pesticides like bifenthrin, diazinon, and permethrin were found remaining in cannabis smoke condensate.¹²² Pesticide residues in cannabis could be substantial and thus pose significant toxicological risks.

It is an unfortunate failing of our federalist system that a Schedule I drug has been legalized in some states prior to the pesticides potentially needed to produce and protect the substance. This gives the appearance that pesticides are more austere regulated in the U.S. than a Schedule I drug. It is imperative for the federal government to establish overall guidelines regarding pesticide legislation and to implement a program for the enforcement of cannabis pesticides.

IV. Potential Marijuana Reform Options

The present situation of conflicting federal and state marijuana laws is suboptimal and will begin to adversely affect consumers if changes are not made. The absence of a sensible, stable federal marijuana policy affects the safety of marijuana products and physicians' comfort in recommending or prescribing them.¹²³ Federal regulation that accommodates, reinforces, and standardizes state marijuana policy would result in a safer, more reliable, and more accessible supply of cannabis products. It is no longer a matter of *whether* marijuana

¹¹⁶*Our Mission and What We Do*, *supra* note 112.

¹¹⁷*Regulation of Pesticide Residues on Food*, U.S. ENVTL. PROT. AGENCY, <https://www.epa.gov/pesticide-tolerances> (last visited Dec. 19, 2019).

¹¹⁸*Id.*

¹¹⁹*Id.*

¹²⁰Sandler et al., *supra* note 41.

¹²¹*Id.*

¹²²Nicholas Sullivan, Sytze Elzinga & Jeffrey C. Raber, *Determination of Pesticide Residues in Cannabis Smoke*, 2013 J. OF TOXICOLOGY 1 (2013).

¹²³Haffajee, Maccoun & Mello, *supra* note 6.

laws will change, but *how* and *when* they will change. This section will outline several federal marijuana reform proposals and pros and cons for each.

A. Federal Exemptions Following State Compliance

One possible federal reform proposal creates exemptions for state-legal marijuana activity from federal prosecution. Meaning, federal marijuana laws simply would not apply to state-compliant activity, potentially requiring the government to prove noncompliance with state law as its main objective for enforcement.¹²⁴ Unlike current legislation, including the Rohrabacher-Farr Amendment which must be approved every year,¹²⁵ this type of policy would provide marijuana users, growers, physicians, etc. with more than temporary protection. Potential federal exemptions would unquestionably apply to and protect any conduct that takes place while they were enacted, even if they were repealed later.

The flaw in this reform proposal is inevitably defining what constitutes “compliance” with state law. For example, a seller who failed to abide by their state’s regulations for packaging or manufacturing could thereby be open to a federal drug prosecution. How will the federal government analyze state compliance? This type of reform policy also does not explicitly address the status of marijuana for federally funded research. Under this legislation, marijuana would still be considered a Schedule I substance, and would still be subjected to those research restrictions. In the end, there would be marijuana policies enacted that still do not have the fundamental science backing to ensure safety for all involved.

B. Rescheduling of Marijuana

A second possible reform option is to reschedule marijuana and all of its derivatives. In doing so, marijuana would become legal for medicinal purposes, but would still be a regulated substance. There is considerable evidence in support of marijuana’s therapeutic benefits in reducing chronic pain, nausea, spasms, and epileptic episodes. Accordingly, there is a compelling argument that marijuana would be more appropriately designated as a Schedule II or III drug. Schedule II substances are defined as drugs with a high potential for abuse, with use potentially leading to severe psychological and physical dependence.¹²⁶ Schedule III substances are defined as drugs with a moderate to low potential for physical and psychological dependence, with drug abuse potential less than Schedule I or II, but more than Schedule IV.¹²⁷ Most importantly, Schedule II or III substances have accepted medical benefits and uses.¹²⁸

Rescheduling would facilitate further study of products for FDA approval, but would not automatically change the severity of penalties for marijuana crimes, to ensure that this substance is only used for legitimate medical and scientific purposes.¹²⁹ However, there are several concerns associated with this reform possibility. One issue relates to how recreational users, in states which allow recreational use of the drug, would proceed with a

¹²⁴Alex Kreit, *What will Medical Marijuana Reform Look Like?*, 65 CASE W. RES. L. REV. 689 (2015).

¹²⁵Haffajee, Maccoun & Mello, *supra* note 8.

¹²⁶*Drug Scheduling*, *supra* note 19.

¹²⁷*Id.*

¹²⁸*Id.*

¹²⁹Haffajee, Maccoun & Mello, *supra* note 8.

new federal distinction of marijuana. Would recreational users still be subject to federal prosecution? Or could their access to marijuana be restricted all together? Another concern arises with accessibility of marijuana products. Rescheduling would subject all marijuana products to FDA approval, which could hinder access initially, but ultimately foster a robust system for regulation and research.¹³⁰ FDA oversight of marketing, packaging, and manufacturing would improve product safety, consistency, and even efficacy.

C. Removal of Marijuana from the CSA

Finally, the most straightforward solution is to completely remove marijuana from the CSA all together. This would effectively eliminate the conflict between state and federal law. The federal government could conceivably retain the federal prohibition in states that want it, while simultaneously regulating marijuana in states that opt to legalize it. Marijuana could be regulated in a similar fashion to how alcohol is regulated in the U.S., and be enforced under the Bureau of Alcohol, Tobacco, Firearms, and Explosives.¹³¹ This approach could entail varying degrees of federal regulation within the marijuana market.

In addition, this dramatic change could also come with FDA oversight of marijuana products, which would effectively regulate their manufacturing to ensure the product's efficacy, safety, and benefit the entire industry. However, this de-scheduling would have to work hand in hand with further research, as removal of marijuana from the CSA would allow for widespread availability for research purposes. Regardless of the level of restrictiveness of a potential federal marijuana regimen, this approach would successfully resolve any state and federal conflict. Replacement of federal prohibition with regulation would leave states free to decide to legalize marijuana on their own terms.

Legalization opponents have cited a range of concerns, chief among them is the possibility of a large-scale commercial marijuana industry.¹³² Some opponents argue that legalization would in effect become like the tobacco industry during the mid-late 20th century.¹³³ “Big Marijuana,” as some refer to it, would invest heavily in promoting and advertising marijuana, which would create addicts and target youth.¹³⁴ However, these claims are unfounded because federal regulation of the marijuana industry would allow for federal control. Federal regulation could strictly limit the amount of marijuana a licensed grower could produce/sell annually, all related packaging/advertising, and even place restrictions on the amount a consumer could purchase in a given time period.

¹³⁰Id.

¹³¹See About the Bureau of Alcohol, Tobacco, Firearms and Explosives, BUREAU OF ALCOHOL, FIREARMS, TOBACCO & EXPLOSIVES, <https://www.atf.gov/> (last visited Dec. 19, 2019).

¹³²NAT'L INST. ON DRUG ABUSE, *supra* note 96.

¹³³David Frum, *Be afraid of Big Marijuana*, CNN (Sep. 10, 2013, 9:17AM), <https://www.cnn.com/2013/09/10/opinion/frum-big-marijuana-cv/index.html>; Kevin A. Sabet, Opinion, *Big Marijuana Copies Big Tobacco’s Playbook. Let’s Not Make the Same Mistake Again*, NEWSWEEK (Apr. 19, 2019, 9:00AM), <https://www.newsweek.com/marijuana-cannabis-legalization-tobacco-industry-mistake-1400440>; German Lopez, *Big Marijuana is coming – and even legalization supporters are worried*, VOX (Apr. 20, 2016, 2:00PM), <https://www.vox.com/policy-and-politics/2015/12/2/9831980/marijuana-legalization-industry-business>.

¹³⁴NAT'L INST. ON DRUG ABUSE, *supra* note 96.

V. Conclusion: The Future of Marijuana Policy

Removal of marijuana from the CSA poses the greatest advantages for the industry as a whole. However, the conundrum in this situation is timing. Timing of legislative changes will be crucial in the creation and enforcement of drug policy that is comprehensive and scientifically sound. As it stands, in order to address some of the central issues surrounding the marijuana industry, the drug needs to be federally legalized. However, in order to federally legalize the drug, the central issues must be addressed first.

The first and most vital step in the federal legalization process is less restrictive research opportunities for marijuana. Research must be opened to a larger community of scientists in order to address the current knowledge gaps associated with its use. Once those questions are answered, the industry would be in a better position to defend and verify the therapeutic use of marijuana. Subsequently, comprehensive and robust research will allow for the creation of effective marijuana policy by scientists and legislators to ensure safety and stability.

The legal status of marijuana is complex and constantly evolving. Moreover, the inevitable policy changes will be guided by multiple competing interests. It is unlikely that any short-term solutions will become the universal formula for the future of marijuana legality in the U.S., as it is abundantly clear we do not have all the answers we need. Key questions for scientists, policy researchers, and decision makers to focus efforts as different paths for the future of marijuana legality are explored include:

- What policies ought to be pursued to speed up research needed to fully exploit the therapeutic potential of marijuana? What specific medical conditions need to be prioritized?
- What effects will chronic users of marijuana suffer and how might they be alleviated?
- How should strain, potency, indications, and routes of administration be regulated and monitored?
- How will the FDA and the EPA go about creating robust cannabis product manufacturing, packaging, and safety testing regulations?
- How would a comprehensive list of all potential drug interactions between marijuana and other substances be determined?
- What governing authority will set standards and regulations associated with the marijuana industry?
- What will the standards for widespread marijuana usage be? (e.g. an age requirement to protect susceptible children from using the drug?)
Limitations for the amount of marijuana one can buy in a certain time period?, etc.)

- Finally, how much will policy makers rely on scientific evidence in creation of new marijuana policy? Scientific involvement should be a requirement for any proposed cannabis legislation, but to what extent and form?

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