

Twenty-First Century Illicit Drugs and Their Discontents: The Troubling Potency of Twenty-First Century Cannabis

Paul J. Larkin

KEY TAKEAWAYS

The cannabis that is available today is 7-30 times more powerful than the cannabis that was available in the 1960s and 1970s.

States have legalized cannabis for medical and recreational use without FDA approval or without performing the necessary safety testing themselves.

Congress and states should address the potential problems created by high-potency cannabis before there is any further discussion of legalization.

The most commonly used—and controversial—illicit drug in the United States is *Cannabis Sativa* L., the technical label for the plant more commonly known by its slang name of marijuana.¹ Advocates for liberalized regulation of cannabis have portrayed it as a mild intoxicant and social lubricant that is not materially more harmful to the body or soul than alcohol, a drug that has played those roles since Noah became the first vintner.² Proponents of legalization also have argued that cannabis has numerous legitimate medical uses for the treatment of disease or alleviation of pain.³ Opponents of legalization have argued that numerous studies and meta-analyses dispute those conclusions.⁴ Those parties have also warned that cannabis’s advocates have ignored or understated various cannabis-use harms, such as increased risk for motor vehicle accidents, psychotic symptoms, violence, and amotivational syndrome.⁵

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Those parties caution against making a radical change to our longstanding cannabis policy that could mistakenly endorse a socially damaging and irreversible new legal régime.⁶

Unfortunately, “cannabis policy has raced ahead of cannabis science.”⁷ Since 1996, when California adopted the first medical-use cannabis régime, 37 states, four territories, and the District of Columbia have revised their laws to permit the use of cannabis products for medical purposes, while 18 states, two territories, and the District of Columbia permit recreational-use cannabis.⁸ In so doing, states adopted medical-use or recreational-use marijuana programs without first analyzing whether today’s cannabis poses health risks not seen in the 1960s, a time when cannabis emerged as an iconic symbol of a generation that thought it could solve every social ill, right every wrong, and eliminate every unjustified restraint on individual liberty.⁹

It is a serious mistake not to analyze the potency of any drug before legalizing it. For more than 80 years, the nation has endorsed the judgment that no one should be free to distribute any “new” drug¹⁰ in interstate commerce unless and until the U.S. Food and Drug Administration (FDA), acting under the authority granted the agency by the Federal Food, Drug, and Cosmetic Act (FDCA) of 1938,¹¹ has found (inter alia¹²) that it is “safe” and “effective” for its intended use.¹³ The FDA did not make any such findings before the states adopted their medical-use and recreational-use cannabis programs. In fact, the FDA and other allied federal health care agencies have consistently found that botanical cannabis is not a legitimate medication.¹⁴ The states decided to take the law into their own hands without bearing the burden that federal law places on the FDA.

That was a grievous error.¹⁵ As Dr. Nora Volkow, Director of the National Institute on Drug Abuse, has noted, “increase in THC content”—THC is the acronym for delta-9-tetrahydrocannabinol, the psychoactive compound in cannabis—“raises concerns that the consequences of marijuana use may be worse now than in the past.”¹⁶ That is why Doctor Volkow has questioned “the current relevance of the findings in older studies on the effects of marijuana use, especially studies that assessed long-term outcomes.”¹⁷ Too often over the past three decades, states have legalized cannabis without waiting for the federal government to conduct that research or performing it themselves. Moreover, much of the debate that we have witnessed during those years was biased toward one side or the other. As Carnegie-Mellon University Professor Jonathan Caulkins, an expert on cannabis, wrote in 2016, “Unfortunately, there is very little in the way of intellectually honest marijuana policy analysis.”¹⁸

This *Legal Memorandum* is the third in a series of Heritage Foundation studies published under the overall title “Twenty-First Century Illicit Drugs and Their Discontents.” This paper highlights the need to consider the far greater potency of today’s cannabis when debating whether to legalize that drug.

Federal Regulation of Cannabis

Before 1996, the potency of cannabis was never an important public policy issue. Although widely available, cannabis was contraband, and its potency was minimal. Since 1996, however, and particularly after 2009, cannabis has become a lawful article of commerce in many states under state law, and its potency has expanded over that period. Yet, despite the fact that numerous states have medical-use programs, the far greater potency of cannabis today has not received the attention that the issue deserves, even though it is standard practice for the government to devote considerable attention to deciding exactly what potency a drug should have to be marketed in interstate commerce. The states’ failure to confront that issue, along with the FDA’s refusal to take control of the regulation of cannabis, has led to the situation that we see today—one in which there is little regulation of the psychoactive ingredients in cannabis despite the risk that highly potent cannabis can have severe adverse effects on long-term users.

Before 1996: Uniformity. Cannabis is an ancient nostrum. Archaeological evidence reveals use of the agricultural form of cannabis more than ten thousand years ago.¹⁹ It was lawfully grown and used in the United States for more than 100 years after 1787. Nonetheless, during the first third of the 20th century, all 50 states outlawed its use for medical or recreational purposes.²⁰ Congress followed suit in legislation enacted in 1937²¹ and 1970.²² The executive branch also entered into several international conventions that require signatories to treat cannabis trafficking as a crime.²³ The legal debate over the status of cannabis appeared to be settled.

It wasn’t.

Cannabis became a controversial social issue by late in the 1960s (if not earlier).²⁴ There was a considerable debate over two issues: whether cannabis had potentially beneficial uses that justified its legalization and whether cannabis possession and use should be decriminalized—treated as a minor infraction rather than a felony—given its dissimilarities to “hard” drugs such as heroin.²⁵ The debate was a lively one.²⁶ Some states and localities reduced the penalty for possession of a small amount of cannabis to a minor infraction.²⁷ At times it appeared that reformers might succeed in legalizing

cannabis.²⁸ Their efforts, however, failed in the 1970s. Although the debate continued,²⁹ cannabis remained contraband.³⁰

1996–2009: The Adoption of Medical Cannabis Initiatives. For advocates of liberalized cannabis use, the Age of Aquarius dawned in 1996. By a popular initiative, California adopted Proposition 215, labelled the Compassionate Use Act of 1996.³¹ The proposition authorized the cultivation, possession, and use of cannabis by patients for medical purposes under California law.³² That proposition established a major beachhead for recreational cannabis use. For the first time, a state had decided to break from the nation’s uniform treatment of cannabis as contraband. Gradually, other states followed California’s lead.³³

Since 2009: The Spread of State Medical and Recreational Cannabis Initiatives. The last critical date is 2009. Starting then, the Obama Administration’s U.S. Department of Justice issued a series of policy memoranda formally stating that it would not enforce federal law against parties who complied with state cannabis regimes.³⁴ The Obama Administration also informally made it clear that it would ignore state compliance efforts as long as a state did not rub the Administration’s face in it.³⁵ Together, those memoranda and the Justice Department’s willful blindness revealed that President Barack Obama, like Pontius Pilate, had washed his hands of the matter.³⁶ Specifically:

President Obama gave the cannabis industry the equivalent of a Papal blessing by almost guaranteeing its members immunity from federal prosecution if they complied with state law—and then studiously ignored whether they were in fact complying. By choosing nonenforcement in lieu of persuading Congress to revise the [Controlled Substances Act], President Obama might have reached a short-term accommodation between what some think is an outdated law and contemporary social values. In Professor [Zachary S.] Price’s words, President Obama might have helped to “unstick a frozen issue” that Congress has proved unwilling to resolve itself. Maybe President Obama thought that he could force Congress to act by making a hash of our cannabis policy. If he did, he was wrong. Strike One. If he thought his actions would energize the public into demanding congressional reform, he was wrong again. Strike Two. If, however, he thought that allowing a massive number of crimes to go unprosecuted on his watch would enable the rise of a billion-dollar industry that no successor would dare seek to eliminate (that’s my guess), he might have been right about that. If that was his plan, perhaps he succeeded. Yet encouraging people to become scofflaws—pardon me, *rich* scofflaws—is hardly a legitimate law enforcement strategy. Strike Three.³⁷

As a result, there has been a sea change in state cannabis laws since 2009. As of 2022, numerous states and territories, as well as the District of Columbia, permit cannabis or its products to be used for medical or recreational purposes. In states with only medical cannabis programs, there is no shortage of physicians willing to recommend cannabis use for a host of ailments. In states with recreational-use programs, businesses are willing to sell it for its euphoric effects.³⁸

Where Are We Today? Three features of that history are noteworthy.

First, cannabis remains contraband under federal law. Ironically, despite the revolution in state cannabis law, the two most relevant federal statutes have remained largely unchanged.³⁹ The Controlled Substances Act of 1970 (CSA) classifies cannabis as a Schedule I controlled substance, the category reserved for drugs that, given their disutility and inherent risks, cannot be prescribed for any purpose.⁴⁰ Cannabis thus is contraband under federal law.⁴¹ In addition to the CSA is the FDCA, which (as noted above) bars the interstate distribution of a drug until the FDA has found it to be safe and effective for its intended use.⁴² The FDA⁴³ may regulate cannabis either as a drug or, when it is added to food and becomes part of an “edible” product, as a food additive.⁴⁴

Nonetheless, the FDA and related federal government health-care agencies have rejected the conclusion that botanical cannabis is a “safe” and “effective” drug for any purpose.⁴⁵ The Biden Administration reiterated that conclusion as recently as April 2022.⁴⁶ Shortly before the 2022 midterm elections, however, the President directed two of his principal lieutenants to reconsider the scheduling of cannabis.⁴⁷ Nonetheless, even if Congress or the Attorney General were to remove the CSA restraint on the distribution of cannabis, interstate distribution would remain a federal offense under the FDCA.⁴⁸

Second, physicians cannot prescribe cannabis. Neither Proposition 215 nor any later state medical cannabis scheme has authorized physicians to “prescribe” cannabis as a medical treatment; no state can modify the federal ban on the distribution of cannabis for any purpose, even one deemed a “medical necessity.”⁴⁹ But the difference between a “prescription” for and “recommendation” of cannabis turned out to be *macht nichts*. Why? The federal courts concluded that, under the First Amendment Free Speech Clause, a physician may legally “recommend” that a patient consider using cannabis as a treatment for disease even though he cannot prescribe it, given federal law.⁵⁰ Of course, the distinction between “prescribing” and “recommending” a drug that is openly sold in state-legal marijuana dispensaries (or readily available in every other state) “is about as precise as the

difference between ‘dusk’ and ‘twilight.’”⁵¹ The result has been that medical-use programs opened the door for recreational-use ones. If you think that medical-use cannabis programs are just a Trojan horse for recreational cannabis use, you’re not alone.⁵²

Third, the debate over the pros and cons of cannabis use has not considered the high potency of today’s drug. A consequence of the states’ legalization of cannabis, coupled with the federal government’s decision to remain on the sidelines, is that businesses have competed to develop products to satisfy consumer demand. That development, as one author put it (likely with unintended sarcasm), is “a real testament to American entrepreneurialism and innovation.”⁵³ The desire to expand market share in the pursuit of profit has led to the development of numerous, high-potency, potentially addictive, THC-infused products,⁵⁴ including “edibles.”⁵⁵ The ironic result of allowing the creative engine of capitalism to devise ever more powerful and dangerous forms of a quasi-legal addictive article of commerce has been damage to the lives of at least 10 percent of long-term users.⁵⁶

What has largely been overlooked in the progression from cannabis as contraband to cannabis as a quasi-legal article of commerce is the effect that this new high-potency cannabis can have on long-term users, particularly adolescents. That is striking. Analysis of the effects of a drug’s potency is critical to any discussion of its safety and effectiveness. This certainly is true in the case of standard pharmaceuticals. Drug companies test the effect of a drug’s potency on animals before conducting tests on humans.⁵⁷ After obtaining those results, pharmaceutical companies then conduct what is known as Phase 1 of the standard three-phase process for the clinical trial of drugs.

The potential toxicity of a drug is an essential feature of the early stages of a drug trial because no drug can be deemed safe if the minimum lethal dose and the potential adverse long-term effects are unknown. Concern with toxicity remains a critical issue throughout the remaining phases of a pharmaceutical trial. A drug that materially reduces the size of tumors is not safe if it is toxic to the liver and kidneys. A drug that provides short-term relief from respiratory distress is not safe if it causes long-term heart failure in everyone who uses it. Yes, there are tradeoffs involved in treatment. Some patients suffering from a fatal, incurable disease might be willing to sacrifice the quality of their remaining days for a larger number of them (or vice versa). But a physician cannot responsibly offer a patient a legitimate choice if there are no known data indicating what the short-term and long-term effects of a potent drug might be. As for cannabis sold for recreational use, where no physician is involved and the only advice comes

from a financially self-interested “ganjapreneur” or “budtender,” the consumer cannot expect to receive a neutral, disinterested product analysis or recommendation for use.

The bottom line is this: The states’ legalization of medical-use and recreational-use cannabis without examining or reexamining the potential harms from high-potency forms of that drug should be seen as the scandal that it is. In the rush to obtain a new source of revenue and to satisfy a vocal constituency clamoring for a substance that has the same painkilling properties as bourbon, the states have chosen to disregard the 80-plus-year judgment that American society has made to forbid large-scale commercialization of a potentially dangerous drug until *after* it has been proved safe and effective by its sponsors. Maybe a few of those legislators thought that they were offering a respite from pain or other consequences of the maladies that the aged and ill can suffer. Nevertheless, even if “[c]aring without science is well intentioned kindness,” it is “not medicine.”⁵⁸ Any claim that smoking a joint “can cure various diseases falls along the spectrum somewhere between risible and fraudulent.”⁵⁹

What Do We Do Now? The debate over the proper legal treatment of cannabis has remained an active one for more than 50 years and shows no sign of fading away. If anything, President Biden’s October 2022 order that the HHS Secretary and Attorney General reconsider the current status of cannabis under the CSA will heighten the controversy.⁶⁰ Hopefully, that review will also bring to the forefront the harms that we are now witnessing from use of the high-octane cannabis being sold today. As Carnegie-Mellon University Professor Jonathan Caulkins, an expert on marijuana policy, has admonished us, legalizing the for-profit sale of marijuana “is an irreversible leap into the unknown” and “would be next to impossible to unwind.”⁶¹ We need to debate whether the private, large-scale, commercial distribution of high-potency cannabis is a course that our society is willing to accept. We have never had that debate in Congress, and it would be criminal for its members to endorse that outcome without fully airing each side of it.

The next section makes two points: First, today’s cannabis is dramatically more potent and potentially more dangerous than grandpa’s. Second, today’s legislators and debaters must be willing to consider, and in some instances reconsider, their old positions in light of the new facts.

Increased Potency of Twenty-First Century Cannabis

Cognac might still be distilled today much as it was in the fifteenth century, but the same cannot be said of the cannabis cultivated nowadays.⁶²

Development of sophisticated indoor and hydroponic cultivation techniques and cross-breeding has increased its potency.⁶³ As noted above, the ganja that grandad toked during the Summer of Love had a THC content of approximately 1–3 percent.⁶⁴ By contrast, the THC content in cannabis products today can far exceed what was used at Woodstock. To be sure, some people believe that cannabis was more potent in the 1960s and 1970s than we give it credit for being.⁶⁵ Nonetheless, there is a consensus that cannabis is available today in far, far more powerful forms than could be obtained during those decades. Think of it as the grain alcohol version of grandad’s near-beer cannabis. Some ganjapreneurs sell forms of cannabis, known by nicknames such as “dabs” or “shatter,” that is nearly 100 percent pure THC.⁶⁶

Several factors can create variation in the amount of THC an individual consumes. To start with, cannabis is not a “standardized good”—that is, it is not a unique chemical compound and does not come with uniform and precise ingredients. Cannabis is not a lab-created pharmaceutical with precise and uniform ingredients. It is “a chemically complex and highly variable” product⁶⁷—or, to quote Dr. Robert DuPont, a former presidential drug policy advisor and Director of the National Institute on Drug Abuse, “a complex chemical slush”⁶⁸—containing hundreds of different chemicals and a variation in the THC potency. That likely is one of the reasons why the FDA has never found that cannabis is a safe and effective drug.

The different forms of cannabis products—such as the botanical flower (and its components), hash, and hash oil—vary in their composition and potency.⁶⁹ The THC content can vary from 12 percent to 20 percent in the plant form or in hashish (dried cannabis resin and crushed plants). Hash oil (an oil-based extract of hashish) has a greater THC content and range, from 15 percent–65 percent. Cannabis oil extracts can be up to 80 percent THC, and crystalline forms of THC can be 99.9 percent pure.⁷⁰

A related factor is the decrease in the amount of a different cannabinoid—cannabidiol, or CBD—in twenty-first century street-level cannabis. The available evidence indicates that the two cannabinoids might produce “different, or mutually antagonistic” molecular, neuropsychiatric, and pharmacologic effects in users by reducing the adverse outcomes that high-potency THC products have on users.⁷¹ Put differently, CBD might buffer the effects of THC on the brain.⁷² A result is that the ratio of THC to CBD might be an important factor to consider in determining the potential adverse effects of high-potency THC.⁷³

Yet the cannabis sold in dispensaries and stores today generally has a low level of CBD. In fact, the THC:CBD ratio can be as high as 80:1.⁷⁴ “[T]he marijuana industry has essentially bred cannabidiol out of street marijuana,”

probably to attract customers by enhancing the effect of the drug.⁷⁵ “That is a critical but largely undiscussed or under-discussed fact in the current debate” and demonstrates a pitfall of legalizing a cannabis industry “without an informed scientific basis.”⁷⁶ That problem needs to be investigated and addressed now.

Think that’s bad enough? It gets worse.

“Synthetic cannabinoids,” known by names such as “K2” or “spice,” are new, non-botanical products synthesized in laboratories.⁷⁷ One study described them as being “currently among the main players in the recreational drug market” and noted that they “represent a major challenge for health-care professionals as well as public health and law enforcement officials.”⁷⁸ They are a potentially greater problem than the agricultural form of the drug. Often sprayed on herbal cannabis ingredients, synthetic cannabis binds more powerfully with CB₁ receptors in the brain than the THC found in traditional joints does.⁷⁹ As a result, synthetic cannabis poses even greater health risks than the botanical form poses.⁸⁰ “A survey of 80,000 drug users showed that those who used synthetic cannabinoids were thirty times more likely to end up in an emergency unit than users of traditional cannabis.”⁸¹

Among the acute adverse physical reactions to synthetic cannabinoid use are agitation, breathlessness, chest pain, tachycardia, nausea, vomiting, convulsions, and renal failure.⁸² Synthetic cannabinoids can be addictive,⁸³ and their use can lead to an overdose or prove fatal.⁸⁴ Adverse effects from long-term use are possible as well.⁸⁵ More than 200 different types of synthetic cannabinoids have been sold over the Internet, each with a slightly different molecular structure, giving them unpredictable side effects,⁸⁶ and more are being produced.⁸⁷ Synthetic cannabinoids can also produce psychiatric symptoms, sometimes called “spiceophrenia.”⁸⁸ Here again, science and business have combined to create a product that was not available in the 1960s and 1970s that must be analyzed from scratch today before we legalize a dangerous product.

Why Cannabis’s Increased Potency Matters

The failure of state governments to address the potential problems created by the development of high-potency cannabis before legalizing medical-use and recreational-use cannabis is a clear failure of legislative responsibility. As noted above, the FDA demands proof that a drug will not be toxic at a particular potency before it can be shipped in interstate commerce. The states have not done so, and that is utterly irresponsible. It is bad enough that the states decided to displace the FDA as the decisionmaker

regarding the safety of medical and recreational cannabis. What makes that worse is that the states refused to accept the accompanying responsibility to conduct the necessary examinations of the drug that they approved for use as medicine or an intoxicant. It is no argument that the states do not have the personnel or resources to conduct the same analysis that the FDA possesses. That only goes to show why the states acted recklessly.

Because there is insufficient information to use as a basis for judgment, we cannot know exactly what the long-term effects of today's high-potency cannabis might be. Consider just the question of whether long-term use of such a drug, particularly when begun early in a person's life, could trigger psychosis. A future *Legal Memorandum* will address that issue at length. Suffice it to say here that studies and commentators have concluded that high-potency cannabis—which NIDA Director Volkow defines as any product containing more than 10 percent THC⁸⁹— is associated with various harms for users and society. People who use cannabis on a long-term basis suffer an increased risk of anomie, cannabis use disorder, psychotic symptoms, and perhaps psychosis itself because long-term use of high-potency cannabis might precipitate psychotic disorders in vulnerable individuals.⁹⁰

That is important in the case of adult users, but it is critical given the potentially life-shattering effects that early initiation and long-term consumption of today's cannabis can have on the labile adolescent brain.⁹¹ Any discussion of the revision of our cannabis law must consider the risks that we run by allowing such a drug to be sold.

Conclusion

Regulation of a subject like pharmacology in which scientific knowledge is essential to sound policymaking demands that the government remain flexible to respond correctly and quickly to developing subject-matter data and trends. In fact, the need for resort to scientific expertise and for flexibility in lawmaking are two of the principal rationales for delegating rulemaking power to administrative agencies. The greater potency of cannabis and its products that we have witnessed over the past five decades demands that we conduct any re-examination of the federal laws governing cannabis mindful of the potentially more severe adverse effects of twenty-first century cannabis. To do anything less would be irresponsible.

Paul J. Larkin is the John, Barbara, and Victoria Rumpel Senior Legal Research Fellow in the Edwin Meese III Center for Legal and Judicial Studies at The Heritage Foundation.

Endnotes

1. Paul J. Larkin, Jr., *Medical or Recreational Marijuana and Drugged Driving*, 52 AM. CRIM. L. REV. 453, 456–57 & n.11 (2015) [hereafter Larkin, *Drugged Driving*].
2. Genesis 9:20 (King James Version).
3. Common claims of the therapeutic uses of cannabis include treatment of chemotherapy-induced nausea and emesis, the neuropathic pain and spasticity caused by multiple sclerosis, and AIDS-induced cachexia. See, e.g., BRITISH MED. ASS'N, THERAPEUTIC USES OF CANNABIS 21–49 (1997); WORLD HEALTH ORG., CANNABIS: A HEALTH PERSPECTIVE AND RESEARCH AGENDA (1997); NAT'L ACAD. OF SCIS., ENG'G, & MED., THE HEALTH EFFECTS OF CANNABIS AND CANNABINOIDS 54 Tbl. 2-2, 128 Box 4-1 (2017) [hereinafter NAT'L ACAD. REPORT] (listing conditions for which marijuana is a treatment for which there are varying degrees of scientific support); Gemayel Lee et al., *Medical Cannabis for Neuropathic Pain*, 22 CURRENT PAIN & HEADACHE REP. 8 (2018) (“Nearly 20 years of clinical data supports the short-term use of cannabis for the treatment of neuropathic pain.”).
4. See, e.g., Gabrielle Campbell et al., *Effect of Cannabis Used in People with Chronic Non-Cancer Pain Prescribed Opioids: Findings from a 4-Year Prospective Cohort Study*, 3 LANCET PUB. HEALTH e341 (2018) (a four-year longitudinal cohort study concluding that cannabis does not provide long-term relief from chronic non-cancer pain); Matt Goldenberg et al., *The Impact of Cannabis and Cannabinoids for Medical Conditions on Health-Related Quality of Life: A Systematic Review and Meta-Analysis*, 174 DRUG ALCOHOL DEPENDENCE 80 (2017); Keith Humphreys & Richard Saitz, *Should Physicians Recommend Replacing Opioids with Cannabis?*, 321 JAMA 639, 639 (2019) (“There are no randomized clinical trials of substituting cannabinoids for opioids in patients taking or misusing opioids for treatment of pain, or in patients with opioid addiction treated with methadone or buprenorphine.... Many factors other than cannabis may affect opioid overdose deaths, such as prescribing guidelines, opioid rescheduling, Good Samaritan laws, incarceration practices, and availability of evidence-based opioid use disorder treatment and naloxone.”); Paul J. Larkin, Jr. & Bertha K. Madras, *Opioids, Overdoses, and Cannabis: Is Marijuana an Effective Therapeutic Response to the Opioid Abuse Epidemic?*, 17 GEO. J.L. & PUB. POL'Y 555, 571–95 (2019) (collecting studies finding that cannabis cannot provide effective analgesic relief from chronic pain); Elizabeth E. Lutge et al., *The Medical Use of Cannabis for Reducing Morbidity and Mortality in Patients with HIV/AIDS*, COCHRANE DATABASE SYSTEMATIC REV. (Apr. 30, 2013), <https://www.ncbi.nlm.nih.gov/pubmed/23633327> [<https://perma.cc/W8RA-7526>]; George G. Mammen et al., *Association of Cannabis with Long-Term Clinical Symptoms in Anxiety and Mood Disorders: A Systematic Review of Prospective Studies*, 79 J. CLINICAL PSYCHIATRY (2018), <https://www.ncbi.nlm.nih.gov/pubmed/29877641> [<https://perma.cc/9U4Z-6GP2>]; Suzanne Nielsen et al., *Opioid-Sparing Effect of Cannabinoids: A Systematic Review and Meta-Analysis*, 42 NEUROPSYCHOPHARMACOLOGY 1752 (2017); Maya E. O'Neil et al., *Benefits and Harms of Plant-Based Cannabis for Posttraumatic Stress Disorder: A Systematic Review*, 167 ANNALS INTERNAL MED. 332 (2017); Pal Pacher et al., *Cardiovascular Effects of Marijuana and Synthetic Cannabinoids: The Good, the Bad, and the Ugly*, 15 NAT. REV. CARDIOLOGY 151 (2018); Chelsea L. Shover et al., *Association Between Medical Cannabis Laws and Opioid Overdose Mortality Has Reversed over Time*, 116 PROCEEDINGS NAT'L ACAD. SCI. 12624 (2019) (National Academy of Sciences study concluding that states with liberal cannabis laws saw an increase in opioid deaths).
5. See, e.g., BRIT. MED. ASS'N, *supra* note 3, at 66 (“Impairment of psychomotor and cognitive performance, especially in complex tasks, has been shown in normal subjects in many tests. Impairments include slowed reaction time, short term memory deficits, impaired attention, time and space distortion, [and] impaired coordination. These effects combine with the sedative effects to cause deleterious effects on driving ability or operation of machinery.” (citations omitted)); *id.* at 19–20 (listing marijuana's pharmacological actions in people); NEW ZEALAND TRANSP. AGENCY, RISKS OF DRIVING WHEN AFFECTED BY CANNABIS, MDMA (ECSTASY) AND METHAMPHETAMINE AND THE DETERRENCE OF SUCH BEHAVIOUR: A LITERATURE REVIEW 6 (2020); Robert L. DuPont et al., *Marijuana-Impaired Driving: A Path Through the Controversies*, in CONTEMPORARY HEALTH ISSUES ON MARIJUANA 183, 186 (Kevin A. Sabet & Ken C. Winters eds., 2018) (“Today there is a wealth of evidence that marijuana is an impairing substance that affects skills necessary for safe driving.”); Mark Asbridge et al., *Acute Cannabis Consumption and Motor Vehicle Collision Risk: Systematic Review of Observational Studies and Meta-Analysis*, 9 BMJ 344, 344–45 (2012); Robert M. Chow et al., *Driving Under the Influence of Cannabis: A Framework for Future Policy*, 128 ANESTHESIA & ANALGESIA 1300, 1301 (2019) (“Several studies have found acute marijuana use to be associated with a ≥2-fold higher risk of crashing while driving a motor vehicle when compared to driving unimpaired. In some cases, drivers under the influence of cannabis were more aware of their deficits and attempted to compensate by driving slower and taking less risks. However, these behaviors do not equate to a reduced risk of accidents. The deleterious cognitive and psychomotor effects of marijuana that increase with multitasking or task complexity cannot be ignored. Studies evaluating the effects of cannabinoids on driving ability have found that participants perform worse on divided attention tasks, during situations with decision-making dilemmas, and during long monotonous drives followed by sudden changes requiring a quick reaction.”) (endnotes omitted); M. Kathryn Dahlgren et al., *Recreational Cannabis Use Impairs Driving Performance in the Absence of Acute Intoxication*, 208 DRUG & ALCOHOL DEPENDENCE, No. 107771, 2020, at 8 (“The current study demonstrates residual driving impairment in nonintoxicated cannabis users, which appears specific to those with early onset cannabis use.”), <https://reader.elsevier.com/reader/sd/pii/S0376871619305484?to-ken=77B6250A44A47439AD0E665BF9C48268BDE0223B> [<https://perma.cc/9538-TB2E>]; Paul J. Larkin, *Driving While Stoned in Virginia*, 59 AM. CRIM. L. REV. ONLINE 1 (2022); Larkin, *supra* note 1.
6. See, e.g., OFFICE OF NAT'L DRUG CONTROL POLICY, NATIONAL DRUG CONTROL STRATEGY 1–2 (2013) (“In recent years, the debate about drug policy has lurched between two extremes. One side of the debate suggests that drug legalization is the ‘silver bullet’ solution to drug control. The other side maintains a law enforcement-only ‘War on Drugs’ mentality.... Neither of these approaches is humane, effective, or grounded in evidence.”); WILLIAM J. BENNETT & ROBERT A. WHITE, GOING TO POT: WHY THE RUSH TO LEGALIZE MARIJUANA IS HARMING AMERICA (2015); ROBERT L. DUPONT, THE SELFISH BRAIN: LEARNING FROM ADDICTION 143–47 (rev. ed., 2000); KEVIN A. SABET, REEFER SANITY: SEVEN GREAT MYTHS ABOUT MARIJUANA (Rev. ed. 2018). See generally Paul J. Larkin, Jr., *Introduction to a Debate: Marijuana: Legalize, Decriminalize, or Leave the Status Quo in Place?*, 23 BERKELEY J. CRIM. L. 73, 78–79 (2018) (“Defenders of the current regulatory regime, such as the federal government—in particular, the Food and Drug Administration (FDA) and the Drug Enforcement Administration—and highly respected medical organizations—the American Medical Association, the American Cancer Society, the American Academy of Ophthalmology, and the National Institute

for Drug Abuse—maintain that today’s marijuana is not only more potent than your grandfather’s marijuana and is addictive, but it also has a number of adverse short- and long-term health effects, particularly for minors. Defenders of the status quo would argue that there is no good reason to exempt marijuana from the approval process demanded by the drug safety laws. The FDA cannot find that marijuana is ‘safe and effective’ for medical use for two simple reasons: there is clear proof that cannabis has actual and potential adverse short- and long-term health effects, and there is no clear proof that it has valuable medical benefits, certainly none that other, approved pharmaceuticals cannot also deliver.”) (endnote omitted).

7. Archie Bleyer & Brian Barnes, Comment & Response, *Opioid Death Rate Acceleration in Jurisdictions Legalizing Marijuana Use*, 178 JAMA INTERNAL MED. 1280, 1280 (2018).
8. *State Medical Cannabis Laws*, NAT’L CONF. OF STATE LEG. (Feb. 3, 2022), <https://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx> [<https://perma.cc/8FTQ-THGR>]. State laws permitting cannabis to be distributed for either purpose differ widely. See DRUG POLICY AND THE PUBLIC GOOD 245–54 (Thomas Babor et al., eds., 2d ed. 2018); Rosalie Liccardo Pacula, Priscillia Hunt & Anne Boustead, *Words Can Be Deceiving: A Review of Variation Among Legally Effective Medical Marijuana Laws in the United States*, 7 J. DRUG POL’Y ANALYSIS 1 (2014).
9. See Paul J. Larkin, Jr., *Reflexive Federalism*, 44 HARV. J.L. & PUB. POL’Y 523, 527 (2021) [hereafter Larkin, *Reflexive Federalism*] (“More and more college-age students experimented with marijuana and found it to be just as much an enjoyable intoxicant and social lubricant as alcohol was to their parents’ generation. Over time, marijuana not only lost its taboo status, but also became a political symbol. On college campuses, openly smoking marijuana, like publicly burning draft cards, came to symbolize a generation rebelling against the Vietnam War, the status quo, and all things square.”) (endnotes omitted).
10. A “new drug” includes “[a]ny drug...[that] is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed....” 21 U.S.C. § 321(p)(1); 21 C.F.R. § 310.3(h) (2021). Despite its age, cannabis would constitute a “new” drug under the FDCA and FDA’s rules. See 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 (Dec. 20, 2018) [hereinafter Gottlieb Statement], <https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-signing-agriculture-improvement-act-and-agencys> [<https://perma.cc/RP9Y-CBDP>] (“Cannabis or cannabis-derived products claiming in their marketing and promotional materials that they’re intended for use in the diagnosis, cure, mitigation, treatment, or prevention of diseases (such as cancer, Alzheimer’s disease, psychiatric disorders and diabetes) are considered new drugs or new animal drugs and must go through the FDA drug approval process for human or animal use before they are marketed in the U.S.”). A pharmaceutical company must conduct extensive clinical testing to prove that a new drug is safe and effective for its intended purposes. That testing generally comes in three phases. Phase I encompasses initial clinical testing in humans to assess toxicity; pharmacodynamics (the effect of a drug on the body); pharmacokinetics (the movement of a drug through a body); and (only preliminarily) potential therapeutic benefits. Phase II testing is designed to explore, and Phase III is designed to confirm or refute, the therapeutic effects of a drug on a particular disease or condition. See 21 C.F.R. § 312.21 (2018). Proof of purity, which ensures that every dose is the same, results from manufacturing controls. See *id.* § 314.50.
11. Federal Food, Drug, and Cosmetic Act, ch. 675 § 1, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. § 301 *et seq.* (2018)).
12. The FDA also examines the drug proponent’s manufacturing practices to ensure that the drug has a consistent quality and the drug’s labeling to satisfy itself that the quantity of active and inactive ingredients is accurate and the directions for use are helpful to a patient. See, e.g., 21 U.S.C. §§ 351(a) (2)(B), 352, 352(b), (c)–(f), 355(a), (b) & (d) (2018); 21 C.F.R. Pt. 200 Subpt. A (2018) (General Labeling Provisions); *id.* Pt. 201 (Labeling); *id.* Pt. 211 (Current Good Manufacturing Practices for Finished Pharmaceuticals); FDA, COMPLIANCE PROGRAM GUIDANCE MANUAL § 7346.832 (2010); Wyeth v. Levine, 555 U.S. 555, 566–68 (2009); BRIAN F. THOMAS & MAHMOUD A EL-SOHLY, THE ANALYTICAL CHEMISTRY OF CANNABIS 11 (2016) (“The quality, safety, and efficacy of starting material are basic prerequisites in the pharmaceutical industry.”).
13. See 21 U.S.C. § 355(a) (2012) (forbidding the distribution of a new drug in interstate commerce without prior FDA approval); Paul J. Larkin, Jr., *States’ Rights and Federal Wrongs: The Misguided Attempt to Label Marijuana Legalization Efforts as a “States’ Rights” Issue*, 16 GEO. J.L. & PUB. POL’Y 495, 499–500 (2018) [hereafter Larkin, *States’ Rights*] (“We do not...make scientific decisions in the same manner that we elect politicians: by ballot. Federal law has flatly or effectively prohibited the cultivation, processing, and distribution of marijuana since the Marijuana Tax Act of 1937. That date is significant because the following year Congress passed the Federal Food, Drug, and Cosmetics Act of 1938 (FDCA). The FDCA prohibited the distribution in interstate commerce of ‘adulterated’ foods and drugs. The act also empowered and directed the Commissioner of Food and Drugs to examine both products to be sure that they were safe for interstate distribution. In 1962, Congress also prohibited the distribution of new drugs unless and until the Commissioner has found that they are not only ‘safe,’ but also ‘effective.’ Ever since, Americans have entrusted the decision whether a particular new drug can be sold throughout the nation to experts at the Food and Drug Administration (FDA). Congress has reaffirmed that judgment on numerous occasions: in 1997, when it passed the Food and Drug Modernization Act of 1997; in 2007, when it enacted the Food and Drug Administration Amendments Act of 2007; in 2012, when it passed the Food and Drug Administration Safety and Innovation Act; and in other years as well. In fact, Congress implicitly but clearly reiterated its judgment every time that it passed an appropriations law underwriting the work of the Commissioner of Food and Drugs and his colleagues at the FDA.”) (footnotes omitted).
14. See, e.g., *FDA Regulation of Cannabis and Cannabis-Derived Products, Including Cannabidiol (CBD)*, FDA (Oct. 1, 2020), <https://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-including-cannabidiol-cbd> [<https://perma.cc/TF56-2GRQ>]; *What You Need to Know (And What We’re Working to Find Out) About Products Containing Cannabis or Cannabis-Derived Compounds, Including CBD*, FDA (Mar. 5, 2020), <https://www.fda.gov/consumers/consumer-updates/what-you-need-know-and-what-were-working-find-out-about-products-containing-cannabis-or-cannabis> [<https://perma.cc/7HGY-KAZ4>]; *FDA and Cannabis: Research and Drug Approval Process*, FDA (Oct. 1, 2020), <https://www.fda.gov/news-events/public-health-focus/fda-and-cannabis-research-and-drug-approval-process> [<https://perma.cc/L2QP-YETU>]; *infra* note 46. See generally Larkin, *Reflexive Federalism*, *supra* note 9, at 593–94 & nn.244–46 (collecting authorities).

15. See, e.g., Larkin, *States' Rights*, *supra* note 13, at 500–01 (“We do not decide by referendum which antibacterial, antiviral, or antifungal drugs should be sold. In fact, no one would seriously offer such a proposal. Why? Perhaps that is because no one wants medical decisions to be made in that manner. Or perhaps that is because the people who would make the argument, and the people whom those advocates hope would be persuaded by it, deep down inside know that it simply will not fly and do not want it to fly. Moreover, the consequences of endorsing that argument pose questions that are mighty difficult to answer. For example, which of the following drugs that were prohibited or recalled by the FDA do we want to leave to a public vote as to whether they should still be distributed nationwide: Diethylstilbestrol? Laetrile? Quaalude? Vioxx? And how do we choose which ones that the FDA can review and which ones go onto the ballot? Ask the members of the ‘States’ Rights’ clan which drugs construction workers, bus drivers, and welfare recipients should have the right to approve or veto and you’re not likely to see many hands go up.”).
16. Nora D. Volkow et al., *Adverse Health Effects of Marijuana Use*, 370 *NEW ENG. J. MED.* 2219, 2222 (2014).
17. *Id.*
18. Jonathan P. Caulkins, *The Real Dangers of Marijuana*, *NAT’L AFF.* 21, 30 (Winter 2016) [hereafter Caulkins, *Marijuana Dangers*].
19. See, e.g., *BRIT. MED. ASS’N*, *supra* note 3, at 7; THOMAS & ELSOHLY, *supra* note 12, at 1; Sunil K. Aggarwal et al., *Medicinal Use of Cannabis in the United States: Historical Perspectives, Current Trends, and Future Directions*, 5 *J. OPIOID MGMT.* 153, 153–57 (2009); Alan J. Budney et al., *Cannabis*, in LOWINSON & RUIZ’S *SUBSTANCE ABUSE: A COMPREHENSIVE TEXTBOOK* 214–15 (Pedro Ruiz & Eric Strain eds., 5th ed. 2011); Tod H. Mikuriya, *Marijuana in Medicine: Past, Present, and Future*, 110 *CAL. MED.* 34 (1969); Solomon H. Snyder, *Foreword* to LESLIE L. IVERSEN, *THE SCIENCE OF MARIJUANA* 12–13, 17–18, 21–24, 116, 121 (2d ed. 2008).
20. See RICHARD J. BONNIE & CHARLES H. WHITBREAD II, *THE MARIJUANA CONVICTION: A HISTORY OF MARIJUANA PROHIBITION IN THE UNITED STATES* (1999) (describing the historical treatment of cannabis in the United States).
21. The Marihuana Tax Act, ch. 553, 50 Stat. 551 (1937) (repealed 1970).
22. The Controlled Substances Act (CSA), Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970, Pub. L. No. 91-513, 84 Stat. 1242 (codified as amended at 21 U.S.C. §§ 801–904 (2018)). A “controlled substance” is “a drug or other substance, or immediate precursor, included in Schedule I, II, III, IV, or V of part B of this title,” except for “distilled spirits, wine, malt beverages, or tobacco, as those terms are defined or used in subtitle E of the Internal Revenue Code of 1954.” 21 U.S.C. § 802(6) (2018). The CSA incorporates the definition of a “drug” from the Food, Drug, and Cosmetic Act, 21 U.S.C. § 201(g)(1) (2018).
23. Single Convention on Narcotic Drugs, Mar. 30, 1961, 18 U.S.T. 1407, *amended by* 1972 Protocol, Mar. 25, 1972, 26 U.S.T. 1439; Convention on Psychotropic Substances, Feb. 21, 1971, 32 U.S.T. 543; United Nations Convention Against Illicit Traffic in Narcotic Drugs and Psychotropic Substances, Dec. 20, 1988, 1582 U.N.T.S. 164.
24. Larkin, *Reflexive Federalism*, *supra* note 9, at 527.
25. See, e.g., Larkin, *States’ Rights*, *supra* note 13, at 528.
26. See, e.g., FIRST REP. OF THE NAT’L COMM’N ON MARIJUANA AND DRUG ABUSE, *MARIJUANA: A SIGNAL OF MISUNDERSTANDING* (1972); U.K. HOME OFF., *ADVISORY COMMITTEE ON DRUG DEPENDENCE*, WOOTTON REP. (1968); E.R. BLOOMQUIST, *MARIJUANA* (1968); *MARIJUANA* (Erich Goode ed., 1969); LESTER GRINSPOON, *MARIJUANA RECONSIDERED* (1971); JOHN KAPLAN, *MARIJUANA: THE NEW PROHIBITION* (1970); HERBERT PACKER, *THE LIMITS OF THE CRIMINAL SANCTION* 333 (1968) (“A clearer case of misapplication of the criminal sanction would be difficult to imagine.”); JOHN ROSEVEAR, *POT: A HANDBOOK OF MARIJUANA* (1967); MICHAEL SCHOFIELD, *THE STRANGE CASE OF POT* (1971); *THE MARIJUANA PAPERS* (David Solomon ed., 1968).
27. See, e.g., JONATHAN P. CAULKINS ET AL., *RAND CORP., CONSIDERING MARIJUANA LEGALIZATION: INSIGHTS FOR VERMONT AND OTHER JURISDICTIONS* 1 (2015) [hereafter CAULKINS ET AL., *MARIJUANA LEGALIZATION INSIGHT*] (“[I]n the 1970s, 12 states removed or substantially reduced criminal penalties for possession of small amounts of marijuana.” (footnote omitted)).
28. President Jimmy Carter signaled interest in decriminalizing simple cannabis possession. Scandals involving his drug advisor Peter Bourne, however, led Carter to withdraw his support for decriminalization. See Robin Williams, *Medical and Recreational Marijuana Policy*, in *MARIJUANA AND MENTAL HEALTH* 39, 45 (Michael T. Compton ed., 2016).
29. See, e.g., INST. OF MED., *MARIJUANA AND MEDICINE: ASSESSING THE SCIENCE BASE* (Janet E. Joy et al. eds., 1999); NAT’L ACAD. REPORT, *supra* note 3; OFFICE OF NAT’L DRUG CONTROL POLICY, *MARIJUANA MYTHS AND FACTS: THE TRUTH BEHIND 10 POPULAR MISCONCEPTIONS* (2004); DIV. OF MENTAL HEALTH AND PREVENTION OF SUBSTANCE ABUSE, WORLD HEALTH ORG., *CANNABIS: A HEALTH PERSPECTIVE AND RESEARCH AGENDA* (1997); CAULKINS ET AL., *MARIJUANA LEGALIZATION INSIGHT*, *supra* note 27; Jonathan Caulkins, *Against a Weed Industry*, *NAT’L REV.* (Mar. 15, 2018, 12:06 PM), <https://www.nationalreview.com/magazine/2018/04/02/legal-marijuana-industry-leap-unknown/> [<https://perma.cc/79W2-FGED>]; Caulkins, *Marijuana Dangers*, *supra* note 18; Wayne Hall & Louisa Degenhardt, *Adverse Health Effects of Non-Medical Cannabis Use*, 374 *LANCET* 1383, 1389 (2009); Mark A.R. Kleiman, *The Public-Health Case for Legalizing Marijuana*, *NAT’L AFF.* 68 (Spring 2019).
30. See 21 U.S.C. §§ 812(c) Schedule I & 841 (2018); 21 C.F.R. § 1308.11(d)(31) (2021) (listing cannabis as a Schedule I controlled substance).
31. Larkin, *Drugged Driving*, *supra* note 1, at 468.
32. See CAL. HEALTH & SAFETY CODE § 11362.5 (West 2022).
33. See, e.g., Larkin, *Reflexive Federalism*, *supra* note 9, at 523–24.
34. See Memorandum from David W. Ogden, Deputy Att’y Gen., to Selected U.S. Attorneys regarding Investigations and Prosecutions in States Authorizing the Medical Use of Marijuana (Oct. 19, 2009); Memorandum from James M. Cole, Deputy Att’y Gen., U.S. Dep’t of Just., for United States Attorneys

- regarding Guidance Regarding the Ogden Memo in Jurisdictions Seeking to Authorize Marijuana for Medical Use 1 (June 29, 2011); Memorandum from James M. Cole, Deputy Att’y Gen., U.S. Dep’t of Just., for United States Attorneys regarding Guidance Regarding Marijuana Enforcement 3 (Aug. 29, 2013); Memorandum from James M. Cole, Deputy Att’y Gen., U.S. Dep’t of Just., for United States Attorneys Regarding Guidance Regarding Marijuana Related Financial Crimes 2 (Feb. 14, 2014).
35. See U.S. GOV’T ACCOUNTABILITY OFF., GAO-16-1, STATE MARIJUANA LEGALIZATION: DOJ SHOULD DOCUMENT ITS APPROACH TO MONITORING THE EFFECTS OF STATE MARIJUANA LEGALIZATION (2015); Larkin, *Reflexive Federalism*, *supra* note 9, at 534 (“To be sure, unlike a statute or regulation, those memoranda did not have the force of law. They merely expressed the Justice Department’s then-current enforcement policy, which President Obama or Attorney General Eric Holder (and any of their successors) could revise or abandon at any time. Nonetheless, since the department essentially turned a blind eye to seeing precisely how compliant cannabis businesses were with state law, the memoranda had the effect of serving as ‘Get Out Of Jail, Free’ cards for any enterprise that did not embarrass the administration by flaunting its illegal conduct.”) (footnotes omitted).
 36. See *Matthew 27:24* (King James Version) (“When Pilate saw that he could prevail nothing, but *that* rather a tumult was made, he took water, and washed *his* hands before the multitude, saying, I am innocent of the blood of this just person: see ye *to it*.”); Larkin, *Reflexive Federalism*, *supra* note 9, at 534 (“The memoranda effectively told the states and marijuana industry that the legal status of marijuana, as well as the vigor with which the criminal law should and would be enforced, was in their hands. Each state was free to decide how to treat marijuana within its own jurisdiction. Put differently, each one could clean its own room or leave it a mess. As long as each state did not foul up a sibling’s room, all was fine with Daddy.”).
 37. Larkin, *Reflexive Federalism*, *supra* note 9, at 539 (footnotes omitted).
 38. See, e.g., DAVID BEARMAN & MARIA PETTINATO, CANNABIS MEDICINE: A GUIDE TO THE PRACTICE OF CANNABINOID MEDICINE (2019); DAVID CASARETT, STONED: A DOCTOR’S CASE FOR MEDICAL MARIJUANA (2015); PATRICIA C. FRYE & DAVE SMITHERMAN, THE MEDICAL MARIJUANA GUIDE: CANNABIS AND YOUR HEALTH (2018); BONNI GOLDSTEIN, CANNABIS REVEALED (2016); MICHAEL H. MOSKOWITZ, MEDICAL CANNABIS (2017); LESTER GRINSPOON & JAMES B. BAKALAR, MARIJUANA: THE FORBIDDEN MEDICINE (1997); MICHAEL H. MOSKOWITZ, MEDICAL CANNABIS: A GUIDE FOR PATIENTS, PRACTITIONERS, AND CAREGIVERS (2017); J. Michael Bostwick, *Clinical Decisions: Medicinal Use of Marijuana—Recommend the Medical Use of Marijuana*, 368 NEW ENG. J. MED. 866, 866–68 (2013); Jerome P. Kassirer, Editorial, *Federal Foolishness and Marijuana*, 336 NEW ENG. J. MED. 366 (1997). Other physicians and scientists disagree that botanical cannabis can be deemed a legitimate medicine. See, e.g., DUPONT, *supra* note 6, at 147–54; ED GOGEK, MARIJUANA DEBUNKED (2015); KEVIN P. HILL, MARIJUANA: THE UNBIASED TRUTH ABOUT THE WORLD’S MOST POPULAR WEED (2015); Gary M. Reisfield & Robert L. DuPont, *Clinical Decisions: Medicinal Use of Marijuana—Recommend Against the Medical Use of Marijuana*, 368 NEW ENG. J. MED. 866, 868 (2013); see also BERTHA K. MADRAS, UPDATE OF CANNABIS AND ITS MEDICAL USE (2015), http://www.who.int/medicines/access/controlled-substances/6_2_cannabis_update.pdf [<https://perma.cc/SA4P-SRA6>] (commissioned monograph to 37th Expert Committee on Drug Dependence, World Health Organization). The debate has proceeded for more than half a century. Neither side has cried “uncle,” and neither one is likely to vanquish the other.
 39. Congress has made one minor incursion into federal enforcement of the cannabis laws. Through the use of riders added to Department of Justice appropriations bills since 2014, Congress has forbidden the department to use federal funds to “prevent” states from “implementing” state medical-use programs. See Consolidated Appropriations Act of 2022, Pub. L. No. 117-103, § 531, 136 Stat. 49 (2022) (providing that “[n]one of the funds made available under this Act to the Department of Justice may be used, with respect to [Maine and other states], to prevent any of them from implementing their own laws that authorize the use, distribution, possession, or cultivation of medical marijuana”); Larkin, *Reflexive Federalism*, *supra* note 9, at 530–31 & n.29–33 (collecting earlier riders). Those bills do not reschedule cannabis out of Schedule I.
 40. Congress placed cannabis in CSA Schedule I, which prohibits its use for any purpose. 21 U.S.C. § 812(b)(1)(A)–(C) (2018) (noting that drugs placed in Schedule I have “a high potential for abuse,” “no currently accepted medical use in treatment in the United States,” and a lack of accepted safety for use of the drug or other substance under medical supervision”); *id.* § 829 (setting prescription standards for drugs in Schedules II–V); *id.* § 841(a) (defining prohibited acts).
 41. See *supra* note 26.
 42. See *supra* notes 11–13 and accompanying text.
 43. See, e.g., FDA Regulation of Cannabis and Cannabis-Derived Products, Including Cannabidiol (CBD), FDA (Oct. 1, 2020), <https://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-including-cannabidiol-cbd> [<https://perma.cc/TF56-2GRQ>]; *What You Need to Know (And What We’re Working to Find Out) About Products Containing Cannabis or Cannabis-Derived Compounds, Including CBD*, FDA (Mar. 5, 2020), <https://www.fda.gov/consumers/consumer-updates/what-you-need-know-and-what-were-working-find-out-about-products-containing-cannabis-or-cannabis> [<https://perma.cc/7HGY-KAZ4>]; *FDA and Cannabis: Research and Drug Approval Process*, FDA (Oct. 1, 2020), <https://www.fda.gov/news-events/public-health-focus/fda-and-cannabis-research-and-drug-approval-process> [<https://perma.cc/L2QP-YETU>].
 44. See “*Cannabis Policies for a New Decade*,” Hearing Before the House Commerce Comm. Subcomm. on Health, 116th Cong. 1–4 (2020) [hereinafter House Cannabis Hearing] (statement of Douglas C. Throckmorton, Dep. Dir. For Reg’y Programs, FDA), <https://docs.house.gov/meetings/IF/IF14/20200115/110381/HHRG-116-IF14-Wstate-ThrockmortonD-20200115.pdf> [<https://perma.cc/Y2PF-X36D>]; 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 (Dec. 20, 2018) [hereinafter Gottlieb Statement], <https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-signing-agriculture-improvement-act-and-agencys> [<https://perma.cc/RP9Y-CBDP>]; Warning Letters and Test Results for Cannabidiol-Related Products: 2015–2019 (Nov. 26, 2019; last accessed Jan. 14, 2020), <https://www.fda.gov/news-events/public-health-focus/warning-letters-and-test-results-cannabidiol-related-products> [<https://perma.cc/55EV-KMLC>]

- (warning letters issued to companies selling unapproved new drugs containing cannabidiol, a non-psychoactive substance in marijuana that the FDA has not approved for use in any drug for any purpose); see also, e.g., Paul J. Larkin, Jr., *Marijuana Edibles and “Gummy Bears,”* 66 *BUFF. L. REV.* 313, 345–48, 373–78 (2018) [hereafter Larkin, *Gummy Bears*] (concluding that the FDA has the authority to regulate cannabis edibles as food “additives”); Sean M. O’Connor & Erika Lietzan, *The Surprising Reach of FDA Regulation of Cannabis, Even After Descheduling,* 68 *AM. U. L. REV.* 823, 851–96 (2019) (same, to regulate cannabis as a drug or food additive); Patricia J. Zettler, *Pharmaceutical Federalism,* 92 *IND. L.J.* 845, 849, 878–79 (2017) (same, to regulate cannabis as a drug).
45. For the FDA’s opinion, see, for example, *FDA Regulation of Cannabis and Cannabis-Derived Products, Including Cannabidiol (CBD)*, FDA (Oct. 1, 2020), <https://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-including-cannabidiol-cbd> [<https://perma.cc/TF56-2GRQ>]; *What You Need to Know (And What We’re Working to Find Out) About Products Containing Cannabis or Cannabis-Derived Compounds, Including CBD*, FDA (Mar. 5, 2020), <https://www.fda.gov/consumers/consumer-updates/what-you-need-know-and-what-were-working-find-out-about-products-containing-cannabis-or-cannabis> [<https://perma.cc/7HGY-KAZ4>]; *FDA and Cannabis: Research and Drug Approval Process*, FDA (Oct. 1, 2020), <https://www.fda.gov/news-events/public-health-focus/fda-and-cannabis-research-and-drug-approval-process> [<https://perma.cc/L2QP-YETU>]. For the views of other federal agencies, see, for example, Alex M. Azar II, HHS Sec’y, Remarks on Surgeon General’s Marijuana Advisory (Aug. 29, 2019), <https://www.hhs.gov/about/leadership/secretary/speeches/2019-speeches/remarks-on-surgeon-general-marijuana-advisory.html> [<https://perma.cc/YBQ8-T4HP>]; *U.S. Surgeon General’ Advisory: Marijuana Use and the Developing Brain*, U.S. Dep’t of Health & Human Servs., Off. of the Surgeon Gen’l (Aug. 29, 2019), <https://www.hhs.gov/surgeongeneral/reports-and-publications/addiction-and-substance-misuse/advisory-on-marijuana-use-and-developing-brain/index.html> [<https://perma.cc/AR4A-5DA8>]; U.S. Dep’t of Health & Human Servs., Off. of the Surgeon Gen’l, *The Surgeon General’s Warning on Marijuana, Morbidity and Mortality Weekly Report* (Aug. 13, 1982), <https://www.cdc.gov/mmwr/preview/mmwrhtml/00001143.htm> [<https://perma.cc/9KLB-FZFU>]; *SUBSTANCE ABUSE & MENTAL HEALTH SERVS. ADM’N (SAMHSA), MARIJUANA RISKS* (Sept. 26, 2019), <https://www.samhsa.gov/marijuana> [<https://perma.cc/DCB3-ZQ7Y>]; *NAT’L INST. ON DRUG ABUSE, MARIJUANA RESEARCH REPORT* (Rev. July 2020), <https://www.drugabuse.gov/download/1380/marijuana-research-report.pdf?v=d9e67cbd412ae5f340206c1a0d9c2bfd> [<https://perma.cc/U5RU-P2HM>].
 46. See Letter from Peter Hyun, Acting Ass’t Att’y Gen’l, to Senators Elizabeth Warren & Cory A. Booker (Apr. 12, 2022) (“Cannabis is a Schedule I controlled substance under the Controlled Substances Act (CSA). This is—in part—due to HHS’s determination that cannabis has not been proven in scientific studies to be a safe and effective treatment for any disease or condition.”).
 47. See *infra* note 59.
 48. See, e.g., Paul J. Larkin, Jr., *Reconsidering Federal Marijuana Regulation*, 18 *OHIO ST. J. CRIM. L.* 99, 115–27 (2020) [hereafter Larkin, *Reconsidering Marijuana*]; O’Connor & Lietzan, *supra* note 44, at 851–96 (2019) (same, to regulate cannabis as a drug or food additive); Zettler, *supra* note 44, at 878–79 (same, to regulate cannabis as a drug); cf. THOMAS & ELSOHLY, *supra* note 12, at xiv (arguing that the FDA needs to be more closely involved in marijuana regulation than the Drug Enforcement Administration is).
 49. The Supremacy Clause of Article VI of the Constitution makes federal law superior to state law when the two conflict. U.S. CONST. art. VI, cl. 2. Accordingly, states cannot exempt their residents from federal law by adopting their own regulatory programs. See *Gonzales v. Raich*, 545 U.S. 1, 23–33 (2005) (rejecting the argument that a state medical marijuana program available only for bona fide state residents should be exempt from federal regulation under the Commerce Clause); *United States v. Oakland Cannabis Buyers’ Coop.*, 532 U.S. 483, 494–95 (2001) (rejecting a medical necessity defense to federal prosecution in a state with a medical marijuana program).
 50. Courts in the Ninth Circuit ruled that the First Amendment Free Speech Clause prohibits the government from adopting a viewpoint-based restriction on private communications between a physician and a patient regarding potential medical treatment options. See *Conant v. McCaffrey*, 172 F.R.D. 681, 694–95 (N.D. Cal. 1997) (issuing preliminary injunction), 2000 WL 1281174 (N.D. Cal. Sept. 7, 2002) (issuing permanent injunction), *aff’d*, *Conant v. Walters*, 309 F.3d 629 (9th Cir. 2002) (upholding permanent injunction).
 51. Larkin, *Reflexive Federalism*, *supra* note 9, at 588 (footnote omitted).
 52. See, e.g., Caulkins, *Marijuana Dangers*, *supra* note 18; Larkin, *Drugged Driving*, *supra* note 1, at 512 (“[A] large segment of the nation’s population justifiably believes that the medical marijuana movement is merely a Trojan Horse for legalization. To them, the sponsors of those initiatives took advantage of the natural sympathy that people have for others in extremis to achieve dishonestly what could not be done openly: legalize marijuana use. Many people quite reasonably believe that medical marijuana initiatives rest on the deceit that their purpose and effect would be limited to alleviating the suffering of parties desperate for relief from unrelenting pain or a crippling malady, some of whom have no hope for anything other than to limit their suffering before they die. Many people would have favored decriminalizing or legalizing marijuana—for example, people who may have supported Colorado and Washington’s decisions to allow marijuana to be consumed for recreational use—but only if it were done openly, with a public debate followed by a vote of the legislature or, more likely, the state’s voters. Now, however, they feel lied to and cheated. Worse still, they feel insulted. In their mind, the supporters of medical marijuana initiatives believe that the average person is so dim-witted that he will never realize what is really going on.”); Hank Campbell, *Junk Science and the Hypocrisy of Medical Marijuana*, *SCIENCE 2.0* (July 23, 2013), http://www.science20.com/science_20/junk_science_and_hypocrisy_medical_marijuana-96254 (“While medical marijuana was sold to states for serious illness, Edward Gogek, M.D. notes, it is not the case in practice. Instead, it is sold for ‘pain’ 90% of the time, which is a symptom so non-specific and subjective that Ferris Buehler got a whole day off school with it.”). Nothing of importance changed during the Trump Administration. In 2018, Trump Administration Attorney General Jeff Sessions revoked the Obama Administration cannabis policies but did not direct the U.S. Attorneys aggressively to enforce federal law. Sessions’ successor, Attorney General Bill Barr, said that Congress should end the back-and-forth by clarifying

federal law. Sarah N. Lynch, *U.S. Attorney General Nominee Will Not Target Law-Abiding Marijuana Businesses*, Reuters (Jan. 15, 2019, 3:30 PM), <https://www.reuters.com/article/us-usa-trump-barr-marijuana/us-attorney-general-nominee-will-not-target-law-abiding-marijuana-businesses-idUSKCNIP92JO> [<https://perma.cc/WQU7-MXDR>]. As a practical matter, the Trump Administration's position was essentially the same as the Obama Administration's. Larkin, *Reflexive Federalism*, *supra* note 9, at 535–36. The result is that the back-and-forth that federal cannabis policy has taken more closely resembles the randomness of Brownian motion than the precision of a NASA flight plan.

53. JOHN HUDAK, *MARIJUANA: A SHORT HISTORY* 18–19 (2d ed. 2020).
54. See, e.g., Paul J. Larkin, Jr., *Cannabis Capitalism*, 69 *BUFF. L. REV.* 101, 113–28 (2021) [hereafter Larkin, *Cannabis Capitalism*] (describing the creation of numerous types of THC-infused products); *id.* at 141–43 (“Unfortunately, for some people the ‘rush’ that marijuana produces is more a curse than a blessing. Heavy or long-term cannabis use can lead to tolerance, which requires increasing amounts of THC to produce the desired effect. Heavy or long-term use can also damage executive mental functioning, as well as lead users to become dependent on the drug, which causes them to suffer withdrawal symptoms when they discontinue its use. The 2013 edition of the American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders defines that condition as ‘Cannabis Use Disorder.’”) (footnotes omitted).
55. “Cannabis ‘came of age,’ so to speak, in the 1960s as a symbol of an intergenerational protest. The image of someone in his or her 20s or 30s smoking a joint could well serve as a representation of that generation’s attitudes toward then-contemporary social and political culture. Users can still smoke cannabis as a ‘joint’ (botanical marijuana in wrapping paper) or a ‘blunt’ (botanical marijuana wrapped in tobacco), by using a ‘bong’ (a pipe or water pipe), or by vaporizing THC via an Electronic Nicotine Delivery Device (ENDD or e-cigarette). Yet, today numerous food products, known as ‘edibles,’ also contain THC. In addition to the Alice B. Toklas brownies popular in the 1960s, numerous food products—such as coffee, tea, soda, cookies, candies, caramels, lozenges, salad dressing, marinara sauce, and others—contain THC. As one commentator put it, a ‘cannabis culinary professional can infuse just about anything you want to eat with THC.’” *Id.* at 124–25 (footnotes omitted); see also, e.g., Larkin, *Gummy Bears*, *supra* note 44, at 318–21.
56. “Like most issues concerning marijuana, the subject of dependency has been a contentious one. Some marijuana supporters have denied that it has any potential for dependency, and some of its opponents have claimed that it always leads to addiction. The truth lies between the extremes. Approximately ten percent of the people who ever smoke marijuana become dependent on it, but that risk goes up for someone who uses cannabis frequently, particularly when regular use began during adolescence. According to cannabis experts Wayne Hall and Rosalie Pacula, ‘the following rules of thumb’ are useful in determining the likelihood of dependence: The risk is one in ten for people who have ever used cannabis. Using the drug on more than a few occasions increases the risk to between one in five and one in three. Use it daily and the risk jumps to approximately one in two. The risk is even higher for someone who begins marijuana use during adolescence, given the labile nature of the adolescent brain.” Larkin, *Cannabis Capitalism*, *supra* note 54, at 143–44; see also, e.g., WAYNE HALL & ROSALIE LICCARDO PACULA, *CANNABIS USE AND DEPENDENCE: PUBLIC HEALTH AND PUBLIC POLICY* 75, 78 (2003); *infra* notes 71–73 and accompanying text.
57. For a summary of the testing and approval process that ordinary pharmaceuticals must undergo before the FDA can approve them as safe and effective, see, for example, RICK NG, *DRUGS: FROM DISCOVERY TO APPROVAL* 136–206 (2d ed. 2009); MIKKAEL A. SEKERES, *DRUGS AND THE FDA* 51, 79–80, 91, 96 (2022).
58. Reisfield & DuPont, *supra* note 38, at 868 (citation omitted).
59. Larkin, *Reconsidering Marijuana*, *supra* note 48, at 118 (footnote omitted); see also, e.g., *id.* at 118–24 (arguing that agricultural cannabis cannot satisfy the FDA requirements to be a safe, effective, and uniform drug); ED GOGEK, *MARIJUANA DEBUNKED: A HANDBOOK FOR PARENTS, PUNDITS, AND POLITICIANS WHO WANT TO KNOW THE CASE AGAINST LEGALIZATION* 111–12 (2015) (“Political campaigns sell marijuana laws to the voting public with ads that feature cancer patients using marijuana for nausea. But it’s a bait and switch.... The patients using medical marijuana in real life are disproportionately young and male, and few of them have serious illnesses.... Data from 2012 show that in Arizona, 90 percent of the marijuana patients claimed pain while only 4 percent got the drug for cancer. In Colorado, 94 percent claimed pain; 3 percent claimed cancer. In Oregon, 94 percent also claimed pain. [¶] A 2014 study that used data from seven states found that 91 percent of all the medical marijuana patients got their marijuana for pain while only 3 percent reported cancer. AIDS, glaucoma, Alzheimer’s, Hepatitis C and ALS accounted for another 2 percent.”) (footnote omitted); Gerard Caplan, *Medical Marijuana: A Study of Unintended Consequences*, 43 *MCGEORGE L. REV.* 127, 130 (2012) (noting that comedian Jon Stewart had remarked that Colorado seemed to have changed almost overnight from “the healthiest state in the country” to “one of the sickest.”); Caulkins, *Marijuana Dangers*, *supra* note 18, at 30 (“Unfortunately, there is very little in the way of intellectually honest marijuana-policy analysis.”); *id.* at 21 (“In the 1990s, several states introduced ‘medical marijuana’ programs. Though marijuana use was made legal only for medical purposes, the regulations were often so loose that essentially anyone could get a physician’s ‘recommendation,’ authorizing that person to purchase marijuana. Suppliers were euphemistically called ‘caregivers’ (even though some never met the ‘patients’ they were caring for), and they sold out of brick-and-mortar retail stores known as ‘dispensaries.’ At one point, there were thousands of dispensaries in California alone.”); Kleiman, *Marijuana and Public Health*, *supra* note 29, at 73 (describing the medical marijuana reform campaign as being “largely fraudulent,” but “worked like a charm”); Larkin, *Gummy Bears*, *supra* note 44, at 374–77 & nn.137–46 (discussing FDA’s issuance of warning letters to companies that had marketed dietary supplements containing cannabidiol for treatment of cancer, Alzheimer’s and other diseases); cf. Larkin, *Drugged Driving*, *supra* note 1, at 511–13 & nn.275–83 (arguing that medical cannabis programs are merely recreational cannabis programs operating under a false flag); Chris Roberts, *Anyone Can Get Their Medicine: California Has Already Pretty Much Legalized Marijuana. And That’s Okay*, *SF WEEKLY* (Sept. 14, 2014) <http://www.sfweekly.com/sanfrancisco/chem-tales-marijuana-legalization-recreational-use/Content?oid=3154256> (“Not long ago, a friend of mine visited the doctor. Afterward, I asked him for the diagnosis. ‘Good news,’ he said with a grin. ‘I’m still sick.’ A clean bill of health would have been a setback. That would mean no more marijuana. I am often asked how to legally obtain some weed in San Francisco, what ailment is required to get a medical marijuana recommendation. This fascinates people to this day, out-of-towners as well as locals. When I am honest, I say, ‘About \$40 and 10 minutes.’”).

60. In October 2022, President Joe Biden directed Health and Human Services Secretary Xavier Becerra and U.S. Attorney General Merrick Garland to reconsider the scheduling of cannabis. White House, Statement from President Biden on Marijuana Reform, Oct. 6, 2022, <https://www.whitehouse.gov/briefing-room/statements-releases/2022/10/06/statement-from-president-biden-on-marijuana-reform/> (“I am asking the Secretary of Health and Human Services and the Attorney General to initiate the administrative process to review expeditiously how marijuana is scheduled under federal law. Federal law currently classifies marijuana in Schedule I of the Controlled Substances Act, the classification meant for the most dangerous substances. This is the same schedule as for heroin and LSD, and even higher than the classification of fentanyl and methamphetamine—the drugs that are driving our overdose epidemic.”).
61. Caulkins, *Against a Weed Industry*, *supra* note 29, at 27.
62. See Larkin, *Gummy Bears*, *supra* note 44, at 318–21, 319 nn.15–16, 337–38 & nn.56–62.
63. See, e.g., Robin Murray et al., *Traditional Marijuana, High-Potency Cannabis and Synthetic Cannabinoids: Increasing Risk for Psychosis*, 15 *WORLD PSYCHIATRY* 195, 196 (2016).
64. See, e.g., Joseph M. Pierre, *Risks of Increasingly Potent Cannabis: The Joint Effects of Potency and Frequency*, 16 *CURRENT PSYCHIATRY* 15, 15 (2017) (noting that the THC level of “street” marijuana was less than 1 percent in the 1970s and 4 percent in the 1990s); Volkow et al., *supra* note 16, at 2222 (“The THC content, or potency, of marijuana, as detected in confiscated samples, has been steadily increasing from about 3% in the 1980s to 12% in 2012.”). There is little uniformity in botanical cannabis, but some estimates can be made. See HALL & PACULA, *supra* note 56, at 14 (“A typical cannabis joint consists of between 0.5 and 1.0 g [gram] of cannabis and contains between 5 and 50 mg [milligrams] of THC (i.e. between 0.5% and 5% of THC). The amount of THC delivered in the smoke varies between 20% and 70%... the rest is burnt or lost in sidestream smoke. The fraction of THC in the joint that reaches the user’s bloodstream varies between 5% and 24% (mean 18.6%)... These variations in the THC content of cannabis and cannabis smoke make it difficult to estimate the typical dose of THC that is received when cannabis is smoked.”). Moreover, factors other than the amount of alcohol consumed, such as body mass, affect a drinker’s response to alcohol. So, too, factors other than THC content affect cannabis users. For example, long-term users develop a tolerance to that drug, requiring consumption of a greater amount to achieve a euphoric effect. See, e.g., *id.* at 133, 215; IVERSEN, *supra* note 19, at 105–13. Moreover, there is considerable variation in the THC content of different cannabis products due to considerations such as the strain, region, cultivation processes, processing stage, storage time, and other considerations. See, e.g., PATRICIA C. FRYE & DAVID SMITHERMAN, *THE MEDICAL MARIJUANA GUIDE: CANNABIS AND YOUR HEALTH* 9 (2018) (“As we now know, the cannabinoid production varies from plant to plant, and ten drops of one batch might be therapeutic, but ten drops of the next batch might have a much higher content of THC and sicken the patient.”); THOMAS & EL-SOHLI, *supra* note 12, at xiii–xiv, 30.
65. Some parties have claimed that factors the cannabis samples tested in the 1960s and 1970s were not as fresh as the ones tested today. See, e.g., Eric L. Sevigny, *Is Today’s Marijuana More Potent Simply Because It’s Fresher?*, 5 *DRUG TESTING ANALYSIS* 62, 62 (2013) [hereafter Sevigny, *Fresher*].
66. See, e.g., OFFICE OF THE SURGEON GENERAL, U.S. SURGEON GENERAL’S ADVISORY: MARIJUANA USE AND THE DEVELOPING BRAIN (Aug. 29, 2019) (“Marijuana has changed over time. The marijuana available today is much stronger than previous versions. The THC concentration in commonly cultivated marijuana plants has increased three-fold between 1995 and 2014 (4% and 12% respectively). Marijuana available in dispensaries in some states has average concentrations of THC between 17.7% and 23.2%. Concentrated products, commonly known as dabs or waxes, are far more widely available to recreational users today and may contain between 23.7% and 75.9% THC.”) (footnotes omitted); WORLD HEALTH ORG., *THE HEALTH AND SOCIAL EFFECTS OF NONMEDICAL CANNABIS* USE 12–13 (2016); AM. PSYCHIATRIC ASS’N, *DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS* 511 (5th ed. 2013) [hereinafter DSM-5] (“During the past two decades, a steady increase in the potency of seized cannabis has been observed.”); JOHN BRICK & CARLTON K. ERICKSON, *DRUGS, THE BRAIN, AND BEHAVIOR: THE PHARMACOLOGY OF DRUG USE DISORDERS* 105 (2d ed. 2013); Desmond Slade et al., *Is Cannabis Becoming More Potent?*, in *MARIJUANA AND MADNESS* (2d ed. David Castle et al. eds., 2012); Alan J. Budney et al., *Cannabis*, in *LOWINSON & RUIZ’S SUBSTANCE ABUSE: A COMPREHENSIVE TEXTBOOK* 216 (Pedro Ruiz & Eric Strain eds., 5th ed. 2011) (the potency of marijuana increased by 60 percent from 2000–2010); ROBIN ROOM ET AL., *CANNABIS POLICY: BEYOND STALEMATE* 6 (2010) (noting that some varieties of marijuana like Sinsemilla (seedless cannabis), also known as skunk and Netherweed, may have THC content as high as 20 percent, that hashish has a THC content in the range of 2 percent–20 percent, and that hash oil has a THC content of 15 percent–50 percent); CAULKINS ET AL., *MARIJUANA LEGALIZATION INSIGHT*, *supra* note 27, at 106–08; Fidelia Cascini et al., *Increasing Delta-9-Tetrahydrocannabinol (Δ -9-THC) Content in Herbal Cannabis Over Time: Systematic Review and Meta Analysis*, 5 *CURRENT DRUG ABUSE REV.* 32 (2012); Suman Chandras et al., *New Trends in Cannabis Potency in USA and Europe During the Last Decade (2008–2017)*, 269 *EUR. ARCHIVES PSYCHIATRY CLINICAL NEUROSCIENCE* 5 (2019) (“[T]he mean D9-THC concentration has increased dramatically over the last 10 years, from 8.9% in 2008 to 17.1% in 2017. The mean D9-THC:CBD ratio also rose substantially from 23 in 2008 to 104 in 2017. There was also marked increase in the proportion of hash oil samples (concentrates) seized (0.5–4.7%) and their mean D9-THC concentration (6.7–55.7%) from 2008 to 2017.”); Wilson M. Compton et al., *Medical Marijuana Laws and Cannabis Use: Intersections of Health and Policy*, 74 *JAMA PSYCHIATRY* 559, 559 (2017) (noting that “[i]n recent years, the potency of cannabis [THC content]...has increased 3-fold to 4 fold”); Mahmoud A. ElSohly et al., *Changes in Cannabis Potency Over the Last 2 Decades (1995–2014): Analysis of Current Data in the United States*, 79 *SOC’Y BIOLOGICAL PSYCHIATRY* 613, 619 (2016) (“[O]ur data show that the potency of illicit cannabis plant material has consistently increased over the last two decades from approximately 4% in 1995 to approximately 12% in 2014....”); Tom P. Freeman et al., *Changes in Delta-9-Tetrahydrocannabinol (THC) and Cannabidiol (CBD) Concentrations in Cannabis Over Time: Systematic Review and Meta-Analysis*, 116 *ADDICTION* 1000, 1006 (2020); Wayne Hall et al., *Cannabis Use and Psychotic Disorders: An Update*, 23 *DRUG & ALCOHOL REV.* 433, 440 (2004) (“Over the past two decades a large-scale illicit cannabis industry has developed in many countries, which aims to meet the demand for cannabis from daily users who prefer more potent forms of cannabis.”); Jennifer McLaren et al., *Cannabis Potency and Contamination: A Review of the Literature*, 103 *ADDICTION* 1100, 1106 (2008) (“There is evidence for a doubling of potency [of cannabis] in the United States.”); Zlato Mehmedic et al., *Potency Trends of Δ 9-THC and Other Cannabinoids in Confiscated Cannabis Preparations from 1998 to 2008*, 55 *J. FORENSIC SCI.* 1209, (2010) (“It is now possible to mass produce plants with potencies

inconceivable when concerted monitoring efforts started 40 years ago... [A]nalysis of the available data in conjunction with the [Potency Monitoring] program results makes a strong case that cannabis is not only more potent than in the past but also that this high-potency product's market share is also growing.”); Pierre, *supra* note 64, at 15 (noting that the THC level of “street marijuana” was less than 1 percent in the 1970s and 4 percent in the 1990s); Eric L. Sevigny et al., *The Effects of Medical Marijuana Laws on Potency*, 25 INT’L J. DRUG POL’Y 308, 309 (2014) (“Although direct empirical evidence is limited, insider and journalistic accounts suggest that [medical marijuana laws—and the medical marijuana industry built up around them—have greatly enhanced the development and diffusion of high-potency cannabis cultivars and sophisticated techniques of production.”); Sevigny, *Fresher*, *supra* note 65, at 67 (“[A]verage marijuana potency in the USA increased more than six-fold since the 1970s and more than two-fold since the mid-1980s.”); Volkow et al., *supra* note 16, at 2222 (“The THC content, or potency, of marijuana, as detected in confiscated samples, has been steadily increasing from about 3% in the 1980s to 12% in 2012. This increase in THC content raises concerns that the consequences of marijuana use may be worse now than in the past and may account for the significant increases in emergency department visits by persons reporting marijuana use... and the increases in fatal motor-vehicle accidents.”). The same phenomenon has occurred in other countries. See, e.g., Mahmoud A. ElSohly et al., *A Comprehensive Review of Cannabis Potency in the United States in the Last Decade*, 6 BIOLOGICAL PSYCHIATRY 603, 604 (2021) (“[O]ur results show an overall increase in potency of illicit cannabis, from approximately 10% in 2009 to approximately 14% in 2019. These results are in agreement with other potency monitoring programs in several European countries.”); Tom P. Freeman et al., *Increasing Potency and Price of Cannabis in Europe, 2006–16*, 114 ADDICTION 1015, 1020 (2018); Murray et al., *supra* note 63, at 196.

67. THOMAS & ELSOHLY, *supra* note 12, at 11.

68. DUPONT, *supra* note 6, at 142.

69. See, e.g., DSM-5, *supra* note 66, at 511 (noting that cannabis potency ranges from 1 percent–15 percent, hashish from 10 percent–20 percent); JONATHAN P. CAULKINS ET AL., MARIJUANA LEGALIZATION: WHAT EVERYONE NEEDS TO KNOW 34 (2d ed. 2016); HALL & PACULA, *supra* note 56, at 17; IVERSEN, *supra* note 19, at 10 (estimating cannabis potency at 10 percent–20 percent); Herbert D. Kleber & Robert L. DuPont, *Physicians and Medical Marijuana*, 169 AM. J. PSYCHIATRY 564, 564, 565 (2012) (estimating cannabis potency at as much as 20 percent); Larkin, *Reconsidering Marijuana*, *supra* note 48, at 120; Pierre, *supra* note 64, at 15 (“Cannabis preparations such as hashish and hash oil extracts containing THC well above average—from 35% to 90% THC—are now more widely available.”); Jeffrey C. Raber et al., *Understanding Dabs: Contamination Concerns of Cannabis Concentrates and Cannabinoid Transfer During the Act of Dabbing*, 40 J. TOXICOLOGICAL SCI. 797 (2015) (finding a range of 53.9 percent–65.5 percent THC in hash seized from 2004 to 2008); Anna Wilcox, *THC-A Crystalline: The World’s Strongest Hash with 99.99% THC*, Herb (Mar. 29, 2017), <https://herb.co/2017/03/29/thc-a-crystalline/>. Dronabinol (marketed as Marinol) is an FDA-approved pill-form drug of 99 percent THC that is used for chemotherapy-induced nausea. See *Dronabinol: Pharmacology and Biochemistry*, Nat’l Ctr. Biotechnology Info., <https://pubchem.ncbi.nlm.nih.gov/compound/Dronabinol#section=Pharmacology-and-Biochemistry> (last accessed Oct. 9, 2022).

70. See CAULKINS ET AL., MARIJUANA LEGALIZATION INSIGHT, *supra* note 27; Beau Kilmer & Rosalie Liccardo Pacula, *Understanding and Learning from the Diversification of Cannabis Supply Laws*, 112 ADDICTION 1128, 1131 (2016); Larkin, *Gummy Bears*, *supra* note 44, at 337–38 & nn.56–62.

71. “Consider the two most common cannabinoids in marijuana, THC and cannabidiol. Over the last two decades, THC levels in street marijuana have risen dramatically, while cannabidiol (CBD) levels have declined, yielding increasing ratios of THC:CBD as high as 80:1. In the current unregulated market, marijuana’s THC:CBD ratios vary from 2:1 to 80:1 or even higher. The changing THC:CBD ratio is quite important for public health purposes. THC and CBD produce different, or possibly antagonistic molecular, neuropsychiatric, and pharmacological effects. The pharmacological effects that limit the therapeutic potential of THC in marijuana are addiction, anxiety, intoxication, impairment of cognition, amotivational syndrome, and psychosis. CBD not only has a wide safety margin, but also no evidence has emerged that it is addictive, produces euphoria or intoxication, or impairs cognition or precipitates psychosis. But with accumulating evidence, it is clear that CBD is not pharmacologically silent. High THC:CBD ratios in marijuana are associated with heightened euphoria, anxiety, and psychotic symptoms, whereas low THC:CBD ratios are linked to sedation and attenuation of THC-induced psychosis, anxiety, and cognitive deficits, leading to the conclusion, that CBD dampens the adverse effects of THC.” Larkin & Madras, *supra* note 4, at 575–76 (footnotes omitted); see also, e.g., Douglas L. Boggs et al., *Clinical and Preclinical Evidence for Functional Interactions of Cannabidiol and Δ(9)-Tetrahydrocannabinol*, 43 NEUROPSYCHOPHARMACOLOGY 142 (2018); Marco Colizzi & Sagnik Bhattacharyya, *Does Cannabis Composition Matter? Differential Effects of Delta-9-tetrahydrocannabinol and Cannabidiol on Human Cognition*, 4 CURRENT ADDICTION RESEARCH 62 (2017); Ahmed Hasbi et al., *Δ-Tetrahydrocannabinol Increases Dopamine D1-D2 Receptor Heteromer and Elicits Phenotypic Reprogramming in Adult Primate Striatal Neurons* 23 SCIENCE 100794 (2020); Bertha K. Madras et al., *Dramatic Increase of Dopamine D1-D2 Receptor Heteromers by Tetrahydrocannabinol (THC) in Primate Caudate Nucleus Is Attenuated by Cannabidiol (CBD)*, NEUROPSYCHOPHARMACOLOGY (2016), <https://acnp.org/videos/bertha-madras/> [<https://perma.cc/RL84-AGVB>]; Christian D. Schubart et al., *Cannabis with High Cannabidiol Content Is Associated with Fewer Psychotic Experiences*, 130 SCHIZOPHRENIA RESEARCH 216 (2011); Kristine Romer Thomsen et al., *Recommendation to Reconsider Examining Cannabis Subtypes Together Due to Opposing Effects on the Brain, Cognition and Behavior*, 80 NEUROSCI. & BIOBEHAVIORAL REVS. 156 (2017); cf. M. Jerry Wright et al., *Cannabidiol Attenuates Deficits of Visuospatial Associative Memory Induced by Δ9Tetrahydrocannabinol*, 170 BR. J. PHARMACOLOGY 1365, 1370 (2013) (same conclusion in animal studies).

72. See Murray et al., *supra* note 63, at 197 (“[I]n a Dutch survey of 2,000 cannabis users, those who preferred cannabis with the highest CBD content had experienced fewer psychotic-like experiences. Morgan and Curran, who tested hair for cannabinoids, showed that users with both detectable THC and CBD had fewer psychotic symptoms than those with only THC. Finally, in an experimental study of 48 healthy volunteers, treatment with oral CBD before administration of intravenous THC significantly reduced the occurrence of psychotic symptoms.”) (footnotes omitted).

73. See, e.g., Bertha K. Madras, *Tinkering with THC-to-CBD Ratios in Marijuana*, 44 NEUROPSYCHOPHARMACOLOGY 215, 215 (2019) (“Over two decades, THC concentrations in retail marijuana rose dramatically, while CBD levels declined, with THC:CBD ratios now 8 times greater than before.”); *id.* (“The Food and Drug Administration has approved low-dose THC (initial oral dose 0.04 mg/kg b.i.d.) for treating nausea/vomiting associated with cancer chemotherapy for non-responders, for

- treating AIDS-associated anorexia/weight loss, and CBD (initial oral dose 2.5 mg/kg, b.i.d.) to treat rare, severe forms of epilepsy.”); *id.* (“Smokable marijuana (~20% THC; ~0.9 mg/kg) delivers THC at ~20 times the FDA-approved initial dose of oral THC and is now obtainable at THC:CBD ratios varying from 1:1 to 80:1. THC doses and ratios are germane to establishing safety standards, as THC and CBD engender markedly different or even antagonistic molecular, pharmacological and neuropsychiatric effects.”) (endnotes omitted); *id.* (“Limiting its therapeutic potential, THC in marijuana acutely elicits psychosis, anxiety, intoxication, and cognitive impairment. With early initiation and prolonged use, marijuana is addictive and is “likely to increase the risk of developing schizophrenia and other psychoses; the higher the use the greater the risk.”) (endnote omitted; quoting NAT’L ACAD. REPORT, *supra* note 3); *id.* (“No comparable evidence implicates CBD in engendering euphoria, psychosis, cognitive impairment, anxiety, or addiction.”); see also Larkin & Madras, *supra* note 4, at 576–77.
74. See ElSohly et al., *supra* note 66.
75. Larkin & Madras, *supra* note 4, at 577.
76. *Id.*
77. See, e.g., NAT’L INST. ON DRUG ABUSE: SYNTHETIC CANNABINOIDS (K2/SPICE) DRUGFACTS (June 2020) [hereinafter NIDA K2/SPICE]; EUROPEAN DRUG MONITORING CENTRE FOR DRUGS & ADDICTION, PERSPECTIVES ON DRUGS: SYNTHETIC CANNABINOIDS IN EUROPE (2017) [hereinafter EUROPEAN DRUG MONITORING CENTRE]; Murray et al., *supra* note 63, at 196.
78. Kathryn A. Seely et al., *Spice Drugs Are More than Harmless Herbal Blends: A Review of the Pharmacology and Toxicology of Synthetic Cannabinoids*, 39 PROG. NEUROPSYCHOPHARMACOLOGY BIOLOGICAL PSYCHIATRY 234, 243 (2012).
79. *Id.*
80. *Id.*
81. *Id.* (footnotes omitted).
82. *Id.*
83. NIDA K2/SPICE, *supra* note 77, at 4 (“Are synthetic cannabinoids addictive? Yes, synthetic cannabinoids can be addictive. Regular users trying to quit may have the following withdrawal symptoms: headaches[,] anxiety[,] depression[,] irritability. Behavioral therapies and medications have not specifically been tested for treatment of addiction to these products. Health care providers should screen patients for possible co-occurring mental health conditions.”) (internal punctuation modified).
84. *Id.* at 4–5 (“Can you overdose on synthetic cannabinoids? Yes. An overdose occurs when a person uses too much of a drug and has a dangerous reaction that results in serious, harmful symptoms or death. Use of synthetic cannabinoids can cause: toxic reactions[,] elevated blood pressure[,] reduced blood supply to the heart[,] kidney damage[,] seizures. Deaths can also occur when dangerous synthetic opioids, such as fentanyl, are added to the packaged mixture without the user knowing it.”) (internal punctuation modified), 6; EUROPEAN DRUG MONITORING CENTRE, *supra* note 77, at 1 (“Little is known about how these substances work and their toxic effects in humans. However, their use has caused many serious poisonings and even deaths—sometimes these have manifested as outbreaks of mass poisonings. It is possible that, along with being highly potent, some may also have long half-lives, potentially leading to a prolonged psychoactive effect.”).
85. See, e.g., Kathryn A. Seely et al., *supra* note 78 (“Long-term heavy cannabis use has also been associated with reduced brain volume, where the hippocampus and the amygdala are the cerebral regions significantly changed, roughly –12% and –7% respectively.... The hippocampus and the amygdala are brain regions involved, respectively, in memory and the pathophysiology of schizophrenia...and emotion processing.... Interestingly, long-term Spice users often experience psychotic episodes as well as irritability and anxiety....”) (citations omitted).
86. *Id.*
87. *Id.* (“The pace at which quasi-legal synthetic cannabinoids are being produced is unprecedented. Since about 2004, products marketed under brand names like K2 or Spice are continually being reformulated with pharmacologically active cannabinoids that avoid regulation and detection in standardized drug tests.”).
88. *Id.* at 197.
89. Angela Bertorelli & Marc Siegel, *Marijuana with High THC Levels Linked to Addiction, Psychiatric Illness, Study Finds*, Fox News, Aug. 30, 2022, <https://www.foxnews.com/health/marijuana-high-thc-levels-linked-addiction-psychiatric-illness-study-finds>.
90. See, e.g., NAT’L ACAD. REPORT, *supra* note 3, at 15; NAT’L INST. ON DRUG ABUSE, RESEARCH REPORT: CANNABIS (MARIJUANA) RESEARCH REPORT 15 (Rev. July 2020) (“Several studies have linked marijuana use to increased risk for psychiatric disorders, including psychosis (schizophrenia), depression, anxiety, and substance use disorders, but whether and to what extent it actually causes these conditions is not always easy to determine. Recent research suggests that smoking high-potency marijuana every day could increase the chances of developing psychosis by nearly five times compared to people who have never used marijuana. The amount of drug used, the age at first use, and genetic vulnerability have all been shown to influence this relationship. The strongest evidence to date concerns links between marijuana use and psychiatric disorders in those with a preexisting genetic or other vulnerability.”) (endnotes omitted); Brooke J. Arterberry et al., *Higher Average Potency Across the United States Is Associated with Progression to First Cannabis Use Disorder Symptom*, 195 DRUG & ALCOHOL DEPENDENCE 186, 189 (2019); Marcel O. Bonn-Miller et al., *Prevalence of Cannabis Use Disorder Diagnoses Among Veterans in 2002, 2008, and 2009*, 9 PSYCHOLOGICAL SERVS. 404 (2012); Marta Di Forti et al., *The Contribution of Cannabis Use to Variation in the Frequency of Psychotic Disorder Across Europe (EU-GEI): A Multicentre Case-Control Study*, 6 LANCET PSYCHIATRY 427 (2019); Marta Di Forte et al., *Proportion of Patients in South London with First-Episode Psychosis Attributable to Use of High Potency Cannabis: A Case-Control Study*, 2 LANCET PSYCHIATRY 233 (2015); Kirsten H. Dillon et al., *Cannabis Use Disorder, Anger, and Violence in Iraq/Afghanistan-era Veterans*, 138 J. PSYCHIATRIC RESEARCH 375 (2021); Julianne C. Flanagan et al., *Association of Cannabis Use with Intimate Partner Violence Among Couples with Substance Misuse*, 29 AM. J. ADDICTION 323 (2020); Suzanne H. Gage et al.,

Association Between Cannabis and Psychosis: Epidemiologic Evidence, 79 *BIOLOGICAL PSYCHIATRY* 549 (2016); Shea-Lee Godin & Sherif Shehata, *Adolescent Cannabis Use and Later Development of Schizophrenia: An Updated Systematic Review of Longitudinal Studies*, 78 *J. CLIN. PSYCHOLOGY* 1331, 1337, 1338 (2022); Wayne Hall & Louisa Degenhardt, Editorial, *High Potency Cannabis: A Risk Factor for Dependence, Poor Psychosocial Outcomes, and Psychosis*, 350 *BMJ* 1205 (2015); Wayne Hall et al., *Cannabis Use and Psychotic Disorders: An Update*, 23 *DRUG & ALCOHOL REV.* 433 (2004); Carsten Hjorthoj et al., *Development Over Time of the Population-Attributable Risk Fraction for Cannabis Use Disorder in Schizophrenia in Denmark*, 78 *JAMA PSYCHIATRY* 1013, 1023 (2021); Carsten Hjorthoj & Christine Merrild Posselt, *Δ-9-Tetrahydrocannabinol Harmful Even in Low Doses?*, 7 *LANCET PSYCHIATRY* 296 (2020); Arianna Marconi et al., *Meta-Analysis of the Association Between the Level of Cannabis Use and Risk of Psychosis*, 42 *SCHIZOPHRENIA BULL.* 1262, 1265 (2016); Theresa H.M. Moore et al., *Cannabis Use and Risk of Psychotic or Affective Mental Health Outcomes: A Systematic Review*, 370 *LANCET* 319, 325–27 (2007); Murray et al., *supra* note 63; Maria Bettina Ortiz-Medina et al., *Cannabis Consumption and Psychosis of Schizophrenia Development*, 64 *INT'L J. SOC. PSYCHIATRY* 690 (2018); Kat Petrilli et al., *Association of Cannabis Potency with Mental Health and Addiction*, 9 *LANCET PSYCHIATRY* P736 (2022).

91. See, e.g., WORLD HEALTH ORG., *THE HEALTH AND SOCIAL EFFECTS OF NONMEDICAL CANNABIS USE* 16 (2016) (“Accumulating evidence reveals that regular, heavy cannabis use during adolescence is associated with more severe and persistent negative outcomes than use during adulthood.”); GEORGE F. KOOB ET AL., *DRUGS, ADDICTION, AND THE BRAIN* 269, 279–87 (2014); ROOM ET AL., *supra* note 66, at 31–39 (describing studies investigating the risk that adolescent marijuana use could adversely affect learning, result in a greater dropout rate, be a prelude to other drug use, or lead to schizophrenia or depression); Bertha Madras, *Drug Use and Its Consequences*, in *THE EFFECTS OF DRUG ABUSE ON THE HUMAN NERVOUS SYSTEM* 14–15 (Bertha Madras & Michael Kuhar eds., 2014); Madeline H. Meier et al., *Cannabis Concentrate Use in Adolescents*, 144 *PEDIATRICS* e20190338, at 9 (2019); Volkow et al., *supra* note 16, at 2220 (noting that negative effects in brain development, educational outcome, cognitive impairment, and life satisfaction are “strongly associated with initial marijuana use early in adolescence”); Jack Wilson et al., *Effects of Increasing Cannabis Potency on Adolescent Health*, 3 *LANCET: CHILD ADOLESCENT HEALTH* 121, 123 (2019); George Sam Wang, *Impact of Cannabis Legalization on Healthcare Utilization for Psychosis and Schizophrenia in Colorado*, 104 *INT'L J. DRUG POL'Y* 103685, 103685 (2022) (“There was a positive association between the number of cannabis dispensaries and rates of psychosis ED visits across all counties in Colorado. Although it is unclear whether it is access to products, or the types of products that may be driving this association, our findings suggest there is a potential impact on the mental health of the local population that is observed after cannabis legalization.”); Leighton Woodhouse, *San Diego ER Seeing Up to 37 Marijuana Cases a Day—Mostly Psychosis*, *N.Y. POST*, Oct. 22, 2022, https://nypost.com/2022/10/22/san-diego-er-seeing-up-to-37-marijuana-cases-a-day/?utm_source=email_sitebuttons&utm_medium=site%20buttons&utm_campaign=site%20buttons (“‘We’re now counting 37 cannabis-related diagnoses a day,’ Dr. Roneet Lev, an addiction medicine doctor at Scripps Mercy Hospital in San Diego, said about her emergency department. ‘It’s been steadily increasing over the years. When I started in the 1990s, there was no such thing. Now I see 1 to 2 cases per shift. The most common symptom is psychosis.’ [¶] ‘We probably see 20 THC-induced psychoses for every amphetamine-induced psychosis,’ said Ben Cort, who runs a drug and alcohol treatment center in Colorado. One study showed an increase of 24% in cases of psychoses in emergency departments in Colorado in the five years following marijuana’s legalization in that state in 2012.”). See generally Larkin, *Cannabis Capitalism*, *supra* note 54, at 144 & n.120 (collecting authorities); Larkin, *Gummy Bears*, *supra* note 44, at 335–38 (“Several respected government and private organizations—the American Medical Association, the American Psychiatric Association, the American Academy of Pediatrics, the American Cancer Society, the American Academy of Ophthalmology, the National Institute for Drug Abuse, and others—have noted those harms and agree that minors should not use cannabis.”) (endnote omitted).