REGULATING THE PSYCHEDELIC RENAISSANCE: FDA'S CRITICAL ROLE IN THE PUSH FOR SCHEDULING REFORM TO EXPAND RESEARCH INTO PSYCHEDELIC MEDICINES

SAUMYA SINHA*

* J.D. Candidate, American University Washington College of Law (2025); B.S. Psychology, University of Washington (2020). I would like to thank my incredible friends for being an endless source of support, encouragement, and inspiration. Additionally, I would like to thank the staff of the *Administrative Law Review*, especially Elena Pomponio, Brooks Marquette, Emilee Daniel, and Mehraz Rahman, for their invaluable feedback and assistance throughout the writing and publication process. Lastly, I would like to dedicate this Comment to my parents, my brother, and Nate for their unwavering love and support—none of this would be possible without you all.

INTRODUCTION

Though Indigenous communities have used psychedelics in a medicinal capacity for centuries,[1] their use in the United States has remained largely illegal since the 1970s as a result of the War on Drugs.[2] In recent years, however, the broader sociocultural and governmental attitudes toward psychedelics have started to shift, leading to a greater push for legislative and regulatory reform—a phenomenon described as the psychedelic renaissance.[3] The resurgence of interest in psychedelics has spread to the scientific world, with several clinical trials being conducted to study the effectiveness of psychedelics in treating mental illnesses.[4] Evidence from these trials indicates that psychedelics hold strong therapeutic potential to treat a wide range of mental health disorders, including some disorders that resist other forms of treatment.[5] Findings from these studies show few, if any, serious adverse effects when these medicines are taken under proper supervision and at

1. *Magic Mushrooms as Medicine*, ALCOHOL & DRUG FOUND. (Mar. 7, 2023), https://adf.org.au/insights/magic-mushrooms-medicine/ ("Psilocybin has been . . . used by some Indigenous communities around the world for over 1[,]000 years.").

2. Rachel Yehuda & Amy Lehrner, *Psychedelic Therapy—A New Paradigm of Care for Mental Health*, 330 JAMA 813, 813 (2023) (explaining the impact of the War on Drugs on psychedelic research and stating that most psychedelic compounds are illegal under federal law).

3. *See* Danielle Schlosser & Thomas R. Insel, *A Renaissance for Psychedelics Could Fill a Long-Standing Treatment Gap for Psychiatric Disorders*, SCI. AM. (Sept. 14, 2021), https://www.scientificamerican.com/article/a-renaissance-for-psychedelics-could-fill-a-long-standing-treatment-gap-for-psychiatric-disorders/ (discussing how the "use of psychedelics, especially psilocybin and MDMA . . . is undergoing a renaissance.").

4. *See* Alan K. Davis, Frederick S. Barrett, Darrick G. May, Mary P. Cosimano, Nathan D. Sepeda, Matthew W. Johnson, et al., *Effects of Psilocybin-Assisted Therapy on Major Depressive Disorder*, 78 JAMA PSYCHIATRY 481, 481 (2021); Nicole L. Galvão-Coelho, Wolfgang Marx, Maria Gonzalez, Justin Sinclair, Michael de Manincor, Daniel Perkins, et al., *Classic Serotonergic Psychedelics for Mood and Depressive Symptoms: A Meta-Analysis of Mood Disorder Patients and Healthy Participants*, 238 PSYCHOPHARMACOLOGY 341, 341 (2021).

5. *See* Reid Robison, *Psychedelics and the Future of Psychiatry*, PSYCHIATRIC TIMES, Feb. 2022, at 1, 6–7 (discussing the growing use of psychedelic medicines to treat mental health disorders).

the recommended dosage.[6]

Several psychedelic compounds—including psilocybin; 3, 4-methylenedioxy-methamphetamine (MDMA); and lysergic acid diethylamide (LSD)—are currently moving through U.S. Food and Drug Administration's (FDA's) clinical trial process as treatments for major depressive disorder (MDD),[7] post-traumatic stress disorder (PTSD),[8] treatment-resistant depression (TRD),[9] and generalized anxiety disorder (GAD).[10] At a time when the mental health crisis in the United States is worsening, access to these beneficial treatments is crucial.[11]

However, despite growing clinical evidence showing the benefits of psychedelics, one of the biggest regulatory hurdles surrounding psychedelic research remains: U.S. Drug Enforcement Agency's (DEA's) scheduling of these substances under the Controlled Substances Act (CSA). DEA currently classifies most psychedelics under Schedule I, which is the most restricted category under the CSA.[12] DEA considers Schedule I substances to have a "high potential for abuse" and "no currently accepted medical use"; thus, these substances are "only legal to produce, dispense, [or] possess . . . in the context of federally approved scientific studies."[13] Schedule I classification

---

6. *See id.*; *see also* Mason Marks & I. Glenn Cohen, *How Should the FDA Evaluate Psychedelic Medicine?*, 389 NEW ENG. J. MED. 1733, 1734 (2023) [hereinafter Marks & Cohen, *FDA Evaluation of Psychedelics?*]; David E. Nichols, *Psychedelics*, 68 PHARMACOLOGICAL REVS. 264, 275 (2016) ("They do not cause addiction, and no overdose deaths have occurred after ingestion of typical doses of LSD, psilocybin, or mescaline.").

7. *A Study of Psilocybin for Major Depressive Disorder (MDD)*, NAT'L LIBR. OF MED. (June 5, 2023), https://clinicaltrials.gov/study/NCT03866174.

8. *A Multi-Site Phase 3 Study of MDMA-Assisted Psychotherapy for PTSD (MAPP2)*, NAT'L LIBR. OF MED. (Jan. 24, 2024), https://clinicaltrials.gov/study/NCT04077437 [hereinafter *Phase 3 Study of MDMA-Assisted Psychotherapy for PTSD*].

9. *The Safety and Efficacy of Psilocybin in Participants with Treatment Resistant Depression (P-TRD)*, NAT'L LIBR. OF MED. (Apr. 24, 2023), https://clinicaltrials.gov/study/NCT03775200.

10. *A Dose-Finding Study of MM-120 (LSD D-Tartrate) for the Treatment of Anxiety Symptoms*, NAT'L LIBR. OF MED. (Dec. 20, 2023), https://clinicaltrials.gov/study/NCT05407064.

11. *See Mental Illness*, NAT'L INST. OF MENTAL HEALTH, https://www.nimh.nih.gov/health/statistics/mental-illness.shtml (last visited May 29, 2024) (stating that one in every five Americans suffer from a mental illness); Hoag Levins, *Worsening Faster Than It's Improving: The U.S. Mental Health Care Delivery System*, LEONARD DAVIS INST. OF HEALTH ECONS. (Sept. 29, 2022), https://ldi.upenn.edu/our-work/research-updates/worsening-faster-than-its-improving-the-us-mental-health-care-delivery-system/.

12. *See* Controlled Substances Act, 21 U.S.C. § 812(c).

13. *See* § 812(b)(1); JOANNA R. LAMPE, CONG. RSCH. SERV., R45948, THE CONTROLLED SUBSTANCES ACT (CSA): A LEGAL OVERVIEW FOR THE 118TH CONGRESS 8 (2023).

creates several barriers to research and limits access to effective treatments.[14]

Given the growing mental health crisis in the United States, a recent push for DEA to reconsider its current scheduling regimes has emerged.[15] The safest way to bring about scheduling reform is through agency action based on an analysis of clinical and scientific data.[16] FDA is the sole agency with the power to effectively bring about such reform for two reasons: (1) FDA has the ability to initiate DEA's administrative pathway for rescheduling, and (2) FDA is tasked with performing a scientific evaluation of the substances being considered for rescheduling under this pathway.[17] Based on its scientific evaluation, FDA can effectuate scheduling reform for psychedelic medicines through two avenues: (1) a recommendation to U.S. Department of Health and Human Services (HHS) to petition DEA to initiate rescheduling proceedings,[18] and (2) the approval of psychedelics that complete FDA's clinical trial process.[19]

This Comment focuses on two psychedelics on the path to FDA approval: MDMA and psilocybin. Part I of this Comment discusses the history of psychedelics, explores the use of psychedelics as treatment for mental illness, and explains the recent push for psychedelic reform. Part II lays out the current regulatory framework surrounding psychedelic research, including the role of DEA and FDA in drug regulation. Part III explains the two administrative avenues for scheduling reform. Part IV analyzes the different issues that arise under the current regulatory framework. Finally, Part V recommends that FDA utilize its administrative authority to initiate scheduling reform for MDMA and psilocybin in an effort to expand research into these substances. Additionally, Part V urges FDA to provide guidance for state licensing boards in order to ensure uniformity in the regulation of these psychedelics upon rescheduling.

---

14. *See* Mason Marks & Carmel Shachar, *Drug Scheduling Limits Access to Essential Medicines and Should be Reformed*, 29 NATURE MED. 294, 296 (2023) (stating that the complex regulatory framework for Schedule I substances "privileges patentable and potentially expensive synthetic substances over inexpensive naturally occurring generics while limiting the scope of research and who can conduct that research.").

15. *See* NAT'L INST. OF MENTAL HEALTH, *supra* note 11.

16. *See infra* text accompanying notes 172–177.

17. *See infra* Part III (explaining FDA's ability to bring about scheduling reform under the CSA).

18. *See infra* Part III.A *(*describing the petition to initiate rescheduling pathway).

19. *See infra* Part III.B (laying out the framework for the FDA approval pathway to rescheduling).

I. BACKGROUND

A. The History of Psychedelics

The term psychedelic was coined in 1956 by psychiatrist Humphry Osmond to describe psychoactive drugs like LSD and psilocybin that "produce radical changes in consciousness."[20] FDA has used the term psychedelics as shorthand to include classic psychedelics such as psilocybin and LSD, as well as entactogens such as MDMA.[21] Classic psychedelics refer to a class of drugs that act as agonists of serotonin 5-hydroxytryptamine 2A (5-HT2A) receptors.[22] This type of agonist mimics the neurotransmitter serotonin by binding to and activating its receptors to produce a similar biological response.[23] As a result of their mechanism of action, these substances have "rapid and profound effects on perception, cognition, and consciousness."[24] Entactogens refer to a class of drugs that primarily stimulate the release of serotonin and produce effects on "self-perception, social interaction, and fear memory."[25] Though entactogens produce responses similar to classic psychedelics, they generally lack hallucinogenic effects.[26]

The history of psychedelics goes back to the centuries-long use of psychedelics by Indigenous communities.[27] In the Western world, however,

---

20. MICHAEL POLLAN, HOW TO CHANGE YOUR MIND: WHAT THE NEW SCIENCE OF PSYCHEDELICS TEACHES US ABOUT CONSCIOUSNESS, DYING, ADDICTION, DEPRESSION, AND TRANSCENDENCE 421 (2018); *Substances*, U.C. BERKELEY CTR. FOR THE SCI. OF PSYCHEDELICS, https://psychedelics.berkeley.edu/substances/ (last visited May 30, 2024) (stating that the term was derived from two Greek words—*psykhē* for "mind" and *dēloun* for "show"—the combination of which roughly translates to the phrase "mind manifesting").

21. CTR. FOR DRUG EVALUATION & RSCH., U.S. FOOD & DRUG ADMIN., 52950908DFT, PSYCHEDELIC DRUGS: CONSIDERATIONS FOR CLINICAL INVESTIGATIONS GUIDANCE FOR INDUSTRY 1 (2023).

22. Nichols, *supra* note 6, at 280 (explaining the mechanism of action for classic psychedelics).

23. *Id.*

24. Yehuda & Lehrner, *supra* note 2, at 813.

25. Boris D. Heifets & David E. Olson, *Therapeutic Mechanisms of Psychedelics and Entactogens*, 49 NEUROPSYCHOPHARMACOLOGY 104, 105 (2023).

26. Franz X. Vollenweider, *Brain Mechanisms of Hallucinogens and Entactogens*, 3 DIALOGUES IN CLINICAL NEUROSCIENCE 265, 266 (2001).

27. *See Psilocybin*, U.C. BERKELEY CTR. FOR THE SCI. OF PSYCHEDELICS, https://psychedelics.berkeley.edu/substance/psilocybin/ (last visited May 25, 2024) (discussing the use of psilocybin by Indigenous communities in Mexico); *Ayahuasca*, U.C. BERKELEY CTR. FOR THE SCI. OF PSYCHEDELICS, https://psychedelics.berkeley.edu/substance/ayahuasca/ (last visited July 13, 2024) (discussing the use of Ayahuasca by Indigenous communities to help with the "diagnosis or treatment of various medical, psychological, or spiritual conditions").

modern psychedelic research began when Swiss chemist Albert Hofmann accidentally discovered the effects of LSD in 1943[28] after first synthesizing LSD-25 in 1938.[29] Hofmann's discovery was followed by a brief period of unrestrained research into the therapeutic potential of psychedelics in the 1950s and 1960s.[30] However, as their use became more recreational, psychedelics quickly became associated with the counterculture—a social movement marked by opposition to the Vietnam War, rejection of traditional authority and societal norms, and resistance to consumerism.[31]

Given the anti-establishment nature of the counterculture movement, psychedelics became the target of governmental interventions across the globe.[32] In the United States, President Richard Nixon launched the War on Drugs to curb the cultural rebellion, "proclaim[ing] that drug use was America's 'public enemy number one.'"[33] Consequently, Congress passed the CSA in 1970, which categorized most psychedelics as Schedule I substances[34] and made psychedelic research nearly impossible for the next several decades.[35] Scientists' inability to conduct further research on psychedelics left many questions about their therapeutic potential unanswered.[36]

---

28. Nichols, *supra* note 6, at 344.

29. Richard E. Doblin, Merete Christiansen, Lisa Jerome & Brad Burge, *The Past and Future of Psychedelic Science: An Introduction to This Issue*, 51 J. PSYCHOACTIVE DRUGS 93, 93 (2019).

30. *See* Nichols, *supra* note 6, at 267 ("Between 1950 and the mid-1960s there were more than a thousand clinical papers discussing 40,000 patients, several dozen books, and six international conferences on psychedelic drug therapy."); Doblin et al., *supra* note 29.

31. *See 1960s Counterculture*, ENCYC. BRITANNICA (May 8, 2024), https://www.britannica.com/topic/1960s-counterculture/additional-info#history; Nichols, *supra* note 6, at 267 (stating that, in the United States, drug use was viewed as the cause for the rise in "[a]ntiwar attitudes and rejection of conventional social norms" by young adults).

32. Nichols, *supra* note 6, at 267; Mason Marks, *Psychedelic Medicine for Mental Illness and Substance Use Disorders: Overcoming Social and Legal Obstacles*, 21 N.Y.U. J. LEGIS. & PUB. POL'Y 69, 89 (2018) [hereinafter Marks, *Psychedelic Medicine for Mental Illness*].

33. Marks, *Psychedelic Medicine for Mental Illness*, *supra* note 32.

34. Controlled Substances Act, 21 U.S.C. §§ 801, 812(c).

35. Nichols, *supra* note 6, at 267 ("[T]he relative dearth of research on psychedelics in the past half century did not result from a lack of scientific interest, but rather occurred as a consequence of political forces that manifested principally in the United States in the 1960s and 1970s . . . .").

36. *Id.*

B. Psychedelics as Treatment for Mental Illness

Psychedelic compounds have emerged as promising treatments for several mental illnesses, including PTSD, TRD, MDD, and GAD.[37] Psychedelics benefit those suffering from mental health disorders by helping facilitate neuroplasticity at the cellular level, thereby allowing the brain to rebuild critical neural "pathways lost to mental health disorders."[38] Increased neuroplasticity impacts crucial areas of cognitive function—such as decisionmaking and impulse control—and ultimately leads to an improvement in symptoms.[39] Psychedelics impact several key brain regions, including the prefrontal cortex, hippocampus, and amygdala.[40] For example, brain imaging of psychedelic study participants shows changes to the amygdala, including "attenuation of amygdala reactivity," which is "significantly correlated with increase of positive mood."[41]

Recognizing the benefits of psychedelics, FDA has granted breakthrough therapy designation (BTD) to manufacturer-specific formulations of two psychedelics—psilocybin[42] and MDMA.[43] BTD is granted to expedite developing and reviewing drugs intended to treat a serious condition when "preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s)."[44]

---

37. *See* Mason Marks & I. Glenn Cohen, *Psychedelic Therapy: A Roadmap for Wider Acceptance and Utilization*, 27 NATURE MED. 1,669, 1,669–70 (2021) [hereinafter Marks & Cohen, *Psychedelic Therapy*].

38. Debra Melani, *This Is Your Brain on Mushrooms: How Does Psychedelic-Assisted Therapy Work*, UNIV. OF COLO. ANSCHUTZ MED. CAMPUS (Aug. 15, 2022), https://news.cuanschutz.edu/news-stories/this-is-your-brain-on-drugs-how-does-psychedelic-assisted-therapy-work.

39. *See id.*

40. *See* Nichols, *supra* note 6, at 281, 305.

41. *See* Nichols, *supra* note 6, at 327.

42. *COMPASS Pathways Receives FDA Breakthrough Therapy Designation for Psilocybin Therapy for Treatment-Resistant Depression*, COMPASS PATHWAYS (Oct. 23, 2018), https://compasspathways.com/compass-pathways-receives-fda-breakthrough-therapy-designation-for-psilocybin-therapy-for-treatment-resistant-depression.

43. MULTIDISCIPLINARY ASSOCIATION FOR PSYCHEDELIC STUDIES (MAPS), FDA Grants Breakthrough Therapy Designation for MDMA-Assisted Therapy for PTSD (Aug. 26, 2017), https://maps.org/news/media/6786-press-release-fda-grants-breakthrough-therapy-designation-for-mdma-assisted-psychotherapy-for-ptsd,-agrees-on-special-protocol-assessment-for-phase-3-trial.

44. *Breakthrough Therapy*, FOOD & DRUG ADMIN. (Jan. 4, 2018), https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/breakthrough-therapy.

As a result of the BTD, COMPASS Pathways' COMP360—a patented, synthetic psilocybin formula designed to address TRD—is currently in Phase III of FDA's clinical trial process.[45] Similarly, the Multidisciplinary Association on Psychedelic Studies (MAPS) has completed two Phase III trials investigating MDMA-assisted psychotherapy as a treatment for PTSD.[46] On December 12, 2023, the MAPS Public Benefit Corporation (MAPS PBC), a wholly owned subsidiary of MAPS, filed a New Drug Application (NDA) with FDA for MDMA capsules used in combination with psychotherapy—also known as MDMA-assisted therapy—for the treatment of PTSD.[47] On February 9, 2024, Lykos Therapeutics (Lykos) (formerly MAPS PBC) announced that FDA had accepted the NDA, granted priority review, and assigned a target action date of August 11, 2024.[48] Psilocybin and MDMA are predicted to receive FDA approval by 2025.[49] However, Lykos' path to approval has not been without challenges.[50]

As part of the NDA review process, FDA's Psychopharmacologic Drugs Advisory Committee (PDAC) met on June 4, 2024, to discuss Lykos' NDA, the drug product's risk-benefit profile, and the potential public health

45. *Efficacy, Safety, and Tolerability of COMP360 in Participants With TRD*, NAT'L LIBR. OF MED. (March 21, 2024), https://clinicaltrials.gov/study/NCT05624268.

46. *Phase 3 Study of MDMA-Assisted Psychotherapy for PTSD*, *supra* note 8; Jennifer M. Mitchell, Michael Bogenschutz, Alia Lilienstein, Charlotte Harrison, Sarah Kleiman, Kelly Parker-Guilbert, et al., *MDMA-Assisted Therapy for Severe PTSD: A Randomized, Double-Blind, Placebo-Controlled Phase 3 Study*, 27 NATURE MED. 1,025, 1,026 (2021).

47. *MAPS PBC Announces Submission of New Drug Application to the FDA for MDMA-Assisted Therapy for PTSD*, PR NEWSWIRE (Dec. 12, 2023), https://www.prnewswire.com/news-releases/maps-pbc-announces-submission-of-new-drug-application-to-the-fda-for-mdma-assisted-therapy-for-ptsd-302011980.html.

48. *Lykos Therapeutics Announces FDA Acceptance and Priority Review of New Drug Application for MDMA-Assisted Therapy for PTSD*, LYKOS THERAPEUTICS (Feb. 9, 2024), https://news.lykospbc.com/2024-02-09-Lykos-Therapeutics-Announces-FDA-Acceptance-and-Priority-Review-of-New-Drug-Application-for-MDMA-Assisted-Therapy-for-PTSD.

49. Mattha Busby, *Biden Administration Plans for Legal Psychedelic Therapies Within Two Years*, INTERCEPT (July 26, 2022), https://theintercept.com/2022/07/26/mdma-psilocybin-fda-ptsd (discussing a letter sent by the Assistant Secretary for Mental Health and Substance Use—on behalf of the Secretary of Department for Health and Human Services (HHS)—acknowledging the anticipated approval of MDMA and psilocybin by FDA within two years).

50. *See* Jane C. Hu, *Breaking News: F.D.A. Panel Votes Against MDMA-Assisted Therapy for PTSD*, MICRODOSE (June 5, 2024), https://open.substack.com/pub/themicrodose/p/breaking-news-fda-panel-votes-against?utm_campaign=post&utm_medium=web [hereinafter Hu, *F.D.A. Panel Votes Against MDMA-Assisted Therapy for PTSD*].

impact.[51] The PDAC panel recommended against approval of Lykos' MDMA product.[52] Notably, though, the recommendation was not binding on FDA.[53] At that point, FDA had the option to either (1) ignore the recommendation and approve the MDMA product[54] or (2) issue a complete

---

51. *See* Psychopharmacologic Drugs Advisory Committee (PDAC); Notice of Meeting; Establishment of a Public Docket; Request for Comments - Midomafetamine Capsules, 89 Fed. Reg 38,903, 38,903–04 (May 8, 2024). The PDAC panel was comprised of eleven independent experts who were tasked with voting on two questions regarding Lykos Therapeutic' (Lykos') NDA after reviewing the data presented to them by FDA, hearing public comments, and hearing from Lykos representatives. John J. Miller, *Medication-Assisted Psychotherapy: Moving Forward*, PSYCHIATRIC TIMES, July 5, 2024, at 9, 9.

52. *See* Food & Drug Admin., *June 4, 2024 Meeting of the Psychopharmacologic Drugs Advisory Committee (PDAC)*, YOUTUBE (June 4, 2024), https://www.youtube.com/live/JqQKP8gcY1E. In a 9–2 vote, the PDAC panel found that the data presented in Lykos' NDA was insufficient to show that proposed intervention—MDMA–assisted therapy (MDMA–AT)—is effective in patients with PTSD. *See id.*; *Live Coverage: FDA Advisory Committee Reviews MDMA-Assisted Therapy for PTSD*, PSYCHEDELIC ALPHA (June 4, 2024), https://psychedelicalpha.com/news/live-coverage-fda-advisory-committee-reviews-mdma-assisted-therapy-for-ptsd. Additionally, in a 10–1 vote, the PDAC panel found that MDMA–AT's benefits do not outweigh the risks for the treatment of PTSD when administered within the context of FDA's proposed risk evaluation and mitigation strategy (REMS). *See June 4, 2024 Meeting*, *supra*; *Live Coverage: FDA Advisory Committee*, *supra*. A majority of the panel's concerns were rooted in Lykos' study design and data, including aspects such as the licensing of providers present in the room during the sessions, the unknown role of expectation bias, the functional unblinding of therapists, the inability to evaluate the relative contribution of psychotherapy, and the history of prior drug use among study participants. *Live Coverage: FDA Advisory Committee*, *supra*. One big concern that has come up repeatedly—both during the panel discussion and in discussions between Lykos and FDA during the trials—is the NDA's inclusion of Lykos' specific psychotherapy process as part of the treatment for which FDA approval is sought. Katie Macbride, *The FDA Might Reject MDMA Therapy—but Not for the Reasons You Think*, SLATE (June 13, 2024), https://slate.com/technology/2024/06/fda-panel-mdma-therapy-lykos-therapeutics-rejection.html. FDA does not regulate the therapeutic context, which currently makes up half of Lykos' treatment. *See id.* Moreover, Lykos is yet to provided data to show the relative contribution of psychotherapy to the drug's efficacy. *See id.* However, both of these issues can be remedied—the first through a reframing of the treatment to bring it more within FDA's regulatory purview and the second through further trials. *See id.*

53. *See* Hu, *F.D.A. Panel Votes Against MDMA-Assisted Therapy for PTSD*, *supra* note 50.

54. *See id.* In 2023, a qualitative study of 409 advisory committee meetings from 2010 to 2021 found that in situations where such committees recommended against approval, FDA followed the recommendation 67% of the time. *See* C. Joseph Ross Daval, Theodore W. Teng, Massimiliano Russo, & Aaron S. Kesselheim, *Association of Advisory Committee Votes with US Food and Drug Administration Decision-Making on Prescription Drugs, 2010-2021*, JAMA HEALTH FORUM (July 7, 2023), https://jamanetwork.com/journals/jama-health-forum/fullarticle/2807050. For example, in 2021, FDA approved the Alzheimer's drug Aduhelm after the

response letter (CRL) and allow Lykos to perform more trials.[55] Based on the issues raised by the PDAC panel, researchers in the field believed that FDA would most likely issue a CRL requiring Lykos to amend the deficiencies in its NDA by conducting another clinical trial prior to approval.[56] As predicted by these researchers, Lykos announced on August 9, 2024, that FDA had issued a CRL requesting that Lykos conduct an additional Phase 3 trial.[57] Moving forward, Lykos intends to meet with FDA officials to seek "reconsideration of the decision and to further discuss the agency's recommendations for a resubmission seeking regulatory approval for [MDMA] capsules."[58]

Scholars and researchers in the field do not view the challenges experienced by Lykos as the end of the road for FDA approval of MDMA.[59] Rather, they understand the decision to be grounded in the shortcomings of Lykos' study design and deficient application.[60] As a result, many researchers

---

Peripheral and Central Nervous System Drugs Advisory Committee voted against its approval in 2020. *See* Jane C. Hu, *MDMA's Next Step Towards FDA Approval: 5 Questions for FDA Advisory Committee Member Suzanne Robotti*, MICRODOSE (June 3, 2024), https://open.substack.com/pub/themicrodose/p/mdmas-next-step-towards-fda-approval?utm_campaign=post&utm_medium=web. [hereinafter Hu, *MDMA's next step towards FDA approval*].

55. 21 C.F.R. §§ 314.100(a), 314.110 (2023).

56. *See* Will Stone, *Trouble for Ecstasy? What MDMA's FDA Setback Could Mean for Psychedelics*, NPR (June 13, 2024), https://www.npr.org/sections/shots-health-news/2024/06/13/nx-s1-4998523/mdma-fda-maps-psychedelic-research [hereinafter Stone, *Trouble for Ecstasy?*].

57. *Lykos Therapeutics Announces Complete Response Letter for Midomafetamine Capsules for PTSD*, PR NEWSWIRE (Aug. 9, 2024), https://www.prnewswire.com/news-releases/lykos-therapeutics-announces-complete-response-letter-for-midomafetamine-capsules-for-ptsd-302219182.html [hereinafter *Lykos Therapeutics Announces CRL*].

58. *Id.*

59. *See FDA Rejects Lykos Therapeutics' MDMA-Assisted Therapy For PTSD*, PSYCHEDELIC ALPHA (Aug. 9, 2024), https://psychedelicalpha.com/news/breaking-fda-rejects-lykos-therapeutics-mdma-assisted-therapy-for-ptsd; Will Stone, *FDA gives thumbs down to MDMA for now, demanding further research*, NPR (Aug. 9, 2024), https://www.npr.org/sections/shots-health-news/2024/08/09/nx-s1-5068634/mdma-therapy-fda-decision-ptsd-psychedelic-treatment [hereinafter Stone, *FDA Gives Thumbs Down for Now*] (discussing early reactions of scholars and researchers in the field to FDA's issuance of the CRL).; Stone, *Trouble for Ecstasy?*, *supra* note 56 (listing the opinions of several scholars and researchers in the field surrounding the Advisory Committee's decision); Jane C. Hu, *The Psychedelics World Reacts after a FDA Advisory Committee Votes Against MDMA for PTSD*, MICRODOSE (June 14, 2024), https://open.substack.com/pub/themicrodose/p/the-psychedelics-world-reacts-to?r=2u9hbh&utm_campaign=post&utm_medium=web (covering the discourse within the community following the vote).

60. *See* Stone, *Trouble for Ecstasy?*, *supra* note 56 ("More than anything though, he

are focusing on the concerns raised by the PDAC panel as lessons to win FDA approval in the future.[61] In fact, scholars believe that Lykos' plight might ramp up competition and provide the impetus for other psychedelic drug manufacturers to take over the market.[62]

Currently, there are also other ongoing clinical trials testing the efficacy of MDMA and its derivatives as treatment for mental health disorders.[63] Two drug products in particular appear promising: atai Life Sciences' EMP-01[64] and MindMed's MM-402.[65] EMP-01 and MM-402 are both synthetic formulations of the R-enantiomer of MDMA.[66] MindMed and atai Life Sciences have both completed Phase I trials testing the safety and efficacy of their respective formulations in human subjects,[67] with atai reporting topline results for the pilot study.[68] Though these drug products are in much earlier

---

[Fredrick Barrett, Director of the Johns Hopkins Center for Psychedelic and Consciousness Research] says the troubles at the FDA are an indictment of how this drug maker, Lykos Therapeutics, ran the trials."); Macbride, *supra* note 52 (providing comments from several scholars in the field, including Professor Mason Marks, criticizing Lykos for failing to address some of the concerns raised by FDA with regards to study design).

61. *See* Stone, *Trouble for Ecstasy?*, *supra* note 56 (stating that, in one researcher's opinion, "certain concerns raised about the research can offer lessons for future efforts to win FDA approval.").

62. *See* Stone, *FDA Gives Thumbs Down for Now*, supra note 59 (quoting Professor Mason Marks, who states that "[i]f anything, [progress] might intensify because the other companies might see an opportunity to really get in there and compete.").

63. NAT'L CTR. FOR BIOTECHNOLOGY INFO., DEP'T OF HEALTH & HUM. SERVS., https://clinicaltrials.gov/ (begin typing "MDMA" in the box labeled "Intervention/treatment"; select "MDMA" when it appears; and click "Search") (last visited July 12, 2024).

64. *atai Life Sciences Announces Initiation of Phase 1 Trial for its MDMA Derivative EMP-01*, ATAI LIFE SCIS. (Sept. 27, 2022), https://atai.life/2022/09/27/atai-life-sciences-announces-initiation-of-phase-1-trial-for-its-mdma-derivative-emp-01/ [hereinafter *atai Life Sciences Initiation of Phase 1*].

65. *MindMed Collaborators Initiate Phase 1 Comparative PK/PD Trial of R-, S- and Racemic MDMA*, PR NEWSWIRE (Oct. 4, 2022), https://www.prnewswire.com/news-releases/mindmed-collaborators-initiate-phase-1-comparative-pkpd-trial-of-r--s--and-racemic-mdma-301639873.html; *Acute Effects of R- and S-MDMA in Healthy Subjects (R-S-MDMA)*, NAT'L LIBR. OF MED. (Jan. 17, 2024), https://clinicaltrials.gov/study/NCT05277636 [hereinafter *MindMend Collaborators Initiate Phase 1*].

66. *atai Life Sciences Announces Positive Topline Results from Single Ascending Dose Phase 1 Study with EMP-01 (R-MDMA)*, ATAI LIFE SCIS. (Jan. 22, 2024), https://atai.gcs-web.com/news-releases/news-release-details/atai-life-sciences-announces-positive-topline-results-single [hereinafter *atai Life Sciences Positive Topline*]; *MindMed Collaborators Initiate Phase 1*, *supra* note 65.

67. *Acute effects of R- and S-MDMA*, *supra* note 65; *atai Life Sciences Positive Topline*, *supra* note 66.

68. *atai Life Sciences Positive Topline Results*, *supra* note 66.

stages of the clinical trial process than the Lykos MDMA product, they present other avenues for FDA approval of MDMA.

C. The Psychedelic Renaissance—Recent Push for Psychedelic Reform

Due to growing evidence demonstrating the therapeutic benefits of psychedelics, there has been a recent push for psychedelic reform across different sectors.[69] Academic institutions have started to establish psychedelic research centers.[70] Though each center has unique programs, "they all study the potential health applications of psychedelics," train healthcare workers on methods of treatment, and promote public education about the benefits of psychedelics.[71]

On the legislative front, efforts to expand psychedelic research and make treatments accessible to vulnerable groups—including veterans—are underway.[72] On March 7, 2023, an updated version of the bipartisan Breakthrough Therapies Act was introduced by Senators Cory Booker (D-NJ) and Rand Paul (R-KY) in the Senate[73] and by Representatives Nancy Mace (R-SC) and Madeleine Dean (D-PA) in the House.[74] In November 2022, Congress also announced the bipartisan Psychedelics Advancing Clinical Treatments (PACT) Caucus to focus on exploring psychedelic research to alleviate

69. Ryan Basen, *Academic Centers Start to Take Psychedelics Seriously*, MEDPAGE TODAY (Nov. 24, 2021), https://www.medpagetoday.com/special-reports/exclusives/95865.

70. *See, e.g.*, *The Project on Psychedelics Law and Regulation (POPLAR)*, PETRIE-FLOM CTR. FOR HEALTH L. POL'Y, BIOTECHNOLOGY, & BIOETHICS AT HARV. L. SCH., https://petrieflom.law.harvard.edu/research/the-project-on-psychedelics-law-and-regulation-poplar (last visited May 25, 2024); *Mission and Vision*, U.C. BERKELEY CTR. FOR THE SCI. OF PSYCHEDELICS, https://psychedelics.berkeley.edu/mission-vision/ (last visited Jan. 26, 2024); JOHNS HOPKINS CTR. FOR PSYCHEDELIC & CONSCIOUSNESS RSCH., https://hopkinspsychedelic.org/ (last visited Apr. 30, 2024).

71. Basen, *supra* note 69.

72. Larry K. Houck, *A Long Strange Trip: Companion Bills Would Facilitate Psychedelics Research*, HYMAN, PHELPS & MCNAMARA P.C.: FDA L. BLOG (Apr. 11, 2023), https://www.thefdalawblog.com/2023/04/a-long-strange-trip-companion-bills-would-facilitate-psychedelics-research/.

73. *See* S.689, 118th Cong. (2023) (proposing to amend the CSA to allow DEA to reclassify drugs—including therapeutic psychedelics—that are granted breakthrough therapy designation (BTD) or expanded access authorization by FDA from Schedule I to Schedule II); *Members of the 118th Congress*, C-SPAN, https://www.c-span.org/congress/members/?chamber=senate&all (last visited July 12, 2024).

74. *See* H.R.1393, 118th Cong. (2023); *Members of the 118th Congress*, C-SPAN, https://www.c-span.org/congress/members/?chamber=house&all (last visited July 12, 2024).

the mental health crisis.[75]

Locally, states and cities are moving to either decriminalize psychedelics or reduce enforcement.[76] Voters in Oregon and Colorado have legalized certain psychedelics through ballot measures.[77] Similarly, Washington, D.C. and Oakland, CA have decriminalized certain psychedelics through ballot measures that make the enforcement of laws criminalizing psychedelics the lowest law enforcement priority.[78] The global attitude is likewise shifting, with Australia recently becoming the first country to legalize the prescription of psilocybin and MDMA for the treatment of TRD and PTSD in a controlled medical setting.[79]

The regulatory landscape surrounding psychedelics is similarly evolving. In June 2023, FDA released its first-ever Draft Guidance for psychedelic drugs titled "Psychedelic Drugs: Considerations for Clinical Investigations; Draft Guidance for Industry."[80] In 2022, following pushback from researchers, DEA withdrew its proposal to add five psychedelics to the Schedule I list.[81] Similarly, in recognition of the need to fulfill research and development

75. Press Release, Lou Correa, Member of the House of Representatives, Correa Launches Bipartisan Congressional Caucus to Explore Psychedelic Research for Mental Health (Nov. 17, 2022), https://correa.house.gov/news/press-releases/correa-launches-bipartisan-congressional-caucus-to-explore-psychedelic-research-for-mental-health.

76. *See* Joshua S. Siegel, James E. Daily, Demetrius A. Perry & Ginger E. Nicol, *Psychedelic Drug Legislative Reform and Legalization in the US*, 80 JAMA PSYCHIATRY 77, 77 (2022) (finding that, as of September 2022, "[t]wenty-five states ha[d] considered [seventy-four] [psychedelic reform] bills . . . ; [ten] bills were enacted, and [thirty-two] were still active").

77. *See* Chris Roberts, *Oregon Legalizes Psilocybin Mushrooms and Decriminalizes All Drugs*, FORBES (Nov. 4, 2020), https://www.forbes.com/sites/chrisroberts/2020/11/04/oregon-legalizes-psilocybin-mushrooms-and-decriminalizes-all-drugs; Tiney Ricciardi, *Colorado Voters Legalize Psilocybin and Psychedelic Therapy*, DENVER POST (Nov. 8, 2022), https://www.denverpost.com/2022/11/08/colorado-results-prop-122-legalizing-psilocybin-psilocin-mushrooms/.

78. *See* Karen Luong & Kimberly Chew, *Legal Developments in Psychedelic Therapeutics*, A.B.A.: HEALTH L. (June 27, 2022), https://www.americanbar.org/groups/health_law/publications/health_lawyer_home/june-2022/legal-developments-in-psychedelic-therapeutics/.

79. *See* Rich Haridy, *Australia Will Be First to Prescribe Psychedelic Drugs for PTSD and Depression*, 619 NATURE 227, 227–28 (2023), https://www.nature.com/articles/d41586-023-02093-8.

80. Psychedelic Drugs: Considerations for Clinical Investigations; Draft Guidance for Industry; Availability, 88 Fed. Reg. 41,407 (June 26, 2023); *see infra* text accompanying notes 155–159.

81. *See* Schedules of Controlled Substances: Placement of 4-hydroxy-N,Ndiisopropyltryptamine (4-OH-DiPT), 5- methoxy-alpha-methyltryptamine (5-MeO-AMT), 5-methoxy-N-methyl-Nisopropyltryptamine (5-MeO-MiPT), 5- methoxy-N,N-

requirements, DEA significantly increased the production quota of certain Schedule I psychedelics.[82]

The shift in the political and regulatory landscape has spurred massive private investment into psychedelic research.[83] There are now more than fifty publicly traded companies involved in the development of psychedelics—at least three of these are valued at over $1 billion.[84] The psychedelic market "is projected to grow from $2 billion in 2020 to $10.75 billion by 2027."[85]

II. REGULATORY FRAMEWORK FOR PSYCHEDELIC REGULATION

A. DEA Framework for Drug Regulation

DEA provides the main regulatory framework for the manufacture, distribution, and use of psychedelic substances through the scheduling of these substances under the CSA. DEA is a law enforcement agency under the U.S. Department of Justice (DOJ) established by an Executive Order from President Nixon in 1973.[86] DEA is charged with enforcing the CSA[87] through delegation from the Attorney General (AG)—the CSA grants the AG the authority to administer its provisions[88] and the AG delegates that authority

diethyltryptamine (5-MeO-DET), and N, Ndiisopropyltryptamine (DiPT) in Schedule I; Withdrawal of Proposed Rule and Notice of Hearing, 87 Fed. Reg. 45,076 (July 27, 2022); Michael Borchard, *DEA Withdraws Rule to Ban Five Psychedelics*, GRAPHITE (Jan. 17, 2023), https://graphite.ucsd.edu/news/2023/01/1832/ (discussing the backlash that led to DEA's withdrawal of its proposed rule). For an example of the arguments raised by researchers challenging the proposed rule during the notice-and-comment process, *see* Matthew W. Johnson, Comment Letter on Proposed Rule to Place 4-Hydroxy-N,N-diisopropyltryptamine (4-OH-DiPT) in Schedule I (Feb. 20, 2022), https://downloads.regulations.gov/DEA-2022-0001-0144/attachment_1.pdf.

82. *Compare* Established Aggregate Production Quotas for Schedule I and II Controlled Substances for 2022, 86 Fed. Reg. 68,513, 68,519–22 (Dec. 2, 2021) (listing the established production quotas of several psychedelics for 2022), *with* Established Aggregate Production Quotas for Schedule I and II Controlled Substances for 2023, 87 Fed. Reg. 74,168, 74,171–74 (Dec. 2, 2022) (increasing the production quota of several psychedelics, such as Dimethyltryptamine (DMT), MDMA, LSD, psilocyn, and other drugs for 2023).

83. *See* Marks & Shachar, *supra* note 14.

84. Joshua Phelps, Ravi N. Shah & Jeffrey A. Lieberman, *The Rapid Rise in Investment in Psychedelics—Cart Before the Horse*, 79 JAMA PSYCHIATRY 189, 189 (2022).

85. *Id.*

86. Exec. Order No. 11,727, 38 Fed. Reg. 18,357, 18,357–58 (July 6, 1973).

87. Controlled Substances Act, 21 U.S.C. §§ 801–971.

88. *See id.* at §§ 811(a), 871(a)–(b).

to the Administrator of DEA.[89]

The CSA establishes the federal policy for the regulation of controlled substances.[90] Specifically, it regulates drugs and substances that are "found to pose a risk of abuse and dependence."[91] Under the CSA, substances are placed into one of five schedules based on the substance's accepted medical uses, potential for abuse, and safety or dependence liability.[92] The schedule "determines the level of restriction imposed on [the] production, distribution, and possession" of the substance, as well as the penalties imposed on any "improper handling."[93] In addition to applying to the listed substances, the CSA restrictions also apply to analogs of controlled substances and certain precursor chemicals commonly used to manufacture controlled substances.[94]

Schedule I substances are considered to 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 . . . under medical supervision."[95] Examples include heroin, LSD, MDMA, and psilocybin.[96] Schedule II substances are considered to have a "high potential for abuse," and a "currently accepted medical use in treatment . . . or a currently accepted medical use with severe restrictions."[97] Abuse may lead to "severe psychological or physical dependence."[98] Examples include cocaine, methamphetamine, fentanyl, and prescription amphetamines, such as Adderall.[99] Schedule III substances are considered to have a "potential for abuse less than the drugs . . . in [S]chedules I and II" and a "currently accepted medical use in treatment," with abuse leading to "moderate or low physical dependence or high psychological dependence."[100] Examples include testosterone, ketamine, Marinol

89. *See* 28 C.F.R. § 0.100(a)–(b) (2023).

90. Nicole R. Ortiz & Charles V. Preuss, *Controlled Substance Act*, NAT'L CTR. FOR BIOTECHNOLOGY INFO. (Mar. 23, 2023), https://www.ncbi.nlm.nih.gov/books/NBK574544/.

91. LAMPE, *supra* note 13, at 2.

92. *See* 21 U.S.C. § 812(b).

93. LAMPE, *supra* note 13, at 6.

94. *Id.* at 8; *see also* 21 U.S.C. § 813 (discussing treatment of controlled substance analogues); 21 U.S.C. § 811(e) (discussing treatment of precursor chemicals).

95. 21 U.S.C. § 812(b)(1).

96. LAMPE, *supra* note 13, at 7; *see also* 21 C.F.R. § 1308.11 (2023) (containing the full list of Schedule I substances controlled under the CSA).

97. 21 U.S.C. § 812(b)(2)(A)–(B).

98. *Id.* § 812(b)(2)(C).

99. LAMPE, *supra* note 13, at 6, fig. 1 (listing examples).

100. 21 U.S.C. § 812(b)(3).

(an FDA-approved dronabinol product), and anabolic steroids.[101] Schedule IV substances are considered to have a "low potential for abuse relative to the drugs . . . in [S]chedule III" and a "currently accepted medical use in treatment."[102] Abuse "may lead to limited physical . . . or psychological dependence."[103] Examples include Xanax, Valium, and Ambien.[104] Lastly, substances with the lowest potential for abuse and physical or psychological dependence, and with current medical uses, are placed in Schedule V.[105] Examples include cough medicines with codeine and FDA-approved drugs containing cannabidiol (CBD).[106]

The most crucial difference in statutory language between Schedule I and Schedules II–V is that Schedule I substances have "no currently accepted medical use."[107] When enacting or amending the CSA, "Congress [has] never defined the phrase 'currently accepted medical use.'"[108] Instead, in its interpretation of the CSA, DEA has devised a conjunctive five-part test for a Schedule I substance to satisfy the "currently accepted medical use" standard.[109] The five necessary elements to satisfy the standard are that (1) the drug's chemistry is known and reproducible; (2) there are adequate safety studies; (3) there are adequate and well-controlled studies proving efficacy; (4) the drug is accepted by qualified experts; and (5) the scientific evidence is widely available.[110] In *Americans for Safe Access v. DEA*,[111] the D.C. Circuit Court ruled that to meet the accepted medical use standard, "the effectiveness of a drug must be established in well-controlled, well-designed, well-conducted, and well-documented scientific studies, including studies performed in a large number of patients."[112] The court indicated that evidence

101. LAMPE, *supra* note 13, at 6, fig. 1 (listing examples); *see also* 21 C.F.R. § 1308.13 (2023) (providing a full list of Schedule IV substances).

102. 21 U.S.C. § 812(b)(4)(A)–(B).

103. *Id.* § 812(b)(4)(C).

104. LAMPE, *supra* note 13, at 6, fig. 1 (listing examples).

105. *Id.* (citing 21 U.S.C. § 812(b)(5)).

106. *Id.*

107. 21 U.S.C. § 812(b)(1)(B).

108. Nabil Al-Khaled, Note, *MDMA and Psilocybin for Mental Health: Deconstructing the Controlled Substance Act's Usage of Currently Accepted Medical Use*, 99 WASH. U. L. REV. 1,023, 1,035 (2021).

109. *Id.*; *see infra* text accompanying notes 196–207 for a discussion of issues surrounding the test.

110. *See* Marijuana Scheduling Petition; Denial of Petition; Remand, 57 Fed. Reg. 10,499, 10,506 (Mar. 26, 1992) (discussing and applying the five factors to a petition to reschedule marijuana); Al-Khaled, *supra* note 108.

111. 706 F.3d 438 (D.C. Cir. 2013).

112. *Id.* at 450.

suggesting the substance's efficacy from Phase II and Phase III FDA clinical trials would meet the standard.[113] The *Americans for Safe Access* framework essentially encapsulates the last four steps of DEA's five-part test.[114] Notably, a drug product approved by FDA for marketing is considered to have a "currently accepted medical use."[115]

After determining that a substance has a "currently accepted medical use" such that it should not be in Schedule I, the determination for which schedule the substance should be placed in is based on the CSA's eight-factor analysis (8-FA), which must be conducted by both DEA and HHS in the rescheduling context.[116] The factors considered include (1) the substance's "actual or relative potential for abuse"; (2) the "[s]cientific evidence of [the substance's] pharmacological effect, if known"; (3) the "state of current scientific knowledge regarding the . . . substance"; (4) "history and current pattern of abuse"; (5) the "scope, duration, and significance of abuse"; (6) "[w]hat, if any, risk there is to the public health"; (7) the substance's "psychic or physiological dependence liability"; and (8) "[w]hether the substance is an immediate precursor" of a controlled substance.[117]

To determine the first CSA factor within the 8-FA, preclinical and clinical data regarding the abuse potential of the substance, including its reinforcing effects, are considered.[118] The second factor involves an evaluation of the substance's various physiological and psychological effects.[119] Similarly, the third factor examines research into the chemistry and medical uses of the substance.[120] The analysis for this factor is almost identical to the "currently accepted medical use" factor listed in § 812 of the CSA, which is satisfied once FDA approves a drug.[121] The fourth, fifth, and sixth factors address the

113. *See id.* at 451.

114. *See id.* at 450.

115. Denial of Petition to Initiate Proceedings to Reschedule Marijuana, 81 Fed. Reg. 53,688, 53,714 (Aug. 12, 2016) ("One way to pass the five-part test for having 'currently accepted medical use' is through submission of an [New Drug Application (NDA)] or [Biologics License Application (BLA)] which is approved by FDA.").

116. *See* 21 U.S.C. § 811(c) (laying out the eight-factor analysis (8-FA) to determine scheduling).

117. *See id.*; Jack E. Henningfield, Marion A. Coe, Roland R. Griffiths, Sean J. Belouin, Ann Berger, Allison R. Coker, et al., *Psychedelic Drug Abuse Potential Assessment Research for New Drug Applications and Controlled Substances Act Scheduling*, 218 NEUROPHARMACOLOGY 3 (Nov. 1, 2022).

118. *See* Denial of Petition to Initiate Proceedings to Reschedule Marijuana, 81 Fed. Reg. 53,688, 53,690 (Aug. 12, 2016).

119. *See id.* at 53,692–93.

120. *See id.* at 53,698–53,701.

121. *See id.* at 53,700.

public health impact of the substance and involve an analysis of public health and epidemiological data.[122] In addressing these factors, both DEA and FDA typically rely on data from the National Survey on Drug Use and Health (NSDUH), the Monitoring the Future (MTF) survey, the Drug Abuse Warning Network (DAWN), and the Treatment Episode Data Set (TEDS).[123] The seventh factor discusses the psychological or physiological dependence liability of the substance, including tolerance and withdrawal.[124] Lastly, the eighth factor considers whether the substance is an "immediate precursor" of another controlled substance.[125]

B. FDA's Role in Drug Regulation

FDA provides the regulatory framework for psychedelic research through its intensive clinical trial process. FDA is an agency within HHS led by the Commissioner of Food and Drugs, responsible for executing the agency's responsibilities on behalf of the Secretary of HHS.[126] FDA is tasked with "ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices."[127] Additionally, FDA is responsible for advancing public health by accelerating innovations to make medicines more effective and providing the public with accurate, science-based information on medicines and food to improve their health.[128]

The Federal Food, Drug, and Cosmetic Act (FDCA) establishes the legal framework within which FDA operates.[129] FDA develops regulations based on the laws set forth in the FDCA or other laws under which FDA operates.[130] FDA follows the procedures required by the Administrative Procedure Act (APA) to issue regulations.[131] Under the APA, when an agency engages in substantive rulemaking, it must engage in notice-and-comment procedures.[132] This process allows for public input on a proposed regulation

122. Henningfield et al., *supra* note 117, at 3, 13.

123. *See* Denial of Petition to Initiate Proceedings to Reschedule Marijuana, 81 Fed. Reg. at 53,702–04.

124. *See id.* at 53,705–06.

125. *See id.* at 53,706.

126. *See* 21 U.S.C. § 393.

127. *What We Do: FDA Mission*, U.S. FOOD & DRUG ADMIN. (Nov. 21, 2023), https://www.fda.gov/about-fda/what-we-do#mission.

128. *Id.*

129. *See* Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. § 301.

130. *See Guidances,* U.S. FOOD & DRUG ADMIN. (Dec. 21, 2023), https://www.fda.gov/industry/fda-basics-industry/guidances.

131. *See* Administrative Procedure Act, 5 U.S.C. § 553.

132. *Id.* § 553(b).

before FDA issues a final regulation.[133]

FDA is involved in all stages of the life cycle of a drug product—during the drug development process, the approval process, and the product's tenure on the market.[134] FDA's drug development process involves a complex framework, requiring coordination between several parties, including "drug sponsors, clinical researchers, and regulatory authorities."[135] Before it can even be marketed to consumers, each drug that goes through FDA's intensive development process must first "move through the pipeline of discovery, investigation, clinical trials, and FDA approval."[136]

To prove a drug's safety and effectiveness, "FDA requires data from clinical trials—formally designed, conducted, and analyzed studies of human subjects."[137] The clinical research process is broken down into four phases, with three phases occurring prior to approval and the final phase falling post-approval.[138] To initiate the clinical testing process, the drug's sponsor files an investigational new drug (IND) application with FDA.[139] FDA has thirty days to review the application, and, unless FDA objects, the sponsor may begin clinical testing once the thirty days have elapsed.[140] Phase I clinical trials are used to determine proper dosage, document the drug's metabolization and excretion, and identify acute side effects.[141] Phase II and III trials involve larger groups of study participants and are used to gather evidence of a drug's efficacy and effectiveness while continuing to monitor safety.[142] After these three phases of clinical trials are completed, the sponsor submits an NDA to FDA's Center for Drug Evaluation and Research.[143]

After a sponsor submits an NDA, FDA has sixty days to determine whether the NDA will be filed.[144] If FDA decides to file the NDA, it typically

---

133. *See id.*

134. AGATA DABROWSKA, VICTORIA R. GREEN & LISA N. SACCO, CONG. RSCH. SERV., R45405, THE SUPPORT FOR PATIENTS AND COMMUNITIES ACT (P.L. 115-271): FOOD AND DRUG ADMINISTRATION AND CONTROLLED SUBSTANCE PROVISIONS 4 (2018).

135. Phillip Zhang & Nicole R. Winston, *Federal Medication Development Regulation*, NAT'L CTR. FOR BIOTECHNOLOGY INFO. (June 12, 2023), https://www.ncbi.nlm.nih.gov/books/NBK574558/.

136. *Id.*

137. AGATA DABROWSKA & SUSAN THAUL, CONG. RSCH. SERV., R41983, HOW FDA APPROVES DRUGS AND REGULATES THEIR SAFETY AND EFFECTIVENESS 4 (2018).

138. *See* Zhang & Winston, *supra* note 135.

139. 21 C.F.R. § 312.20 (2023).

140. *See* DABROWSKA & THAUL, *supra* note 137, at 5.

141. *Id.*

142. *See id.*

143. *See id.*

144. 21 C.F.R. § 314.101(a)(1) (2023).

has 180 days from the receipt of the NDA—referred to as the "initial review cycle"—to review the application and take action.[145] Upon completion of its review, FDA can send the applicant either an approval letter or a CRL.[146] Typically, FDA sends the applicant a CRL if it believes that the NDA cannot be approved in its current form for one or more reasons, including insufficiency of data, lack of evidence, noncompliant labeling, and deficient methodology.[147] Upon receiving a CRL, an applicant can take one of three actions: (1) resubmit the application addressing all of the deficiencies laid out in the CRL, (2) withdraw the application without prejudice, or (3) request an opportunity for hearing "on the question of whether there are grounds for denying approval of the application."[148] In the past, FDA has approved several drugs after the drug sponsor resubmitted the NDA addressing the deficiencies noted by FDA in the CRL.[149] For example, Sunlenca, an HIV drug developed by Gilead Sciences, received a CRL from FDA in March 2022 after submitting its NDA and receiving BTD in 2021; after Gilead Sciences resubmitted its NDA in June 2022, the drug was approved by FDA in December 2022.[150] FDA can only refuse to approve an NDA if FDA sends a CRL to the applicant, the applicant requests an opportunity for hearing, and FDA finds that one of the grounds for refusal listed in 21 C.F.R. § 314.125(b) applies.[151]

Outside of the clinical trial process, FDA routinely issues guidance to the industry to inform industry actors, such as drug manufacturers, about FDA's current thinking on a regulatory issue.[152] FDA follows the procedures required by its "Good Guidance Practice" regulation to issue guidance.[153] However, FDA guidance is not legally binding on the public or FDA.[154] On June 26, 2023, FDA issued its Draft Guidance for psychedelics, highlighting considerations for sponsors developing psychedelic drugs for the treatment

145. *Id.* at § 314.100(a).

146. *Id.*

147. *See* 21 C.F.R. § 314.101 (a), (d)–(e).

148. *Id.* at § 314.100(b).

149. *Complete Response Letter*, PINK SHEET: CITELINE, https://pink.citeline.com/PS120021/Complete-Response-Letters (last visited July 14, 2024) (listing examples of instances where drug sponsors have received complete response letters (CRLs) for their drug products, the indication stated in the NDA, the issues outlined in the CRL, and the activity following receipt of the CRL, including resubmission and eventual approval).

150. Judith Stewart, *Sunlenca FDA Approval History*, DRUGS.COM (Jan. 17, 2023), https://www.drugs.com/history/sunlenca.html.

151. 21 C.F.R. § 314.125 (2023).

152. 21 C.F.R. § 10.115(b); *Guidances*, *supra* note 130.

153. 21 C.F.R. § 10.115(a).

154. *Guidances*, *supra* note 130.

of medical conditions and for clinical trials to be conducted under an IND application.[155] The release of the Draft Guidance was well-received within the scientific and legal communities, with commentators interpreting it to demonstrate FDA's recognition of the therapeutic potential of psychedelics.[156] One critique of the Draft Guidance concerned FDA's decreased emphasis on the psychotherapy aspect of psychedelic-assisted therapy.[157]

According to Mason Marks and Glenn Cohen, two of the leading legal scholars in the area of psychedelic law, the Draft Guidance included a mix of well-founded and controversial recommendations.[158] Discussing some of the concerns surrounding the Draft Guidance, these scholars interpret FDA's controversial approach to psychological monitoring and support in a less skeptical light—that is, as an attempt to expand research into psychedelic medicines by encouraging researchers to consider a more comparative approach and study these medicines over a variety of contexts, including without psychotherapy, to understand their efficacy best.[159]

III. ADMINISTRATIVE PATHWAYS FOR SCHEDULING REFORM

Controlled substances can be moved from the schedule in which they were originally placed.[160] Two entities maintain the authority to place a substance under control, change its classification, or remove it from control altogether: the DEA Administrator (as delegated by the AG) and Congress.[161]

One way to change the legal status of a controlled substance is through legislative amendment of the CSA.[162] Congress can pass laws placing a substance under control, alter the classification of a controlled substance, or

155. Psychedelic Drugs: Considerations for Clinical Investigations; Draft Guidance for Industry; Availability, 88 Fed. Reg. 41,407 (June 26, 2023).

156. *See* Clara Greaney, Lauren Carboni, Monica Chmielewski & Kyle Faget, *Key Takeaways from the FDA's First Draft Guidance on Clinical Trials with Psychedelic Drugs*, FOLEY & LARDNER LLP (July 17, 2023), https://www.foley.com/insights/publications/2023/07/key-takeaways-fda-draft-guidance-psychedelic-drugs/; Marks & Cohen, *FDA Evaluation of Psychedelics?*, *supra* note 6, at 1,735 ("The FDA's guidance for psychedelics research is a policy landmark and reflects shifting attitudes toward controversial substances.").

157. *See* Marks & Cohen, *FDA Evaluation of Psychedelics?*, *supra* note 6, at 1,734.

158. *Id.*

159. *Id.* ("We interpret the FDA's guidance not as dismissing the therapeutic role of psychological support and continuity of care, but rather as underscoring the need to rigorously study these variables.").

160. *See* LAMPE, *supra* note 13, at 5.

161. LAMPE, *supra* note 13, at 5.

162. *See id.*; 21 U.S.C. § 811.

remove the substance from control entirely.[163] Because Congress is not subject to the procedural requirements for administrative scheduling,[164] it does not need to incorporate scientific and medical findings into the scheduling legislation.[165] In the past, Congress has used its scheduling power to respond quickly to drugs that pose an urgent concern.[166] However, the congressional pathway is slow, infrequently utilized, and does not require incorporating scientific and medical findings, making it less appealing than the administrative pathway.[167]

Alternatively, DEA can exercise its administrative authority to make scheduling decisions through the two pathways discussed below: the petition to initiate rescheduling pathway and the FDA approval pathway.[168] Additionally, any final scheduling decision by DEA—whether it be a decision to reschedule a substance or to deny a petition—is subject to judicial review.[169] The petition to initiate rescheduling pathway and the FDA approval pathway are discussed below.

A. Scheduling Reform Through a Petition to Initiate Rescheduling

The petition to initiate rescheduling pathway involves collaboration between several agencies.[170] DEA may initiate such administrative scheduling on its own initiative, at the request of HHS, or following a petition to initiate rulemaking proceedings for rescheduling by an interested party.[171] Prior to initiating rulemaking proceedings, DEA must request a scientific and medical evaluation of the drug from the Secretary of HHS.[172] The authority to prepare the scientific and medical evaluation is delegated to FDA.[173] FDA's evaluation involves an assessment of the substance under the CSA's 8-FA to

163. *See* LAMPE, *supra* note 13, at 8; United States v. Ways, 832 F.3d 887, 893–94 (8th Cir. 2016) (summarizing the addition of certain substances to Schedule I by legislation).

164. *See infra* Part III.A (listing the procedural requirements for administrative scheduling).

165. *See* LAMPE, *supra* note 13, at 8.

166. *See, e.g.*, Synthetic Drug Abuse Prevention Act of 2012, Pub. L. No. 112-144, 126 Stat. 1130 (2012) (adding two synthetic cathinones and certain cannabimimetic drugs permanently to Schedule I); Temporary Reauthorization and Study of the Emergency Scheduling of Fentanyl Analogues Act, Pub. L. No. 116-114, 134 Stat. 103 (2020) (placing a broad class of fentanyl analogues in Schedule I on a temporary basis).

167. *See* LAMPE, *supra* note 13, at 9.

168. Marks & Shachar, *supra* note 14.

169. *Id.*

170. *See* 21 U.S.C. § 811(a).

171. *See id.*

172. LAMPE, *supra* note 13, at 9.

173. *Id.*

determine scheduling,[174] as well as an assessment of DEA's five-part test to determine whether the substance has a "currently accepted medical use."[175] Based on its evaluation, FDA recommends whether the substance should be controlled and, if so, in which schedule it should be placed.[176] Pursuant to the CSA, FDA's findings are binding on DEA with respect to scientific and medical matters, and, if FDA recommends against controlling a drug, DEA shall not control it.[177]

After receiving FDA's recommendation, DEA conducts its own investigation of the relevant data to determine whether the substance should be rescheduled.[178] In order to reach a scheduling decision, DEA Administrator must make specific findings to determine that the drug meets the applicable criteria for the relevant schedule.[179] Finally, DEA is required to engage in the notice-and-comment procedures required under the APA,[180] thereby allowing interested parties the opportunity to submit comments on the decision before it is finalized.[181]

The DEA Administrator may deny a petition for review.[182] Once a petition is denied, the petitioner can seek judicial review.[183] Pursuant to the CSA, DEA's "findings of fact are 'conclusive' on judicial review if the findings are supported by substantial evidence."[184] As for DEA's interpretation of the CSA, courts followed the *Chevron* doctrine until recently, and accepted the interpretation as long as it was reasonable.[185] With the Supreme Court's recent overruling of the *Chevron* doctrine in *Loper Bright Enterprises v. Raimondo*,[186] the resolution of statutory ambiguity is now entirely within judicial

174. 21 U.S.C. § 811(c)(1)–(8).

175. *See* Denial of Petition to Initiate Proceedings to Reschedule Marijuana, 81 Fed. Reg. 53,688, 53,714 (Aug. 12, 2016) (discussing and applying the test to a petition to reschedule marijuana); *see also* Mason M. Marks, *Controlled Substance Regulation for the Covid-19 Mental Health Crisis*, 72 ADMIN. L. REV. 649, 674 (2020) [hereinafter Marks, *Controlled Substance Regulation*].

176. *See* 21 U.S.C. § 811(b).

177. *See id.*; Marks & Shachar, *supra* note 14.

178. *See* 21 U.S.C. § 811(b).

179. *See* 21 U.S.C. § 812(b).

180. *See* 5 U.S.C. § 553(b).

181. 21 U.S.C. § 811(a); *see also* Touby v. United States, 500 U.S. 160, 162–63 (1991).

182. 21 C.F.R. § 1308.43 (2023) (permitting denial based on a finding that "the grounds upon which the petitioner relies are not sufficient to justify the initiation of proceedings").

183. Marks & Shachar, *supra* note 14, at 294.

184. LAMPE, *supra* note 13, at 11.

185. *See* Chevron U.S.A., Inc. v. Nat. Res. Def. Council, Inc., 467 U.S. 837, 843–45 (1984).

186. Loper Bright Enters. v. Raimondo, 144 S. Ct. 2,244, 2,254 (2024).

discretion, regardless of the agency's interpretation.[187] Though the implications of *Loper Bright* on judicial review of the denial of rescheduling petitions are yet to be seen, courts will now have more latitude to dictate the outcome of these situations.[188] Moreover, under the APA, a reviewing court is required to overturn DEA's denial of a petition if the denial was "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law."[189] For example, the Ninth Circuit recently reversed DEA's denial of a petition to transfer psilocybin to Schedule II and remanded the petition to DEA to "either clarify its pathway for denying [the] petition or reevaluate [the] petition on an open record."[190] This framework indicates that judicial review of scheduling decisions can constrain agency power and, accordingly, prove to be a valuable tool to effect scheduling reform for psychedelics in the future.

The petition to initiate rescheduling pathway was recently triggered following a 2022 statement from President Joseph Biden urging review of marijuana scheduling.[191] On August 29, 2023, HHS sent a letter to DEA recommending that marijuana be moved from Schedule I to Schedule III.[192] On May 21, 2024, DEA's notice of proposed rulemaking (NPRM) proposing to transfer marijuana from Schedule I to Schedule III of the CSA was published in the Federal Register.[193] The NPRM stated that the decision to propose the transfer was "consistent with the view of the Department of Health and Human Services . . . that marijuana has a currently accepted medical use as well as HHS's views about marijuana's abuse potential and level of physical or psychological dependence."[194] Given that recommendations by

187. *See id.* at 2,266–67.

188. *See id.*

189. *See* Ams. For Safe Access v. DEA, 706 F.3d 438, 449 (D.C. Cir. 2013) (quoting 5 U.S.C. § 706(2)(A)).

190. Aggarwal v. DEA, No. 22-1718, 2023 WL 7101927, at *1–2 (9th Cir. Oct. 27, 2023) (holding that DEA's denial was "arbitrary and capricious" because DEA has never explicitly stated that a substance could not meet the Schedule II "currently accepted medical use with severe restrictions" standard "unless it met the DEA's five-part test for 'currently accepted medical use'").

191. Press Release, The 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/.

192. Natalie Fertig & Paul Demko, *Slightly Higher Times: Biden Administration Moves to Loosen Weed Restrictions*, POLITICO (Aug. 30, 2023), https://www.politico.com/news/2023/08/30/marijuana-review-move-to-schedule-iii-00113493.

193. Schedules of Controlled Substances: Rescheduling of Marijuana, 89 Fed. Reg. 44,597, 44,597 (May 21, 2024).

194. *Id.*

HHS as to scientific and medical matters—based on FDA's evaluation—are binding on DEA, it was no surprise that DEA followed the HHS recommendation.[195] However, DEA's decision to propose rescheduling only after the HHS recommendation underscores a larger concern that commentators have continually raised: the reasonableness of DEA's stringent five-part test for "currently accepted medical use."[196]

In the rescheduling context, both FDA's scientific evaluation and DEA's review involve an assessment of the five-part test for "currently accepted medical use," which is based on DEA's interpretation of the CSA.[197] Despite stating that FDA approval is not the only path to meet the "currently accepted medical use" standard,[198] DEA has repeatedly denied petitions to reschedule marijuana in the past, stating that marijuana did not meet the standard and indicating that rescheduling would have been possible if marijuana was FDA approved.[199] Moreover, the five-factor test has not been subject to judicial review because courts have generally deferred to DEA's interpretation based on the *Chevron* doctrine.[200] However, with the recent overruling of the *Chevron* doctrine in *Loper Bright*, DEA's interpretation of the CSA is no longer due judicial deference.[201] Though the impact of the decision is yet to be seen, lower judicial deference could result in reduced reliance on DEA's stringent five-factor test, ultimately leading to favorable outcomes for psychedelic scheduling reform.[202]

---

195. *See* 21 U.S.C. § 811(b).

196. *See* Marks, *Psychedelic Medicine for Mental Illness*, *supra* note 32, at 109; Al-Khaled, *supra* note 108, at 1,050; Kennedy Dickson, *Blunt Forces: A Case Study of Administrative Exhaustion Under the Controlled Substances Act*, 73 CASE W. RES. L. REV. 503, 525 (2022) ("[DEA's] interpretation is flawed and creates a Catch-22 situation.").

197. *See* Denial of Petition to Initiate Proceedings to Reschedule Marijuana, 81 Fed. Reg. 53,688, 53,714 (Aug. 12, 2016).

198. *Id.*

199. *See* Marijuana Scheduling Petition; Denial of Petition; Remand, 57 Fed. Reg. 10,499, 10,507–08 (Mar. 26, 1992); Notice of Denial of Petition, 66 Fed. Reg. 20,038, 20,038 (Apr. 18, 2001); Denial of Petition to Initiate Proceedings to Reschedule Marijuana, 76 Fed. Reg. 40,552, 40,552 (July 8, 2011); Denial of Petition to Initiate Proceedings to Reschedule Marijuana, 81 Fed. Reg. at 53,688.

200. *See, e.g.*, Grinspoon v. DEA, 828 F.2d 881, 891 (1st Cir. 1987); All. for Cannabis Therapeutics v. DEA, 930 F.2d 936, 937 (D.C. Cir. 1991); All. for Cannabis Therapeutics v. DEA, 15 F.3d 1131, 1135 (D.C. Cir. 1994); Ams. for Safe Access v. DEA, 706 F.3d 438, 440–41 (D.C. Cir. 2013); *see also* Dickson, *supra* note 196, at 526–28.

201. *See* Loper Bright Enters. v. Raimondo, 144 S. Ct. 2,244, 2,266–67 (2024).

202. *See id.*

B. Scheduling Reform Through FDA Approval

Schedule I substances can also be rescheduled following FDA approval.[203] Typically, this involves the approval of a drug product that is either a synthetic formulation of a Schedule I substance or contains a Schedule I substance as an active ingredient.[204] Once such a drug product has completed the clinical trial process and received FDA authorization, the HHS Secretary recommends scheduling the product in Schedules II–V.[205] The Secretary's decision is based on FDA's scientific evaluation, which includes an assessment of the drug product using the CSA's 8-FA and, for central nervous system active drugs, an abuse potential assessment.[206] Because FDA-approved drug products are considered to have a "currently accepted medical use," an assessment of DEA's five-part test is not required.[207] After FDA approval, DEA must take appropriate scheduling action to reschedule the approved product.[208]

Under the APA, DEA generally issues notice-and-comment procedures before a rule is finalized.[209] However, in cases where FDA approves a Schedule I drug and the HHS Secretary recommends control in Schedules II–V, the CSA requires DEA (as delegated by the AG) to first issue an Interim Final Rule (IFR) scheduling the drug within ninety days.[210] Under the CSA, the IFR becomes immediately effective without requiring DEA to demonstrate good cause for forgoing the thirty-day waiting period required by the APA.[211] The IFR gives interested persons the opportunity to comment and request a hearing, after which the DEA Administrator must issue a final rule in accordance with the CSA's scheduling criteria.[212]

In the past, DEA has rescheduled certain FDA-approved medications that

---

203. Marks & Shachar, *supra* note 14, at 295.

204. *See* Ismail L. Ali, Joy S. Cooper & Leslie Booher, *Making MDMA a Medicine (II): (Re)Scheduling for Schedule I Substances*, MAPS BULL., 2022, at 19, 21.

205. Henningfield et al., *supra* note 117, at 6–7.

206. *Id.*

207. *See* Denial of Petition to Initiate Proceedings to Reschedule Marijuana, 81 Fed. Reg. 53,688, 53,740 ("A drug that is the subject of an approved new drug application (NDA) or abbreviated new drug application (ANDA) . . . is considered to have a currently accepted medical use in treatment in the United States for purposes of the CSA.").

208. LAMPE, *supra* note 13; Webb Wright, *Rescheduling Psilocybin: A Beginner's Guide*, MUD/WTR (Nov. 9, 2022), https://mudwtr.com/blogs/trends-with-benefits/rescheduling-psilocybin-beginners-guide; Marks & Shachar, *supra* note 14.

209. 5 U.S.C. § 553(b).

210. 21 U.S.C. § 811(j)(1).

211. *Id.* § 811(j)(3).

212. *Id.*

either contain or are derived from Schedule I substances.[213] In 1985, FDA approved Marinol—a drug product containing dronabinol, the synthetic form of delta-9-tetrahydrocannabinol (delta-9-THC).[214] Delta-9-THC, an isomer of tetrahydrocannabinol (THC), is the principal psychoactive substance in the marijuana plant.[215] Following FDA approval, DEA issued a final rule on May 13, 1986, transferring FDA-approved products of the same formulation as Marinol from Schedule I to II.[216] In July 1999, following a petition to reschedule, DEA rescheduled Marinol to Schedule III based on FDA's recommendation.[217] Notably, DEA retained THC and marijuana on Schedule I.[218]

IV. REGULATORY IMPEDIMENTS TO PSYCHEDELIC RESEARCH

Despite mounting clinical evidence showing the therapeutic benefits of psychedelics, several regulatory impediments deter psychedelic research.[219] Perhaps the largest regulatory impediment to psychedelic research is DEA's current scheduling system, under which most psychedelics are classified as Schedule I substances.[220] Schedule I classification leads to various restrictions; as a result, researchers' access to the drug is "tremendously hindered, delayed, and often cost-prohibitive."[221] Clinical research on Schedule I substances is subject to the dual oversight of FDA and DEA, which typically results in unique and lengthy delays.[222] DEA limits the number of researchers that can obtain the required registration to work with Schedule I substances and the quantity of these substances produced for such research.[223] Moreover, Schedule I status results in an inability to acquire federal funding, thereby limiting funding to private donors.[224] Each fiscal year, Congress allocates funding to agencies through a series of appropriations bills, which often contain riders—clauses prohibiting the agency from "using any of the

213. *See, e.g.*, 64 Fed. Reg. 35,921, 35,928–30 (July 2, 1999).

214. *Id.* at 35,928.

215. *Id.*

216. *Id.*

217. *Id.*

218. *See id.* at 35,929; 21 C.F.R. § 1308.11 (2023).

219. *See* Marks & Shachar, *supra* note 14, at 294–95 (discussing some of the regulatory impediments that deter psychedelic research).

220. *Id.*

221. Al-Khaled, *supra* note 108, at 1,027.

222. Marks & Shachar, *supra* note 14, at 294–95.

223. Mason Marks, *The Varieties of Psychedelic Law*, NEUROPHARMACOLOGY, Mar. 15, 2023, at 1, 2.

224. Marks & Cohen, *Psychedelic Therapy*, *supra* note 37, at 1,670; LAMPE, *supra* note 13, at 39.

funds included in the bill to perform a certain action that legislators oppose."[225] An appropriations rider for fiscal year 2023 prohibits the use of appropriated funds for "any activity that promotes the legalization of any drug . . . included in [S]chedule I."[226] Such a funding limitation allows large pharmaceutical companies to monopolize the market and charge exorbitant prices, which, in turn, limits access to useful treatments.[227]

Apart from moving psychedelics from Schedule I, one way to overcome the federal funding hurdle is through Congressional elimination of the rider.[228] Appropriations riders must be renewed annually, and they can be eliminated if they are not renewed or are repealed by Congress.[229] Prior legislative efforts to eliminate the rider have failed.[230] However, in 2021, Johns Hopkins Medicine was awarded a grant by the National Institute on Drug Abuse (NIDA) of the National Institutes of Health (NIH) to study psilocybin as a treatment for tobacco addiction—the first federal grant awarded in fifty years to investigate the therapeutic benefits of a classic psychedelic.[231] Given that the lack of federally funded research has been a big point of contention in the context of legislative efforts surrounding marijuana, NIH's award of this grant has the potential to convince lawmakers about the benefits of psychedelics.[232]

Schedule I classification also leads to individualized local and state-level measures to decriminalize psychedelics, making it difficult to create a consistent regulatory scheme.[233] The concept of federalism allows some level of

225. *A Brief Guide to the Federal Budget and Appropriations Process*, AM. COUNCIL ON EDUC., https://www.acenet.edu/Policy-Advocacy/Pages/Budget-Appropriations/Brief-Guide-to-Budget-Appropriations.aspx (last visited May 29, 2024).

226. LAMPE, *supra* note 13, at 39; Consolidated Appropriations Act, 2023, Pub. L. No. 117-328, § 509, 136 Stat. 4459, 4909.

227. *See* LAMPE, *supra* note 13, at 39; Marks & Cohen, *Psychedelic Therapy*, *supra* note 37, at 1,670.

228. *See* Marks & Cohen, *Psychedelic Therapy*, *supra* note 37, at 1,670.

229. *See A Brief Guide to the Federal Budget and Appropriations* Process, AM. COUNCIL ON EDUC., https://www.acenet.edu/Policy-Advocacy/Pages/Budget-Appropriations/Brief-Guide-to-Budget-Appropriations.aspx (last visited May 29, 2024).

230. Marks & Cohen, *Psychedelic Therapy*, *supra* note 37, at 1,670.

231. Press Release, Johns Hopkins Med., Johns Hopkins Med. Receives First Fed. Grant for Psychedelic Treatment Rsch. in 50 Years (Oct. 18, 2021), https://www.hopkinsmedicine.org/news/newsroom/news-releases/2021/10/johns-hopkins-medicine-receives-first-federal-grant-for-psychedelic-treatment-research-in-50-years.

232. *See* Rahul Jakati, *Hopkins Receives Grant for Psychedelic Research from NIH*, JOHNS HOPKINS NEWSL. (Nov. 10, 2021), https://www.jhunewsletter.com/article/2021/11/hopkins-receives-grant-for-psychedelic-research-from-nih.

233. *See* LAMPE, *supra* note 13, at 39–40 ("[T]here is a growing gulf between federal and

conflict to exist between state and federal regulations without warranting federal intervention.[234] However, several state psychedelic programs today blur "the lines between psychedelics and health care services . . . which may exceed the scope of permissible conflict and pose a higher risk of federal intervention."[235]

Additionally, FDA's clinical trial process poses issues of its own, thereby making psychedelic research even more difficult. FDA's notoriously expensive clinical trial process, compounded by the lack of federal funding for Schedule I substances, further disincentivizes drug manufacturers from investing in psychedelic research.[236] The limitation to private funding alone favors large companies and promotes ethically ambiguous, competitive behaviors.[237] One example includes the patenting of psychedelics, particularly naturally occurring psychedelics like psilocybin that Indigenous communities have used for centuries.[238] The clinical trial process also raises other issues in the context of psychedelics.[239] Several psychedelic treatments currently going through the FDA clinical trial process involve a combination of drug intake and psychotherapy.[240] However, FDA does not regulate the therapeutic context.[241]

---

state law with respect to Schedule I controlled substances with potential medical benefits."); Mason Marks, *State-Regulated Psychedelics on a Collision Course with FDA*, 330 JAMA 2,337, 2,337 (2023) [hereinafter Marks, *State-Regulated Psychedelics*] ("In addition to being expensive, redundant, and potentially misleading, many state-regulated psychedelic programs are on a collision course with FDA law.").

234. *See* Marks, *State-Regulated Psychedelics*, *supra* note 233, at 2,337–38.

235. *See id.* at 2,337 (discussing Colorado as an example because Colorado's National Medicine Advisory Board, which helps regulators draft rules for Colorado's psychedelic program, interprets Colorado law to "require state health insurance, funded by federal Medicaid, to cover health services offered in conjunction with unapproved psychedelic medicines.").

236. *See* Amy L. McGuire, Holly Fernandez Lynch, Lewis A. Grossman & I. Glenn Cohen, *Pressing Regulatory Challenges for Psychedelic Medicine*, 380 SCIENCE 347, 349–50 (2023).

237. *See* Marks & Cohen, *Psychedelic Therapy*, *supra* note 37, at 1,670 (discussing the negative impacts of patenting psychedelics); Quentin Barbosa, *America Is Tripping: Psychedelic Pharmaceutical Patent Reforms Fostering Access, Innovation, and Equity*, 88 BROOK. L. REV. 1,129, 1,132 (2023) ("[T]he patent system can be abused such that only a few companies gatekeep psychedelic medicine, discouraging competitors, impeding research, restraining innovation, and limiting access to psychedelic therapy.").

238. *See* Marcelo Leite, *Capitalism Goes Rogue with Patent Claims on Psychedelics*, CHACRUNA (Mar. 17, 2021), https://chacruna.net/psychedelic-patents-capitalism/; Carolyn Gregoire, *Inside the Movement to Decolonize Psychedelic Pharma*, PROTO.LIFE (Oct. 29, 2020), https://proto.life/2020/10/inside-the-movement-to-decolonize-psychedelic-pharma/.

239. *See* McGuire et al., *supra* note 236, at 347–48.

240. *Id.*

241. *See id.* at 348.

V. RECOMMENDATIONS

A. Scheduling Recommendation for MDMA and Psilocybin Upon Approval

Two psychedelic drug products are in the later stages of the FDA clinical trial process—Lykos' MDMA product and COMPASS Pathways' synthetic psilocybin formula, COMP360.[242] COMPASS Pathways is currently conducting Phase III trials with the intention of submitting an NDA upon completion.[243] Though Lykos has experienced some setbacks,[244] researchers in the field believe that the eventual approval of MDMA is likely.[245] Based on statements made by Lykos in the wake of the PDAC recommendation and FDA's issuance of the CRL, Lykos seems committed to continue working with FDA to provide additional relevant information.[246] Based on the actions FDA and Lykos can take at this stage, Lykos remains on the path to gain approval—the only aspect in question is the timing.[247] Additionally, interagency correspondences indicate regulators' belief that psilocybin and MDMA are expected to receive FDA approval in the next couple of years.[248] Moreover, two other drug products—atai Life Sciences' EMP-01[249] and MindMed's MM-402[250]—that are currently going through the clinical trial process are both synthetic formulations of MDMA derivatives.[251] As a result, these drug products present alternate avenues for FDA approval of MDMA.

Upon approval of the MDMA and psilocybin drug products, FDA should recommend rescheduling. Schedule I substances can be rescheduled following FDA approval.[252] Once these drug products are approved, FDA must provide the Secretary of HHS with an evaluation of them and a

---

242. *See* LYKOS THERAPEUTICS, *supra* note 48; COMPASS PATHWAYS, *supra* note 42.

243. COMPASS PATHWAYS, *supra* note 42.

244. *See supra* text accompanying notes 50–61.

245. *See* Stone, *supra* note 56.

246. *Lykos Therapeutics Statement on FDA Advisory Committee Meeting*, LYKOS THERAPEUTICS, https://news.lykospbc.com/2024-06-13-Lykos-Therapeutics-Statement-on-FDA-Advisory-Committee-Meeting (last visited July 13, 2024); *Lykos Therapeutics Announces CRL*, supra note 57.

247. *See supra* text accompanying notes 144–151.

248. Busby, *supra* note 49 (discussing a letter sent by the Assistant Secretary for Mental Health and Substance Use—on behalf of the Secretary of Department for Health and Human Services (HHS)—acknowledging the anticipated approval of MDMA and psilocybin by FDA within two years).

249. *See atai Life Sciences Initiation of Phase 1*, *supra* note 64.

250. *MindMed Collaborators Initiate Phase 1*, *supra* note 65.

251. *See id.*; *atai Life Sciences Initiation of Phase 1*, *supra* note 64.

252. *See supra* text accompanying notes 205–208.

recommendation for their scheduling based on the 8-FA.[253] Based on FDA's evaluation and scheduling determination, the HHS Secretary will recommend that DEA reschedule the drug products.[254] At this stage, DEA must take appropriate scheduling action to reschedule the approved product.[255] Based on the 8-FA, FDA should recommend that the approved MDMA and psilocybin drug products be placed in Schedules III and IV, respectively.

The third factor of the 8-FA will be satisfied because, as soon as FDA approves an MDMA or psilocybin drug product, that drug product will be considered to have a currently accepted medical use in the United States.[256] An assessment of both drugs under the remaining factors is discussed below.

1. Recommendation that the Approved MDMA Product be Placed in Schedule III

Upon approval of an MDMA product, FDA should recommend that the MDMA product be placed in Schedule III. Schedule III controlled substances are considered to have a "currently accepted medical use in treatment in the United States" and a "potential for abuse less than the drugs or other substances in schedules I and II," with abuse leading to "moderate or low physical dependence or high psychological dependence."[257] An assessment of MDMA using the CSA's 8-FA weighs in favor of this recommendation.

MDMA has been evaluated in many preclinical and clinical studies over several decades.[258] In fact, given the quantity of data available, FDA informed Lykos that it would not need to conduct any new dedicated animal and human abuse potential studies to guide FDA's rescheduling recommendation if the MDMA product is approved for therapeutic use.[259] Existing data does not indicate that MDMA poses a high risk of abuse when administered in the clinical setting.[260] Findings from animal studies suggest that although MDMA appears to have higher reinforcing effects than classic psychedelics, these effects are still substantially lower than for Schedule II substances such as amphetamines and cocaine.[261]

253. *See id.*

254. *Id.*

255. *Id.*

256. Denial of Petition to Initiate Proceedings to Reschedule Marijuana, 81 Fed. Reg.at 53,714.

257. 21 U.S.C. § 812(b)(3)(A)–(C).

258. Henningfield et al., *supra* note 117, at 8.

259. *Id.*

260. *Id.* at 14; Mitchell et al., *supra* note 46 (concluding that the MDMA treatment was safe, well-tolerated, and did not induce abuse potential); Ben Sessa, Laurie Higbed & David J. Nutt, *First Study of Safety and Tolerability of 3,4-Methylenedioxymethamphetamine-Assisted Psychotherapy in Patients with Alcohol Use Disorder*, 35 J. PSYCHOPHARMACOLOGY 375, 376 (2021).

261. Henningfield et al., *supra* note 117, at 14.

MDMA's mechanism of action and pharmacological effects have been thoroughly investigated.[262] MDMA is a synthetic drug known to "increase feelings of empathy and prosociality, heighten mood states, and facilitate the processing of difficult emotions."[263] It has also been shown to "enhance fear memory extinction, modulate fear memory reconsolidation . . . and bolster social behavior in animal models."[264] Though MDMA primarily induces the release and selective reuptake of serotonin, it also increases the activity of dopamine (which produces increased energy and acts in the reward system to reinforce behaviors) and norepinephrine (which increases heart rate and blood pressure).[265] The chemical structure of MDMA is similar to both stimulants and hallucinogens.[266] However, MDMA does not share the same mechanism of action as hallucinogens and, thus, does not cause hallucinogenic effects.[267]

Epidemiological data indicates that use of MDMA poses a low risk to the public health because prevalence of MDMA use is relatively low.[268] According to data from the 2022 MTF survey, only 3.2% of young adults aged nineteen to thirty reported MDMA use.[269] Moreover, instances of adverse events or substance use disorders are uncommon.[270] In 2022, DAWN reported one emergency department visit pertaining to MDMA.[271] According to the 2021 TEDS survey, "other amphetamines" (a category that includes MDMA)

---

262. *See* Danilo De Gregorio, Argel Aguilar-Valles, Katrin H. Preller, Boris Dor Heifets, Meghan Hibicke, Jennifer Mitchell, et al., *Hallucinogens in Mental Health: Preclinical and Clinical Studies on LSD, Psilocybin, MDMA, and Ketamine*, 41 J. NEUROSCIENCE 891, 892–93 (2021).

263. Grant Jones & Matthew Nock, *Lifetime Use of MDMA/Ecstasy and Psilocybin is Associated with Reduced Odds of Major Depressive Episodes*, 36 J. PSYCHOPHARMACOLOGY 557 (2021).

264. Mitchell et al., *supra* note 46; *see also* Sessa et al., *supra* note 260 ("3,4-methylenedioxymethamphetamine (MDMA) is a phenethylamine that raises levels of monoamine neurotransmitters in the brain. MDMA elevates mood, increases sociability and feelings of closeness to others, and can facilitate imagination and memory.").

265. *See* Sessa et al., *supra* note 260; Mitchell et al., *supra* note 46; De Gregorio et al., *supra* note 262, at 895.

266. *MDMA (Ecstasy/Molly) DrugFacts*, NAT'L INST. ON DRUG ABUSE, https://nida.nih.gov/research-topics/mdma-ecstasymolly (last visited Feb. 10, 2024).

267. De Gregorio et al., *supra* note 262, at 891.

268. *See* Megan E. Patrick, Richard A. Miech, Lloyd D. Johnston & Patrick M. O'Malley, *Monitoring the Future Panel Study Annual Report: National Data on Substance Use Among Adults Ages 19 to 60, 1976–2022*, MONITORING THE FUTURE 1, 34 (2023).

269. *Id.*

270. *See Findings from Drug-Related Emergency Department Visits, 2022*, U.S. SUBSTANCE ABUSE & MENTAL HEALTH SERVS. ADMIN., DRUG ABUSE WARNING NETWORK (DAWN) 1, 47 (June 20, 2023), https://store.samhsa.gov/sites/default/files/pep23-07-03-001.pdf.

271. *Id.*

constituted only 0.8% of admissions to substance use treatment services.[272]

Current evidence does not indicate a high risk for psychological or physical dependence in the clinical setting.[273] For example, in a study of MDMA-assisted therapy as a treatment for alcohol use disorder, none of the participants reported any desire to obtain or use illicit MDMA following their participation in the trial.[274] Finally, though MDMA itself is classified as a Schedule I substance, it is not a known precursor for any other controlled substance.[275]

FDA should recommend that DEA place the approved MDMA product in Schedule III because MDMA has low potential for abuse relative to other Schedule I and II substances, low risk of dependence, low risk to the public health, and an abundance of scientific evidence surrounding its pharmacological effects and medical uses. However, MDMA should be placed in a higher schedule than psilocybin. Notably, MDMA's potential for abuse, reinforcing effects, and potential for physical and psychological dependence are higher than those of classic psychedelics, such as psilocybin.[276] Additionally, there is some evidence to indicate that MDMA could lead to psychological dependence or produce serious adverse effects—including potentially fatal serotonin syndrome—if consumed chronically, excessively, or at high doses.[277] On the other hand, the lethal dose for psilocybin appears to be approximately 1,000 times the highest therapeutic dose—a dose that is likely impossible to consume recreationally.[278] Consequently, though MDMA should be moved to a lower schedule, it should still be placed in a more restrictive schedule than psilocybin.

---

272. *Treatment Episode Data Set (TEDS) 2021: Admissions to and Discharges from Substance Use Treatment Services Reported by Single State Agencies*, U.S. SUBSTANCE ABUSE & MENTAL HEALTH SERVS. ADMIN. 1, 10 (Nov. 29, 2023), https://www.samhsa.gov/data/sites/default/files/reports/rpt42794/2021-teds-annual-report.pdf.

273. *See* Henningfield et al., *supra* note 117, at 14; Sessa et al., *supra* note 260, at 381.

274. Sessa et al., *supra* note 260, at 381.

275. *See* 21 U.S.C. § 802(23).

276. Henningfield et al., *supra* note 117, at 14; Marks, *Controlled Substance Regulation*, *supra* note 175, at 712.

277. Benjamin Illingworth, Declan Lewis, Andrew Lambarth, Kate Stocking, James Duffy, Luke Jelen, et al., *A Comparison of MDMA-Assisted Psychotherapy to Non-Assisted Psychotherapy in Treatment-Resistant PTSD: A Systematic Review and Meta-Analysis*, 35 J. PSYCHOPHARMACOLOGY 501, 502 (2021); David J. Heal, Jane Gosden & Sharon L. Smith, *Evaluating the Abuse Potential of Psychedelic Drugs as Part of the Safety Pharmacology Assessment for Medical Use in Humans*, 142 NEUROPHARMACOLOGY 89, 109 (2018).

278. *See* Matthew W. Johnson, Roland R. Griffiths, Peter S. Hendricks & Jack E. Henningfield, *The Abuse Potential of Medical Psilocybin According to the 8 Factors of the Controlled Substances Act*, 142 NEUROPHARMACOLOGY 143, 150 (2018).

2. Recommendation that the Approved Psilocybin Product be Placed in Schedule IV

Similarly, following approval, FDA should recommend that the psilocybin product, COMP360, be placed in Schedule IV. Schedule IV substances have a "low potential for abuse relative to the drugs . . . in [S]chedule III" and a "currently accepted medical use in treatment," with abuse possibly leading to "limited physical . . . or psychological dependence."[279] An assessment of psilocybin using the CSA's 8-FA weighs heavily in favor of the recommendation.

Psilocybin has been the subject of thousands of scientific and clinical studies, both prior to the War on Drugs and in recent years.[280] Preclinical and clinical data from trials show that psilocybin has a very low potential for abuse.[281] Psilocybin similarly has a lower potential for abuse relative to substances listed in Schedule III, including ketamine.[282]

Additionally, there is an abundance of scientific evidence regarding psilocybin's neurochemistry and pharmacology.[283] Psilocybin has "little to no psychoactive effects on its own."[284] However, upon ingestion, psilocybin is converted into its active metabolite, a chemically similar compound called psilocin, which interacts directly with the serotonin 5-HT2A receptors in the brain.[285] Typical effects of psilocybin consumption include "distorted perception or hallucinations, an altered sense of space and time, and a loss of the normal boundaries of personhood, often accompanied by euphoria."[286]

---

279. 21 U.S.C. § 812(b)(4).

280. Johnson et al., *supra* note 278, at 148 ("It has been estimated that there were more than one thousand scientific and clinical studies of classic psychedelics including LSD and psilocybin published through the 1960s, and several thousand more published since the 1960s.").

281. *Id.* at 146, 157; *see, e.g.*, David Bender & David J. Hellerstein, *Assessing the Risk–Benefit Profile of Classical Psychedelics: A Clinical Review of Second-Wave Psychedelic Research*, 239 NEUROPHARMACOLOGY 1,907, 1,921 (2022) ("Classical psychedelics are not considered addictive, and . . . do not have significant reinforcing effects.").

282. *See* Johnson et al., *supra* note 278, at 162 ("In contrast to Schedule III drugs and even to many drugs placed in Schedule IV, the reinforcing effects in preclinical studies are marginal.").

283. *See generally* Bender & Hellerstein, *supra* note 281 (analyzing methodology of recent scientific studies of classical psychedelics).

284. Broderick Daniel, *Psilocybin vs. Psilocin: Understanding the Magic Behind the Mushrooms*, MEDIUM (May 7, 2023), https://medium.com/@broderickdaniel0/psilocybin-vs-psilocin-understanding-the-magic-behind-the-mushrooms-76c6dd9ab7c0.

285. *Id.*

286. *Psilocybin*, NEWSCIENTIST, https://www.newscientist.com/definition/psilocybin/ (last visited May 31, 2024).

Epidemiological data regarding the use of psilocybin indicate that the risks posed to the public health are low.[287] According to the 2022 NSDUH results, the reported lifetime use of psilocybin among people aged twelve or older was 11.3%.[288] Though the NSDUH results do not include data for psilocybin use disorder specifically, prevalence of hallucinogen-based substance use disorder among people aged twelve or older in 2022 was 0.2%.[289] Comparatively, prescription stimulant use disorder was 0.6%.[290] The 2022 MTF survey results were similar.[291] Though the MTF survey does not ask specifically about psilocybin use, it does ask about "hallucinogens," which is broken down into LSD and "hallucinogens other than LSD," including psilocybin.[292] According to data from the 2022 MTF survey, "[7%] of young adults reported use of hallucinogens other than LSD in the past [twelve] months."[293]

Scientific data indicates that the psychological or physiological dependence liability of psilocybin is low—though tolerance has been observed, no signs of physical dependence or withdrawal have been documented.[294] Psilocybin is also considered to have a "low potential for acute toxicity due to overdose."[295] As mentioned above, a lethal dose of psilocybin is

287. *See* Johnson et al., *supra* note 278, at 162.

288. *2022 NSDUH Detailed Tables*, U.S. SUBSTANCE ABUSE & MENTAL HEALTH SERVS. ADMIN. tbl.1.108B, (*Nov.* 13, 2023), https://www.samhsa.gov/data/report/2022-nsduh-detailed-tables (choose "Clickable Table of Contents"; then choose the second "PE" from left next to "[s]pecific hallucinogen, inhalant, needle, and heroin use, by standard age categories").

289. *2022 NSDUH Detailed Tables*, U.S. SUBSTANCE ABUSE & MENTAL HEALTH SERVS. ADMIN., tbl.5.1B, (Nov. 13, 2023), https://www.samhsa.gov/data/report/2022-nsduh-detailed-tables (choose "Clickable Table of Contents"; then choose the second "PE" from left next to "SUD for specific substances, by standard age categories;" and scroll down one page).

290. *Id.*

291. *See* Patrick et al., *supra* note 268, at 27.

292. Richard A. Miech, Lloyd D. Johnston, Megan E. Patrick, Patrick M. O'Malley, Jerald G. Bachman & John E. Schulenberg, *Monitoring the Future National Survey Results on Drug Use, 1975-2022: Secondary School Students*, MONITORING THE FUTURE 1, 25 (2023), https://monitoringthefuture.org/wp-content/uploads/2022/12/mtf2022.pdf.

293. Patrick et al., *supra* note 268, at 27.

294. *See* Johnson et al., *supra* note 278, at 162; Craig Pearson, Joshua Siegel & Jessica A. Gold, *Psilocybin-Assisted Psychotherapy for Depression: Emerging Research on a Psychedelic Compound with a Rich History*, 434 J. NEUROLOGICAL SCIS. 1, 6 (Mar. 15, 2022); Shawn Ziff, Benjamin Stern, Gregory Lewis, Maliha Majeed & Vasavi Rakesh Gorantla, *Analysis of Psilocybin-Assisted Therapy in Medicine: A Narrative Review*, 14 CUREUS 1, 3 (Feb. 5, 2022).

295. Seetal Dodd, Trevor R. Norman, Harris A. Eyre, Stephen M. Stahl, Arnie Phillips, André F. Carvalho, et al., *Psilocybin in Neuropsychiatry: A Review of its Pharmacology, Safety, and Efficacy*, 28 CNS SPECTRUMS 416, 419 (2022).

approximately 1,000 times the highest therapeutic dose and is likely impossible to consume recreationally.[296] Lastly, though psilocybin and psilocin are currently placed in Schedule I, there is no evidence to suggest that they are used as precursor chemicals as defined by the CSA.[297]

Accordingly, an assessment of psilocybin under the CSA's 8-FA indicates that it has a low potential for abuse relative to Schedule III substances, is well-researched with regards to its pharmacological effects, poses a low risk to public health, and has low dependence liability. As a result, FDA should recommend that the approved psilocybin product be placed in Schedule IV.

B. Recommendation to HHS to Initiate a Petition for Rescheduling MDMA and Psilocybin as a Whole

FDA should recommend that HHS petition DEA to initiate rescheduling proceedings for MDMA and psilocybin as a whole.[298] Schedule I substances can be rescheduled using the petition to initiate rescheduling pathway.[299] Before initiating rulemaking proceedings, DEA will request a scientific and medical evaluation of the drug, as well as a recommendation for scheduling, from HHS.[300] FDA is charged with preparing this evaluation, and it includes an assessment of the CSA's 8-FA to determine scheduling and DEA's five-part test to determine if the substance has a "currently accepted medical use."[301] FDA's scientific and medical findings are binding on DEA.[302] After FDA approves the two drug products and recommends rescheduling for the products, FDA should also recommend that HHS initiate a rescheduling petition for MDMA and psilocybin suggesting that DEA reschedule the two compounds as a whole, rather than just the specific FDA-approved formulations.

FDA's recommendation to HHS will be based on the eight CSA factors analyzed above, as well as the finding that MDMA and psilocybin satisfy DEA's five-part test for the "currently accepted medical use" standard.[303]

---

296. Johnson et al., *supra* note 278.

297. Silvia N. Calderon, Katherine R. Bonson, Chad J. Reissig, Joshua M. Lloyd, Steven Galati & Dominic Chiapperino, *Considerations in Assessing the Abuse Potential of Psychedelics During Drug Development*, 224 NEUROPHARMACOLOGY 1, 6 (Nov. 28, 2022).

298. *See supra* text accompanying notes 170–177.

299. *Id.*

300. *Id.*

301. *Id.*

302. *See* 21 U.S.C. § 811(b); Marks & Shachar, *supra* note 14.

303. *See* Denial of Petition to Initiate Proceedings to Reschedule Marijuana, 81 Fed. Reg. 53,688, 53,714 (Aug. 12, 2016) (discussing and applying the test to a petition to reschedule marijuana); Marks, *Controlled Substance*, *supra* note 175, at 656.

The five necessary elements to satisfy the standard are: that (1) the drug's chemistry is known and reproducible; (2) there are adequate safety studies; (3) there are adequate and well-controlled studies proving efficacy; (4) the drug is accepted by qualified experts; and (5) the scientific evidence is widely available.[304] As discussed above, the *Americans for Safe Access* court found that the last four elements of DEA's five-part test can be satisfied using evidence suggesting the substance's efficacy from Phase II and Phase III FDA clinical trials.[305]

For substances like marijuana, the currently accepted medical use standard has been difficult to meet.[306] However, both MDMA and psilocybin are in a better position for rescheduling. First, as opposed to the marijuana plant, MDMA and psilocybin can easily meet the first step of the five-part test because they are both chemical compounds whose chemistry is "known and reproducible."[307] Moreover, MDMA and psilocybin meet the *Americans for Safe Access* framework for clinical studies.[308] In addition to results from Phase III trials conducted by Lykos and COMPASS Pathways to prepare for their NDAs, there are numerous ongoing and completed Phase II trials testing the efficacy of these substances.[309] For example, nearly a dozen Phase II studies have been conducted to test the efficacy of MDMA in patients experiencing treatment-resistant PTSD, and these studies have consistently yielded encouraging results.[310] MAPS is also conducting a Phase II study testing the efficacy of MDMA as treatment for eating disorders.[311] Similarly, there are over thirty ongoing and completed Phase II studies evaluating psilocybin as treatment for several mental health disorders, including PTSD, TRD, MDD, GAD, OCD, and alcohol use disorder.[312] Ultimately, clinical evidence from

304. Marijuana Scheduling Petition; Denial of Petition; Remand, 57 Fed. Reg. 10,499, 10,506 (Mar. 26, 1992).

305. Ams. for Safe Access v. DEA, 706 F.3d 438, 450–51 (D.C. Cir. 2013).

306. Marks, *Psychedelic Medicine for Mental Illness*, *supra* note 32, at 117.

307. *Id.* at 117–18.

308. *See* Am. for Safe Access v. DEA, 706 F.3d 438, 450 (D.C. Cir. 2013).

309. *See Psychedelic Drug Development Tracker*, PSYCHEDELIC ALPHA, https://psychedelicalpha.com/data/psychedelic-drug-development-tracker (last visited June 2, 2024) (listing ongoing FDA clinical trials for several psychedelic substances).

310. De Gregorio et al., *supra* note 39, at 896.

311. *A Multi-Site Study of MDMA-Assisted Psychotherapy for Eating Disorders (MED1)*, NAT'L LIBR. OF MED. (Jan. 4, 2024), https://clinicaltrials.gov/study/NCT04454684.

312. *See Psychedelic Drug Development Tracker*, *supra* note 309; NAT'L LIBR. OF MED., https://clinicaltrials.gov/ (begin typing "Psilocybin" in the box labeled "Intervention/treatment"; select "Psilocybin" when it appears; click "More Filters;" then select "Phase 2" under "Study Phase" and "Active, not recruiting" and "Completed" under "Study Status"; and finally, click "Search") (last visited July 13, 2024).

these trials indicates that MDMA and psilocybin meet the standard for "currently accepted medical use" under the CSA.[313]

Notably, FDA's own changing attitude toward psychedelic medicines has proved beneficial in gathering the clinical evidence required to meet the *Americans for Safe Access* bar.[314] First, FDA granted BTD to both MDMA and psilocybin, thereby accelerating the clinical trial process and allowing these substances to reach the approval stage sooner.[315] Second, for the first time ever, FDA released its Draft Guidance for research on psychedelic drugs, which provides a useful frame of reference for sponsors to create studies that meet FDA's expectations.[316] Additionally, the notice-and-comment procedure for the June 2023 Draft Guidance has allowed researchers to influence FDA's current thinking and provide feedback on elements of the Draft Guidance.[317] As a result, FDA's recommendation to HHS to initiate a petition for rescheduling will be supported not just by its scientific and medical evaluation using the CSA's 8-FA and DEA's five-part test, but also by its own recognition of the therapeutic benefits of these substances.

Accordingly, FDA should recommend that HHS initiate a rescheduling petition for MDMA and psilocybin urging DEA to reschedule the two compounds as a whole, rather than just the specific FDA-approved formulations. It is important to note that rescheduling alone will not lead to increased access to these medicines.[318] Under the FDCA, the various psychedelic treatments must be approved by FDA before they can be marketed by psychedelic companies and prescribed by doctors.[319] However, rescheduling will expand further research into these medicines by removing the numerous barriers that come with Schedule I classification.[320]

C. Guidance for State Licensing Boards

As discussed above, local and state psychedelic programs are treading the fine line that separates permissible and impermissible conflict between state

313. *See Am. for Safe Access*, 706 F.3d at 450.

314. *See id.*

315. *See* COMPASS PATHWAYS, *supra* note 42; LYKOS THERAPEUTICS, *supra* note 48.

316. *See* Psychedelic Drugs: Considerations for Clinical Investigations; Draft Guidance for Industry; Availability, 88 Fed. Reg. 41,407, 41,407–08 (June 26, 2023).

317. *See, e.g.*, MAPS Pub. Benefit Corp., Comment Letter on FDA Draft Guidance on Psychedelic Drugs: Considerations for Clinical Investigations; Draft Guidance for Industry (Aug. 21, 2023), https://www.regulations.gov/comment/FDA-2023-D-1987-0109.

318. *See* Marks, *Psychedelic Medicine for Mental Illness*, *supra* note 32, at 125.

319. *See id.*

320. *See supra* text accompanying notes 219–227.

and federal law.[321] If MDMA and psilocybin are rescheduled for broader clinical use, FDA should follow the procedures required by its Good Guidance Practice regulation and issue guidance for state licensing boards to execute a strict regimen for the use of psychedelics as treatment for mental illnesses.[322] Given that FDA does not regulate the therapeutic context, such guidance will help direct states to adopt a more uniform regulatory scheme and promote safe use of these substances.[323]

CONCLUSION

Psychedelics show great promise in treating a host of mental illnesses. Amid the worsening U.S. mental health crisis, expanding research into psychedelic medicines is crucial. One of the biggest regulatory hurdles surrounding psychedelic research is DEA's current scheduling of most psychedelics as Schedule I substances under the CSA. Schedule I classification not only creates barriers to meaningful research, but it also leads to an inconsistent regulatory scheme in situations where states choose to decriminalize such controlled substances.[324] The overly restrictive classification of psychedelics is a direct result of the War on Drugs, which has already prevented research into these useful treatments for several decades—treatments that could have helped curb the worsening mental health crisis today.[325]

The most effective solution to the regulatory issues surrounding psychedelic research is the rescheduling of psychedelics by DEA. The safest way to bring about scheduling reform is through agency action based on an analysis of clinical and scientific data, and FDA is the sole agency with the power to effectuate such reform effectively.[326] This Comment recommends that FDA utilize its authority to initiate scheduling reform for MDMA and psilocybin. FDA's role in scheduling reform is crucial to the expansion of psychedelic research. As the only agency with the ability to bring about scheduling reform safely and effectively, FDA must act now to remedy the ongoing negative consequences of the War on Drugs.

321. *See supra* notes 233–235 and accompanying text.

322. *See* McGuire et al., *supra* note 236.

323. *See id.* at 348.

324. LAMPE, *supra* note 13, at i, 8.

325. *See* Marks, *Psychedelic Medicine for Mental Illness*, *supra* note 32, at 73, 87.

326. *See* DABROWSKA & THAUL, *supra* note 137, at i.