Texas A&M Journal of Property Law

Volume 10
Number 2 *Student Articles Edition*

Article 8

4-11-2024

Far Out: The Extended Denial of Public Access to Psychedelic Therapeutics

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FAR OUT: THE EXTENDED DENIAL OF PUBLIC ACCESS TO PSYCHEDELIC THERAPEUTICS

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Abstract

The United States patent regime is designed to promote dissemination of information that undergirds a particular innovation. To incentivize disclosure, inventors are granted a time-limited right to exclude others from practicing the invention, thereby affording the inventor a period in which to commercialize and financially benefit from their inventive contribution. The disclosure provides information sufficient for one of skill in the relevant art to make and use the invention, and the public may freely do so upon the patent's expiry.

Global advancement of human medicine is fundamentally intertwined with the United States patent system; medical progress largely depends upon the exclusionary protections United States patents confer. Ordinarily, the expiry of patents covering therapeutic products and methods yields substantial price reduction, as new market participants seek to establish market share by undercutting the expired patent holder and others. The patent system also yields to the public not only access to new and improved medical technology but also a delayed, unencumbered freedom to make and use the invention upon the patent's exhaustion.

Recently, psychoactive chemical compounds have garnered renewed and international attention. Although many psychedelic substances have had a long history of human use, including within therapeutic contexts, the Controlled Substances Act and related legislation significantly stifled research directed toward developing these substances for medical use. This "artificial" impediment to therapeutic innovation effectively delayed public access to the fruits of earlier innovation.

DOI: https://doi.org/10.37419/JPL.V10.I2.8

[†]J.D., Texas A&M University School of Law, 2023. Ph.D., The University of Texas at Austin. The Author sincerely thanks Professor Casado Perez for her guidance as a faculty advisor. The Author also thanks John Gillette for providing encouragement throughout the writing process as Note and Comment Editor. Finally, the Author would like to thank his family and his classmates at Texas A&M University School of Law for their thoughtful perspectives and support.

As researchers investigate and discover improved therapies employing well-known psychedelic substances and their derivatives, they understandably seek patent protection. But coupled with delay resulting from the imposition of strict regulatory oversight and the threat of criminal prosecution, patent protection largely extends the denial of public access to these therapeutics. Should the United States government continue to both effectively deny public access to medical innovation and simultaneously permit individuals and corporations to accumulate further exclusionary rights in that same innovation? Is there a more equitable framework that considers the interests of innovators and patients, accounts for historical context, and balances safety with access?

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I. INTRODUCTION

Despite long-standing prohibitions outlawing the possession, use, or sale of psychedelic drugs, various therapies employing psychedelics have recently gained support, having demonstrated success in the treatment of neurological conditions, such as post-traumatic stress disorder and depression.[1] For example, Australia's

1. *See, e.g.*, Jennifer M. Mitchell et al., *MDMA-Assisted Therapy for Severe PTSD: A Randomized, Double-Blind, Placebo-Controlled Phase 3 Study*, 27 NATURE MED. 1025, 1025 (2021); Alan K. Davis et al., *Effects of Psilocybin-Assisted Therapy on Major Depressive Disorder*, 78 JAMA PSYCHIATRY 481, 481 (2021).

Department of Health and Aged Care recently rendered a final decision effectively legalizing MDMA- and psilocybin-based medical treatments.[2] Such successes and accompanying governmental messaging encourage competition among pharmaceutical developers and manufacturers to patent therapeutic methods using these compounds. But is it right that treatments using compounds known to, but denied to, the public for decades should now continue to be effectively denied to the public pursuant to the exclusionary rights of patent holders? How can the United States legal system balance the incentive of market exclusivity—which ostensibly drives drug developers to conduct the clinical trials necessary to win regulatory approval to market their products for human use—with the public's right to enjoy the benefits of substances long known to possess therapeutic potential?

First, this Comment provides a brief overview of the use of psychedelics in human medicine, the effect of later regulation and prohibition, and the resulting conflict between innovation, safety, and health. Second, this Comment considers the statutory requirements for patentability in the context of psychedelic therapeutics, highlighting the tension underlying the governmental grant of exclusive rights concerning psychedelics while that government itself has disincentivized, and continues to disincentivize, associated inventive endeavor. Finally, this Comment proposes an alternative lens through which the patentability of psychedelic therapies may be analyzed that is designed to improve the public's access to fruits of innovation to which it has long been entitled while minimizing undesirable market ramifications for drug developers.

II. BACKGROUND

A. Origins of Modern Psychedelic Therapeutics

Human use of plants and fungi producing mind-altering effects has been known for millennia.[3] For example, cave murals discovered in

2. *Notice of Final Decisions to Amend (or Not Amend) the Current Poisons Standard in Relation to Psilocybin and MDMA*, DEP'T OF HEALTH AND AGED CARE: THERAPEUTIC GOODS ADMIN. (Feb. 3, 2023), https://www.tga.gov.au/resources/publication/scheduling-decisions-final/notice-final-decision-amend-or-not-amend-current-poisons-standard-june-2022-acms-38-psilocybine-and-mdma [https://perma.cc/LE9T-UYTZ].

3. DAVID O. KENNEDY, PLANTS AND THE HUMAN BRAIN 116 (2014); Giorgio Samorini, *The Oldest Archeological Data Evidencing the Relationship of Homo*

Algeria, estimated to have been created between 5,000 and 7,000 B.C.E., are suspected to depict *Psilocybe mairei* mushrooms.[4] This and many other *Psilocybe* species contain psilocybin—a prodrug of the psychoactive compound psilocin, known for producing psychological effects in humans including aural and visual hallucinations.[5] Similarly, oral histories collected from members of Mexican indigenous tribes, which span back over 2,000 years, describe human use of the peyote cactus (*Lophophora williamsii*), which contains the psychoactive compound mescaline.[6]

Since the mid-19th century, rapid scientific progress in the chemical arts has afforded improved methods for the isolation, identification, and synthesis of chemical compounds.[7] Such developments facilitated the recognition of the specific chemical compounds responsible for the psychological effects reported by ingesting various plants and fungi.[8] Correspondingly, advances in synthetic methodology permitted chemists to design and prepare a wide array of chemical structures previously unexplored, including those exhibiting psychoactive effects in humans. One notable example is the synthesis of lysergic acid diethylamide ("LSD") by Albert Hoffmann in 1938 and his recognition of its psychoactive effect in humans in 1943.[9]

By the mid-1900s, these developments were accompanied by an appreciation for the therapeutic potential conferred by psychoactive compounds, which was underscored by numerous studies conducted using such compounds to evaluate their effect and efficacy in various

Sapiens with Psychoactive Plants: A Worldwide Overview, 3 J. PSYCHEDELIC STUDIES 63, 70 (2019).

4. *Id.*

5. Ricardo Jorge Dinis-Oliveira, *Metabolism of Psilocybin and Psilocin: Clinical and Forensic Toxicological Relevance*, 49 DRUG METABOLISM REVS. 84, 85, 87 (2017).

6. Kennedy, *supra* note 4, at 109.

7. Brian J. Yeh & Wendell A. Lim, Commentary, *Synthetic Biology: Lessons from the History of Synthetic Organic Chemistry*, 3 NATURE CHEM. BIOLOGY 521, 521 (2007).

8. *See, e.g.*, Albert Hofmann et al., *Psilocybin and Psilocin*, 42 HELVETICA CHIMICA ACTA 1557, 1560–61 (1959); Arthur Heffter, *Ueber Cacteenalkaloïde*, 29 BERICHTE DER DEUTSCHEN CHEMISCHEN, 216, 223 (1896); Kakisawa et al., *Structure of Grayanotoxin-I and -III*, 2 TETRAHEDRON LETTERS 59, 67 (1961).

9. Ivan Oransky, *Albert Hoffmann*, 371 THE LANCET 2145, 2168 (2008).

military and clinical contexts, including LSD,[10] mescaline,[11] and 3,4-methylenedioxymethamphetamine ("MDMA").[12]

B. The Effects of Illegality on the Progress of the Useful Arts

In the 1960s, LSD and other psychedelic substances were frequently associated with the counterculture movement,[13] which included many strongly opposed to the ongoing United States involvement in the Vietnam War.[14] In 1970, Congress enacted the Controlled Substances Act ("CSA"). Ostensibly, the CSA's initial purpose was, in part, to consolidate numerous federal drug laws, particularly those concerning narcotics.[15] The Act lists specific chemical substances subject to regulatory control, referred to as schedules I–V.[16] Save for obligations flowing from international treaties, authority to add a substance to—or to remove a substance from—a schedule rests primarily with the United States attorney general.[17] Additionally, the United States attorney general may transfer a listed chemical substance from one schedule to another.[18] These schedules are updated each year.[19]

LSD, along with myriad other psychoactive compounds, was among the first substances that the Drug Enforcement Agency (DEA) included as part of Schedule I pursuant to the CSA,[20] a decision that garnered swift criticism from scholars.[21] Consequently, scientific inquiry into the therapeutic potential of these compounds, while not prohibited outright, was severely impeded by the imposition of

10. *See, e.g.*, Erika Dyck, *'Hitting Highs at Rock Bottom': LSD Treatment for Alcoholism, 1950–1970*, 19 SOC. HIST. MED. 313, 317–18 (2006).

11. *See, e.g.*, David E. Nichols & Hannes Walter, *The History of Psychedelics in Psychiatry*, 54 PHARMACOPSYCHIATRY 151, 159 (2020).

12. *See, e.g.*, Alana R. Pentney, *An Exploration of the History and Controversies Surrounding MDMA and MDA*, 33 J. PSYCHOACTIVE DRUGS 213, 214–15 (2001).

13. Matt Lamkin, *Prescription Psychedelics: The Road from FDA Approval to Clinical Practice*, 135 AM. J. MED. 15, 15 (2022).

14. Donald R. Wesson, *Psychedelic Drugs, Hippie Counterculture, Speed and Phenobarbital Treatment of Sedative-Hypnotic Dependence: A Journey to the Haight Ashbury in the Sixties*, 43 J. PSYCHOACTIVE DRUGS 153, 153–55 (2011).

15. 21 U.S.C.S. § 801 (LexisNexis, LEXIS through Pub. L. No. 117-214).

16. § 812(a).

17. § 811(a)(1).

18. *Id.*

19. § 812(a).

20. Katherine B. Bonson, *Regulation of Human Research with LSD in the United State*s (1949-1987), 235 PSYCHOPHARMACOLOGY 591, 602 (2018).

21. *See, e.g.*, Carol A. Smith, *Lysergic Acid Diethylamide (LSD), Clinical Use and Research: A Proposal for Legislative Change*, 7 U.C.D. L. REV. 113, 113 (1974).

additional regulatory requirements, including review and approval by both the DEA and the United States Food and Drug Administration ("FDA").[22] Both agencies were largely unconstrained by mandatory time periods in which to review and evaluate trial protocols, the facilities in which studies would be conducted, and the adequacy of investigators.[23] In fact, the DEA was not mandated to provide any response to an applicant seeking a license to possess controlled substances for research purposes within any particular time period, which effectively permitted the agency to delay legitimate investigational studies indefinitely.[24] Given emerging therapeutic successes in the preceding years, the results of studies abandoned because of prohibition may have further demonstrated and emphasized the therapeutic efficacy of psychedelic compounds, such as LSD. Such a demonstration of utility in human medicine may have bolstered a rebuttal to classification within Schedule I.

These agencies' wanton ability to impede the pace at which scientific investigation could be performed very likely discouraged academic and industrial interest in these compounds. And it likely stifled research seeking to optimize pharmacological characteristics that otherwise could have been explored by derivatization, formulation, and combination with other psychotherapeutic or pharmacological treatments to evaluate synergistic potential. Impeded access to these substances likely had a profoundly deleterious effect on the mores of academic research, such as the publish or perish adage, which reflects that tenure decisions are largely a function of publication success.[25] In concert with the relative newness of synthetic psychedelics and the limited rigorous study of their use in humans, these regulatory barriers dissuaded multifarious scholars from straying from more established research into the inchoate field of psychedelic therapeutics.[26]

22. Bonson, *supra* note 20, at 591.
23. *Id.* at 602.
24. *Id.*
25. Mark de Rond & Alan N. Miller, *Publish or Perish: Bane or Boon of Academic Life?*, 14 J. MGMT. INQUIRY 321, 322 (2005).
26. Craig Pearson et al., *Psilocybin-Assisted Psychotherapy for Depression: Emerging Research on a Psychedelic Compound with a Rich History*, 434 J. NEUROLOGICAL SCI. 1, 2 (2022) ("[Schedule I] designation contributed to a decline in the number of studies performed using psychedelics, in part because they were much harder to get approved, and the stigma towards these compounds persisted for decades.").

Moreover, although regulatory hindrance initially applied only to controlled substances falling within Schedule I, the scope of this prohibition was later greatly expanded by Congress through the enactment of the Federal Analogue Act, which permitted any compound "substantially similar" to a Schedule I controlled substance to be treated as if it were so classified.[27] But despite expanding legislative and executive measures seeking to deter drug use, illicit use of psychoactive compounds continues.[28] And the broad therapeutic potential of psychedelic compounds against myriad ailments in humans has been discussed and investigated by clandestine researchers for decades.[29]

C. The Present Psychedelic Renaissance and Conflicting Agency Messaging

Although largely hindered by the United States government, other nations' approaches to therapeutic research employing psychoactive compounds have been less restrictive, at least for a time.[30] This permissiveness has spurred numerous investigations into the psychotherapeutic efficacy of various psychoactive compounds.[31] For example, when the United States classified 3,4-methylenedioxymethamphetamine ("MDMA") as an illicit substance with no recognized medical use in 1985, Switzerland continued legal, prescription access to the drug "to enhance the effectiveness of psychotherapy."[32]

Despite regulatory hurdles imposed by the DEA's classification system, the therapeutic potential emphasized by these results abroad

27. 21 U.S.C.S. § 813 (LexisNexis, LEXIS through Pub. L. No. 117-214).

28. *See, e.g.*, R. Andrew Yockey, *Trends in LSD Use Among US Adults: 2015–2018*, 212 DRUG & ALCOHOL DEPENDENCE 1, 1 (2020).

29. *See, e.g.*, R. Andrew Sewell et al., *Response of Cluster Headache to Psilocybin and LSD*, 66 NEUROLOGY 1920, 1920–21 (2006) (reporting cluster headache support group members identified the efficacy of psilocybin or LSD in the treatment of their headaches).

30. Peter Gasser, *Psycholytic Therapy with MDMA and LSD in Switzerland*, MAPS BULL., Winter 1995, at 3, 3 (summarizing Swiss research into MDMA and LSD therapies during the period from 1988–1993 when the compounds were legal there).

31. *See* Jørgen Due Madsen & Asle Hoffart, *Psychotherapy with the Aid of LSD*, 50 NORDIC J. PSYCHIATRY 477, 477–78 (1996).

32. Peter Oehen et al., *A Randomized, Controlled Pilot Study of MDMA (± 3,4-Methylenedioxymethamphetamine)-Assisted Psychotherapy for Treatment of Resistant, Chronic Post-Traumatic Stress Disorder (PTSD)*, 27 J. PSYCHOPHARMACOLOGY 40, 40–41 (2013).

may reasonably be assumed to have encouraged researchers around the world, including in the United States, to continue related studies, such as those investigating psilocybin for the treatment of depression. Perplexingly, despite the DEA's continued classification of psilocybin as a Schedule I controlled substance, reflecting the agency's position that the compound "has no currently accepted medical use in treatment in the United States,"[33] the FDA has recently granted "breakthrough therapy" status for psilocybin-based treatments for both treatment-resistant depression[34] and major depressive disorder.[35] Thus, there is notable tension among these executive agencies. Yet, another federal agency is deeply intertwined with the development of psychedelic therapeutic agents—the United States Patent and Trademark Office ("USPTO").

Patent law systems in diverse jurisdictions throughout the world provide regimes conferring market exclusivity, which greatly incentivizes technological innovation. Such exclusivity is of striking importance in the United States. The overall size of its market, together with its citizens' relative wealth and access to medical services—to say nothing of the intricate interplay of the economically gargantuan United States healthcare and insurance industries[36]—make pharmaceutical patent exclusivity immensely attractive to drug manufacturers. Scientists and doctors continue to develop, create, and test compounds and therapies. Accordingly, they seek patents to protect intellectual property rights underlying their discoveries.

The USPTO remains effectively agnostic to the legality of products or methods falling within the scope of the claims of the patents it grants.[37] This is understandable given the USPTO's position within the Department of Commerce and its relatively narrow role limited to patent examination and issuance. As such, FDA and USPTO messaging appear to stand in stark contrast to that of the DEA. But the effects of DEA and USPTO involvement vis-à-vis human use of

33. 21 U.S.C.S. § 812(b)(1) (LexisNexis, LEXIS through Pub. L. No. 117-214).

34. *FDA Grants Breakthrough Therapy Designation to Usona Institute's Psilocybin Program for Major Depressive Disorder*, BUS. WIRE (Nov. 22, 2019, 1:15 PM), https://www.businesswire.com/news/home/20191122005452/en/FDA-grants-Breakthrough-Therapy-Designation-to-Usona-Institutes-psilocybin-program-for-major-depressive-disorder [https://perma.cc/5EKN-2JGH].

35. *Id.*

36. *See, e.g.*, Adam Olson et al., *Lobbying Expenditures of the Health Sector During the COVID-19 Pandemic*, 35 J. GEN. INTERNAL MED. 3133, 3134 (2020).

37. *See, e.g.*, U.S. Patent No. 11,478,447; U.S. Patent No. 10,426,772; U.S. Patent No. 11,447,510.

psychoactive substances are unified in at least one respect—the threat of criminal prosecution and patent infringement liability together result in the public's continued denial of access to the benefits of psychoactive compounds long known to exhibit promising therapeutic value.

III. PSYCHEDELIC THERAPEUTICS AND THE PATENT SYSTEM

American legislators recognized early in the Nation's history the value of innovation. A strong proponent of the idea that innovation should be made to benefit all, Thomas Jefferson believed that financial incentive was the optimal mechanism for ensuring the disclosure of innovative ideas. So foundational is the concept of exclusionary rights for the protection of intellectual contributions that the Constitution confers upon Congress the power to provide exclusive rights to inventors to "promote the Progress of Science and useful Arts."[38] Accordingly, it is often argued that the underlying goal of the patent system is to facilitate society's scientific and technological advancement. In large part, the patent system is designed to afford the public access to previously unknown technological developments and information, thereby permitting them to make, use, and generally benefit from that new technology, at least after the patent expiry, as well as to use any additional information disclosed but not claimed by the patent applicant. The time-limited right of exclusivity afforded by a patent is given, in part, in exchange for public disclosure of the invention, and the invention becomes freely available to make and use upon the patent's expiry.

Patents are granted only for processes, machines, articles of manufacture, and compositions of matter possessing differentiating qualities over existing technologies. Moreover, the subject matter sought to be patented must be novel and nonobvious over any existing information in the public domain before the patent application's filing.[39] Additionally, patent law requires the invention to have some utility,[40] and the examination procedures employed by patent examiners at the United States Patent and Trademark Office stipulate that such utility be specific and substantial—the assertion by an inventor that the invention is merely useful as landfill is insufficient to

38. U.S. CONST. art. I, § 8, cl. 8.
39. 35 U.S.C.S. § 103 (LexisNexis, LEXIS through Pub. L. No. 117-214).
40. § 101.

satisfy the statutory utility requirement.[41] This requirement of substantial and specific utility has sparked an interesting discussion of whether a compound that cannot legally be possessed or used possesses satisfactory utility.[42]

Novelty, in the context of patentability, requires that the element or combination of elements that make up a given patent claim have not previously appeared in the public domain.[43] In the context of previously identified compounds that exhibit psychoactive properties, patent claims covering these compounds per se lack novelty—the provisions of the America Invents Act preclude the issuance of a patent claiming subject matter that was "patented, described in a printed publication, or in public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention."[44] LSD, MDMA, and psilocybin were identified, characterized, and published[45]—as well as on sale and in public use—many decades ago; thus, claims directed to the compounds per se are not patentable today. But methods of using these drugs may be patentable, such as methods of treating a disease, ameliorating a symptom, or reducing endogenous expression of a particular substance. Moreover, later identification of additional therapeutic uses of a known compound may also yield patentable subject matter; commonly, patents are sought and issued for second medical uses—that is, a compound previously known to be effective in the treatment of one disease may later be found to be useful for the treatment of another indication, whether wholly unrelated or perhaps even just slightly so.[46] And further, claims to methods of treatment using known compounds for known indications but in previously unrecognized and beneficial dosing regimens may also be patented.[47]

41. MPEP § 2107(B) (9th ed. Rev. 07.2022, Feb. 2023).

42. Manuela Cabal Carmona, *Dude, Where's My Patent?: Illegality, Morality, and the Patentability of Marijuana*, 51 VAL. U.L. REV. 651 (2017).

43. *See* 35 U.S.C.S. § 102 (LexisNexis, LEXIS through Pub. L. No. 117-214).

44. *Id.*

45. Ivan Oransky, *Albert Hoffmann*, 371 THE LANCET 2145, 2168 (2008); Roland W. Freudenmann et al., *The Origin of MDMA (Ecstasy) Revisited: The True Story Reconstructed from the Original Documents*, 101 ADDICTION HIST. 1241, 1242 (2006); Albert Hofmann et al., *Psilocybin und Psilocin, Zwei Psychotrope Wirkstoffe aus Mexikanischen Rauschpilzen*, 42 HELVETICA CHIMICA ACTA 1557, 1560–61 (1959).

46. Mitali Bhagwat et al., *Second Medical Use Patenting: A Review of Practices Across Different Jurisdictions*, 21 J. INTELL. PROP. RIGHTS 260, 262 (2016).

47. *Id.* at 261.

The patent system also requires that a claimed invention be nonobvious.[48] As negative public sentiment surrounding the use of psychoactive compounds for the treatment of disease has generally relaxed,[49] inventors have increasingly sought to patent methods of using known compounds like LSD, MDMA, and psilocybin in the treatment of diseases in humans. The present lens through which current statutory standards and judicially created tests for obviousness[50] are applied may support nonobviousness. But arguably, many of these uses are at least generally discernable or predictable from the research conducted in the years before the CSA's enactment, as well as later reports published in fora targeting both academic researchers and underground producers and users. Beyond pressures felt by scholars,[51] clandestine experimentalists had little to gain—and much to lose—by informing the public of the results concerning their experiments with substance use, either alone or in combination with other substances of any legal status, at least because of the risk that such publication would facilitate personal identification and their prosecution. Fear of prosecution likely suppressed motivation to investigate and disclose useful information to the public concerning therapeutic methods employing these psychedelic compounds. Prior disclosure determent should be considered in evaluating the patentability of claims to related subject matter in later-sought patents that would further impede the public's enjoyment of earlier innovation.

The current standard for nonobviousness as applied to second medical use claims permits claims to be issued that do not reasonably fall within the spirit of the government's promotion of innovation when considered in view of such strong disincentives as the regulatory barriers and prosecutorial threats enforced by that same government. For example, a patent issued in 2022 claims:

A method of enhancing positive therapeutic effects of a psychedelic, including the steps of: administering an empathogen/enactogen and a psychedelic in a same single oral dosage

48. 35 U.S.C.S. § 103 (LexisNexis, LEXIS through Pub. L. No. 117-214).

49. *See* John Haltiwanger, *Over a Third of US Voters Say Magic Mushrooms and Other Psychedelics Have a Medical Use, New Poll Shows*, INSIDER (June 1, 2021), https://www.businessinsider.com/over-third-of-us-voters-magic-mushrooms-medical-use-poll-2021-6 [https://perma.cc/NRC3-LSKU].

50. Graham v. John Deere Co., 383 U.S. 1, 17–18 (1966); KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 419–22 (2007).

51. de Rond & Miller, *supra* note 25.

form to an individual, wherein the empathogen/enactogen induces a positive psychological state in the individual and is administered in a dose of 20-200 mg; and enhancing a positive response to the psychedelic.[52]

The issued dependent claims focus on psychedelic compounds, including prototypical examples of LSD, mescaline, and psilocybin; the empathogen/entactogen is narrowed to MDMA and its relatives.[53] Thus, this claim generally covers "candy-flipping,"[54] the combination of LSD and MDMA, albeit within a single dosage form containing a specific mass of MDMA. Reports from drug users that purport to have experimented with this combination appear at least as early as 1993 on various early internet sites.[55]

Common with second medical use claims, the dosage amount and form, although seemingly peripheral limitations, are effectively the hook for patentability. If claim 1 of the 221 patent is novel, then no one has ever previously disclosed the claimed method's exact combination of features. And to rebut a rejection that the combination of features would be obvious to a person of skill in the art at the time the application was effectively filed, an applicant may produce evidence that the invention, taken as a whole, produces surprising and unexpected results.[56] But considering the history of these substances and the substantial barriers that discouraged academic investigation, it is quite reasonable to conclude that the rather straightforward limitations of dosage form and active ingredient proportions, and their associated benefits, likely would have been identified and disclosed long ago. And any patents covering such methods of treatment would likely be expired or approaching expiration. Arguably, a determination that such a method is nonobvious may unfairly rely on the benefit of governmental deterrence and its anti-innovative effect of discouraging investigation and disclosure.

Standing opposed to the goals of the patent system, in the context of the development of new therapeutic agents and methods, the DEA's keenness to place compounds within Schedule I and its enforcement of the Federal Analogue Act together act to deter scientific and

52. U.S. Patent No. 11,364,221.

53. *Id.*

54. Martin D. Schechter, *'Candyflipping': Synergistic Discriminative Effect of LSD and MDMA*, 341 EUR. J. PHARMACOLOGY 131, 131 (1998).

55. NICHOLAS SAUNDERS, E IS FOR ECSTASY 17 (1993).

56. *See* KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 419–22 (2007); In re Dillon, 919 F.2d 688, 691–92 (1990).

commercial endeavor in the critical and ever-growing field of human medicine. Categorization of compounds like psilocybin and LSD as Schedule I controlled substances largely prevented continued scientific study into their potential therapeutic benefits for decades. In addition to deterring—if not outright prohibiting—formal academic and medical study of the therapeutic potential of such compounds, criminalization also deterred non-scientists who continued to use the illicit substances from disclosing any information gleaned from self-experimentation.

To be placed on Schedule I, a compound must be judged to: (1) have a high abuse potential; (2) possess "no currently accepted medical use"; and (3) lack "accepted safety for use under medical supervision."[57] Many Schedule I compounds clearly have some medical use, as evidenced by their past and present successes in human trials, both official and clandestine. But more crucially, much of this information was known back in the '60s. Such compounds, namely LSD, were known to cause mind-altering effects. They were tested for efficacy in treating various diseases and were employed by the military in humans for other purposes as part of the MKULTRA program.[58] These trials arguably demonstrated the impropriety of a Schedule I designation. Once part of Schedule I, researchers seeking to synthesize or otherwise procure such compounds without first obtaining a license from the DEA risked criminal prosecution.

Not only were the primary substances themselves effectively prohibited, but also their analogues.[59] Controlled substance analogues are defined as having "chemical structures . . . substantially similar to the chemical structure of a controlled substance in Schedule I or II," and the possessor either knows that the compound has similar or stronger effects or intends for or represents that compound has similar or stronger effects.[60] Exceptions are made for substances part of an approved new drug application or those exempted by the Secretary of the Department of Health and Human Services for use in an investigational research program.[61] The analogue provisions to the CSA thus further broadened the scope of compounds prohibited from

57. 21 U.S.C.S. § 812(b)(1) (LexisNexis, LEXIS through Pub. L. No. 117-214).
58. Bonson, *supra* note 20.
59. 21 U.S.C.S. § 813 (LexisNexis, LEXIS through Pub. L. No. 117-214).
60. 21 U.S.C.A. § 802(32)(A) (West, Westlaw through Pub. L. No. 117-262).
61. 21 U.S.C.S. § 802(32)(C) (LexisNexis, LEXIS through Pub. L. No. 117-285); *see* 21 U.S.C.S. § 355(i) (LexisNexis, LEXIS through Pub. L. No. 117-285); 21 U.S.C.A. § 802(32)(A) (West, Westlaw through Pub. L. No. 117-262).

therapeutic research, preventing the possible discovery of new and useful therapeutic methods.

But considering the encouraging recent results of research into psychiatric therapies employing these and other drugs,[62] scientists and the universities or industry companies that employ them have correspondingly sought to patent these new therapies.[63] Thus, although academic researchers appear more willing to navigate regulatory hurdles to conduct studies on psychedelic therapy, the ramifications flowing from the height of the war on psychoactive compounds are still clearly felt, as benefits known to, or easily discernible by, persons of skill in the art as of the mid-1900s continue to be effectively withheld from the public at large. In essence, regulatory deterrence and the threat of criminal prosecution in conjunction with the subsequent conveyance of patent exclusivity synergistically weaken the possibility for public access, which is a fundamental aspect of the patent bargain.

Clearly, many psychoactive compounds have been known to induce psychological effects in humans. The patent system is designed to ensure that a patent is only granted on a method of using such a known compound if the method as a whole is novel and nonobvious. However, given the decades of prohibition and simultaneous underground culture of continued use, it is reasonable to suggest that many psychotherapeutic uses of such compounds would likely have been discovered and advanced much earlier, to the relief of many suffering from various diseases or disorders. Moreover, even had patents covering such developments been issued at that time, many likely would have expired long ago; thus, still, progress in this field would be well further along than it currently is. Importantly, the details and data contained in patent applications would have been made available to the public upon publication. This information very well could have driven further innovation and improved the methods of treatment as well as the design and construction of new compounds that reduce or enhance effects disclosed in or suggested by the published data.

As a result of the confluence of exclusivities flowing from criminalization and patents, the public continues to be deprived of methods employing psychoactive therapeutics long known to demonstrate psychological effects in humans. But there is certainly

62. *See* Mitchell et al., *supra* note 2.
63. *See supra* note 52.

innovation associated with present research into the use of these compounds. For example, the discovery of the optimal dosing regimen to produce a desired result in a patient may be novel and nonobvious. Suggesting that one should not be able to patent methods of treatment that employ a known psychoactive Schedule I controlled substance would again act to deter innovation underlying the development of therapeutic methods that may greatly improve the lives of so many. Thus, this Article suggests that the framework for examining patent applications should be adapted, specifically in the context of Schedule I controlled substances, to balance the incentives associated with patent rights—which motivate companies to develop and conduct clinical trials necessary to acquire regulatory approval for human use—with the public's right to access treatments employing compounds long known to possess related therapeutic potential.

IV. POSSIBLE SOLUTIONS TO BALANCE INNOVATION AND PUBLIC ACCESS

The discussion above largely concerns two statutory mechanisms by which the public has been delayed access to compounds that have demonstrated psychoactive effects. First, the CSA significantly disincentivizes research into the possible therapeutic uses of scheduled substances, including criminalization—arguably one of the strongest possible forms of disincentive. Second, the patent statute grants patentees the right to exclude others from using a patented method that employs such compounds. The balance between incentivizing innovation and public access sought by the patent system is substantially thrown off where the patented subject matter also was or currently is subject to substantially burdensome regulation under the CSA.

It is important to note that the scope of this problem is limited to subject matter falling within the area of overlap between the patent and the food and drug statutory schemes.[64] As such, a proposed solution aimed at addressing the issues presented herein should be tailored commensurately, and thus narrowly, because an overly broad solution would likely also disincentivize efforts to innovate human medicine using psychedelic compounds. Thus, a reasonable solution must traverse a narrow gap; it must increase public access without ruinously undermining the capitalistic motivations that spur

64. *See* 35 U.S.C.A. § 100; 21 U.S.C.A. § 801.

innovation—motivations that are particularly pronounced in the context of human medicine.

Mason Marks and I. Glenn Cohen suggest that part of the explanation for recent patent grants concerning psychedelic compounds or methods for their use is ignorance of history on the part of patent examiners and a lack of facile access to prior art often published in foreign languages in jurisdictions having lesser restrictions concerning such compounds.[65] They largely present two proposals for addressing the issuance of psychedelic patents that are of questionable inventiveness: (1) third-party efforts and (2) legislative efforts.[66] Improving the availability and accessibility of prior art publications concerning psychedelic compounds and their effects would make it easier for examiners to locate and apply references in rejecting patent claims.[67] Alternatively, prohibiting patents concerning psychedelics would facilitate patient access to treatments once approved.[68] But placing the onus on third parties to assist the patent examiners at the United States Patent and Trademark Office misallocates the burden. And the outright prohibition of patents directed to psychedelic compounds would severely undermine the commercial incentive to develop next-generation therapies employing psychedelics, to say nothing of the challenges associated with shepherding the legislative action required to ban subject matter, even psychedelics. This Author proposes a third option, which requires neither third-party commitment nor legislative action—an enhanced standard for evaluating nonobviousness.

A. An Enhanced Standard of Nonobviousness as Applied to Scheduled Drugs

The very nature of the problem outlined above is the extended denial, to the public, of not just the fruits of past innovation but also those of innovations that would likely have been identified much earlier. Once placed within Schedule I, it is reasonable to suspect that researchers would have hesitated, if not have outright refused, to wade into the regulatory quagmire required to investigate psychedelic compounds,[69] and that such aversion substantially limited the

65. Mason Marks & I. Glenn Cohen, *Patents on Psychedelics: The Next Legal Battlefront of Drug Development*, 135 HARV. L. REV. F. 212, 220–21 (2022).
66. *Id.* at 230–32, 234.
67. *Id.* at 230–32.
68. *Id.* at 234.
69. *See* 21 U.S.C.A. § 821–26 (West, Westlaw through Pub. L. No. 117-262).

scientific community's understanding of these compounds and their therapeutic potential in human medicine.

This assertion is susceptible to a very reasonable challenge—it relies on the mere possibility that such research and the discoveries that have now recently stemmed therefrom *would have been* conducted and recognized decades ago. Perhaps, moreover, to assume specific technological advancement would have occurred had a different set of events transpired is no more than an exercise in imagination. But the Author suggests that only a relatively small step of logic, as opposed to a great leap, is needed to arrive at the proposed assertion. Although the scope of understanding concerning the broader safety and therapeutic efficacy of these compounds likely was limited by the time the CSA was enacted, some fundamental therapeutic characteristics were known that overwhelmingly suggested psychological treatment potential—namely that psychedelic compounds caused marked and varied neurological effects. At present, to patent treatment methods employing these compounds in the context of psychological or neurological diseases requires little more—though more, to be sure—than simply administering the compound to the patient. But limitations sufficient to overcome the current standard of obviousness may simply append a particularized dosing regimen, criteria for optimal patient selection or exclusion, administration frequency, or use in combination with other medicines.

In the context of a wholly new chemical entity, which inherently has no history of any effects or tolerability in humans, these additional limitations appear to be much more reasonable insofar as they may suffice to warrant a patent separate from, and typically enjoy a term of exclusivity extending beyond that of, the chemical entity itself or even the first medical use employing that entity, in which such additional limitations are absent. But the long history of human use of psychedelic compounds, and the bright spotlight shined upon their psychological and neurological effects during the mid-to-late 1900s, should substantially undermine the effectiveness of such claim limitations in the context of these therapies. Had the CSA not so impeded psychedelic therapeutic research, such dosing regimen, criteria for optimal patient selection or exclusion, administration frequency, or identification of tolerable or synergistic combinations with other existing medications almost assuredly would have been thoroughly explored. Thus, one possible solution is to raise the standard for nonobviousness, or at least recast its framework, in the context of method claims that employ compounds subject to, or ever

having been subject to, regulation that has effectively precluded public access—for example, substances of Schedule I.

For example, consider a hypothetical invention for which a patent is being sought today. The general thrust of the claim sought to be patented is a method for improving cognitive focus by administering psilocybin to a patient in need of such medical intervention. Under the current standard of obviousness, such a claim may well be patentable, even if, for example, an academic paper describing the use of psilocybin to treat depression had been published decades earlier. The rationale supporting nonobviousness asserted by the applicant could be that the academic publication, although disclosing the use of psilocybin to treat depression, provides no teaching, suggestion, or motivation (or any other post-*KSR* rationale)[70] to use psilocybin to improve cognitive focus. Alternatively, the applicant may assert that depression and cognitive focus are the results of largely disparate underlying neurological mechanisms and pathways.

But now consider the same framework for nonobviousness through a wider lens. For the sake of this example, assume psilocybin was placed in Schedule I shortly after the academic paper had been published and, as a result, research surrounding psilocybin effectively stopped. Is it unreasonable to imagine that, had it not been for that regulatory impediment, the scientific community—having observed the effective impact of psilocybin in the context of one neurological condition—likely would have dedicated considerable investigation into the use of psilocybin for the treatment of other neurological conditions, perhaps even including lack of cognitive focus? One casting of the present proposal is that, in the limited context described throughout this Article, a method of using such a compound for the treatment of a particular condition associated with a physiological system should not be sufficient to overcome the obviousness bar where it was previously known that the same compound was useful for the treatment of a different condition associated with that same physiological system. Indeed, the claim should fail to overcome the obviousness bar even were the claim to further recite various limitations that in the context of wholly unknown therapeutics might well surpass the nonobviousness bar, such as specific dosages, formulations, or administration intervals as previously discussed concerning U.S. Patent No. 11,364,221.[71]

70. KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 419–22 (2007).
71. U.S. Patent No. 11,364,221.

Thus, at the time psilocybin was placed in Schedule I, it was public knowledge that psilocybin exhibited significant neurological effects and, unsurprisingly, that substantially burdensome regulation—which arguably amounts to an effective prohibition on research—then impeded further investigation. That effective prohibition should be considered, to at least some extent, later in determining whether to confer patent rights to but a handful of persons or entities because enforcement of these rights serves to further extend the denial to the larger public of enjoying the benefits of human endeavor that had largely occurred long before. Such a patent would largely reflect innovation that the effective prohibition substantially delayed from free public access—a delay that would necessarily be magnified by that very patent's grant.

B. Minimizing Possible Negative Ramifications

The direct effect of raising the standard for overcoming the obviousness bar in this context is, of course, that it would likely become considerably more difficult for an inventor to patent methods of treatment employing substances that are, or have ever been, placed within Schedule I of the CSA. This difficulty may attenuate the pharmaceutical industry's willingness to investigate these compounds, and thus a promising field would be left to wither. To combat this attenuation, drug developers could be granted more favorable tax treatment for later income from psychedelic therapeutics sales corresponding to the costs associated with development.[72] Beyond research and development and clinical costs, permitting reasonable costs associated with patent filing and prosecution in the United States to be eligible for favorable tax treatment may be sufficient to incentivize start-up drug developers and large, established pharmaceutical manufacturers.

Another way to mitigate the cooling effect the proposed higher standard for overcoming the obviousness bar may have on the development of treatments using known psychoactive compounds could be to offer additional term for inventions that are sufficiently innovative to overcome the heightened standard. Extending the period during which a patentee may exclude others from using their invention is already well-established in the field of human medicine. The Hatch-Waxman Act established patent term extension, which permits a

72. *See generally* Amy C. Madl, Note, *Using Value-Agnostic Incentives to Promote Pharmaceutical Innovation*, 71 STAN. L. REV. 1305, 1334–36 (2019).

patentee to extend their patent term to compensate for the delay in the applicant's ability to market a drug product covered by the issued patent incurred through the acquisition and submission of information required by the FDA during the drug approval process.[73] As a result of such delays, the patent term may be extended up to five years.[74] Pediatric data exclusivity under section 505A of the Federal Food, Drug, and Cosmetics Act is somewhat analogous, at least in effect.[75] In general, data exclusivity protects data underlying a drug developer's new drug application for a new chemical entity, such as data obtained from clinical trials, and it prevents other applicants from referencing that data in the later applicant's applications for regulatory approval.[76] Pediatric data exclusivity extends this period of protection by an additional six months.[77] Unlike some other forms of data exclusivity, pediatric data exclusivity is additive—where a new drug has been patented before regulatory approval, six months of pediatric data exclusivity does not run concurrently with the patent's term, but rather it extends "six months after the date the patent expires (including any patent extensions)."[78] Thus, a drug developer may receive patent term extension followed by a period of pediatric data exclusivity, further extending the effective monopoly period. Pediatric data exclusivity incentivizes drug developers to endeavor upon clinical trials to test new drugs in pediatric patients, a population often avoided when designing drug safety and efficacy trials, perpetuating the dearth of medicines available to children.

Like patent term extension or pediatric exclusivity, the presently proposed reframing of the obviousness bar could similarly be accompanied by additional term or exclusivity. The ideal outcome would be twofold: (1) a reduction in patent applications directed to minor, less innovative changes to psychedelic therapies related to the psychoactive compound's long-recognized psychological effects; and (2) an incentive to research wholly new derivatives that possess markedly improved characteristics, or methods of using known psychedelic compounds in the treatment of diseases *wholly unrelated*

73. 35 U.S.C.S. § 156(a) (LexisNexis, LEXIS through Pub. L. No. 117-262).
74. § 156(g)(6)(A).
75. 21 U.S.C.S. § 355a(b) (LexisNexis, LEXIS through Pub. L. No. 117-262).
76. 21 U.S.C.S. § 355(c)(3)(E)(ii) (LexisNexis, LEXIS through Pub. L. No. 117-285).
77. § 355(b)(1)(A)(i)(I).
78. 21 U.S.C.S. § 355a(b)(B)(i) (LexisNexis, LEXIS through Pub. L. No. 117-262).

to such compounds' known activity. As an illustrative example, a method of preventing immune system rejection after organ transplant using LSD would need not be burdened with strong consideration of historical prohibition insofar as LSD, at the time it was prohibited, was not known to possess immunological activity. Similarly, a known psychoactive compound so chemically modified as to be distinct from even a "controlled substance analogue"[79] would also not require significant consideration of historical deterrents. The award of additional patent term or regulatory exclusivity for therapies sufficiently innovative to overcome the enhanced obviousness standard would counterbalance disincentives this proposed standard might otherwise introduce.

C. Potential Downstream Effects on Scheduling

Beyond softening the negative effects an enhanced obviousness standard may have on innovation, applying the enhanced standard to methods employing compounds ever having been classified as Schedule I controlled substances—as opposed to only those currently listed as Schedule I—may serve to deter the DEA from so readily categorizing additional compounds as Schedule I controlled substances because the future commercial effect of doing so would be substantially greater. Moreover, as the nature of the administrative state is apt to fluctuate in four- or eight-year cycles, decisions having irreversible consequences may more strongly support keeping new psychedelic therapeutics off of Schedule I. In this way, studies of these compounds may continue without the roadblocks that have delayed the methods being investigated today using LSD and psilocybin.

For example, if a DEA decision to place within Schedule I a psychoactive compound that is otherwise pharmacologically promising results in the loss of tax revenue, pressure from within the executive or legislative branch may be applied to the agency to discourage such characterization. Moreover, raising the patentability bar for methods employing compounds ever having been placed in Schedule I may promote pharmaceutical industry lobbyists to pressure the administrative state to stop compounds from being characterized as Schedule I controlled substances, thus preserving drug developers' ability to market and realize a financial return from the expensive and uncertain drug development endeavor.

79. 21 U.S.C.S. § 802(32) (LexisNexis, LEXIS through Pub. L. No. 117-285).

But the largest players in the pharmaceutical industry may willingly accept an enhanced patentability challenge for such methods because these companies may have their own promising candidates for treating conditions for which long-established psychedelic compounds are now being employed. Even if not, large pharmaceutical companies' greater financial flexibility may permit significant additional development to design around the controlled substance or its analogues.[80] Thus, this proposal may increase the disparity in market access between smaller startups or mid-stage drug development companies and established Big Pharma.[81]

But pharmaceutical science's inherent unpredictability, coupled with the time-limited nature of patents and significant marketability delays due to clinical trials, likely would obviate Big Pharma's quiet acquiescence. For example, structurally modified derivatives of compounds known to exhibit particular effects in humans may fail to exhibit similar effects or any effect at all. Worse yet, such derivatives could demonstrate substantial undesired off-target effects. Unsurprisingly, a compound that is potent, efficacious, and well-tolerated in humans and that possesses properties strongly suggestive of a path to marketability is quite rare—in the pharmaceutical industry, a bird in the hand may be worth hundreds or thousands in the bush. As such, there may be staggering costs, both known and unknown, for designing and synthesizing derivatives that are not "substantially similar" to a corresponding controlled substance and that work as well as, or better than, the controlled substance itself.

Further, despite 20-year patent exclusivity afforded to claims covering a drug,[82] the drug's marketability period is typically much shorter due to requisite clinical trials, which "should ensure the safety and effectiveness of drugs before they make it into the hands of patients."[83] For an approved drug, competition is largely inevitable once patents covering the drug expire. Competitor generics manufacturers need not price their products to cover the costs incurred by the developer associated with the approved drug and all drug candidate failures across the developer's programs. As such, generics manufacturers can provide the same drugs at much lower prices. Thus,

80. 21 U.S.C.S. § 813 (LexisNexis, LEXIS through Pub. L. No. 117-214).
81. *See* Marks & Cohen, *supra* note 65, at 219.
82. 35 U.S.C.S. § 154(a)(2) (LexisNexis, LEXIS through Pub. L. No. 117-285).
83. Michelle Llamas, *Big Pharma's Role in Clinical Trials*, DRUGWATCH (Apr. 24, 2015), https://www.drugwatch.com/featured/clinical-trials-and-hidden-data/ [https://perma.cc/22EJ-VQV6].

the pharmaceutical industry heavily relies on patent exclusivity and is unlikely to willingly accept an administrative agency's cavalier placement of promising, but as-yet unvetted, therapeutics within Schedule I, making it more difficult to obtain treatment method patents under the current proposal.

As such, the pharmaceutical industry's reaction to an enhanced nonobviousness analysis described throughout this Article may include fighting to keep compounds out of Schedule I. Further pitting the pharmaceutical industry against the DEA may also have ramifications in the criminal justice system. Well-funded lobbying against compound placement within Schedule I would mean that illicit production, sale, and use of such compounds likely would carry lesser punishments, the result of which may be a lessened burden on the prison system, to say nothing of general societal aims of rehabilitation and liberty.

V. CONCLUSION

As unpalatable as it may be to some, patent exclusivity is the bedrock upon which pharmaceutical innovation in the United States rests. The investigation of psychedelic compounds—well known to produce marked neurological effects—has long been encumbered by barriers erected through the Controlled Substances Act. These barriers likely have discouraged and delayed innovation that has only recently begun to be developed in earnest. As such, these barriers have undermined the patent system's implicit *quid quo pro* of exclusivity for disclosure and have unjustly delayed new and useful subject matter from entry into the public domain for the benefit of the People.

This Article's proposal—to raise the standard for establishing nonobviousness—provides a framework through which administrative and judicial interpretation of obviousness is applied to compositions and uses of known psychedelic therapeutics, which seeks to account for historical barriers and the subversion of academic and industrial incentive. Apprehension concerning this proposal's adoption as having the potential to disincentivize investment to develop these therapies is reasonable. But this cooling effect may be mitigated through preferential tax treatment or additional opportunities for patent term extension or data exclusivity for those innovations that surpass the heightened standard. These concessions may position industry lobbyists to champion policy change that affords freer public access to anachronistic but effective treatments

using traditional psychedelics and may incentivize the development of next-generation psychedelic therapies.