

October 23, 2026

Drug Enforcement Administration
Attn: DEA Federal Register Representative/DPW
8701 Morrisette Drive
Springfield, Virginia 22152
Via regulations.gov

Re: Schedules of Controlled Substances: Placement of 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT in Schedule I (Docket No. DEA1715)

Dear Administrator Cole:

These comments are submitted in response to the Drug Enforcement Administration's (DEA) notice of proposed rulemaking (NPRM) to place 4-hydroxy-*N,N*-diisopropyltryptamine (4-OH-DiPT), 5-methoxy- α -methyltryptamine (5-MeO-AMT), 5-methoxy-*N*-methyl-*N*-isopropyltryptamine (5-MeO-MiPT), 5-methoxy-*N,N*-diethyltryptamine (5-MeO-DET), and *N,N*-diisopropyltryptamine (DiPT) in Schedule I of the Controlled Substances Act (Docket No. DEA1715).

Through Pinney Associates the authors consult on pharmaceutical drug development and regulatory submissions to the Food and Drug Administration (FDA) on a broad range of CNS-active substances and drug products such as psychedelic substances, new chemical entities, and alternative formulations and routes of delivery, and the development and regulation of potential dietary ingredients and supplements. Our work includes abuse potential assessments for New Drug Applications (NDAs), Eight-Factor Analyses (8FAs) to guide controlled substance scheduling recommendations under the Controlled Substances Act (CSA), and risk management. We consult to companies pursuing therapeutic uses of compounds that would be directly impacted by this proposed rule.

These comments are our own and do not represent those of any company for which we provide or have provided consulting services. Additionally, these comments were not vetted with anyone outside of our company, nor did any outside organization compensate us for our time preparing these comments.

We urge DEA to withdraw the proposed rule. Schedule I placement would set back several clinical-stage development programs and National Institutes of Health (NIH) funded research that is contributing to the development of potentially life-saving medicines that address unmet medical needs. Patient welfare and lives are at stake because of the well-known barriers to clinical research imposed by Schedule I placement (see discussions by Comer et al. 2021; Henningfield, Coe, Griffiths et al. 2022).

We also disagree with the DEA analysis of factors 4, 5, and 6 of the CSA shows a meaningful current or imminent threat to public health and safety that would justify Schedule I placement. There is little evidence of overdose risk, addiction, or diversion of these drugs in the existing data. Thus, Schedule I's bureaucratic requirements are unlikely to substantially reduce any existing levels of misuse, let alone offer benefits that would outweigh their substantial burdens.

Moreover, FDA already rigorously regulates clinical research, with additional oversight at many levels, including by Institutional Review Boards and for research funded by NIH

and the Department of Veterans Affairs (VA). This oversight ensures that research meets requirements for participant safety and diversion prevention. Schedule I placement would impose an unnecessary burden on this research. The additional bureaucratic requirements would significantly increase development costs and greatly delay development programs.

Schedule I placement would delay drug development that is already well underway

In its Regulatory Flexibility Act analysis, the NPRM assumes few researchers will be affected because the substances are not the subject of an investigational new drug application (IND). However, at least two of the five substances, 4-OH-DiPT and 5-MeO-MiPT, are active compounds in clinical-stage programs¹². FDA granted 4-OH-DiPT Breakthrough Therapy designation in February 2026³. Additionally, the bipartisan Congressional Psychedelics Advancing Therapies (PATH) Caucus has made clear that development of medicines in this category is of vital importance to medicine and public health.

Both the 4-OH-DiPT and 5-MeO-MiPT clinical development programs predate the Department of Health and Human Services' April 2, 2026 evaluation, yet the NPRM mentions neither program. If the rule is finalized, every manufacturer, laboratory, and clinical site handling these compounds would need a Schedule I registration and would have to meet Schedule I security, quota, and recordkeeping requirements. These registrations add significant cost, extend timelines, and deter participation by sites that do not already hold them. In addition, Schedule I requirements for FDA and DEA site inspections, staffing evaluations, and approval of protocols and protocol changes can cumulatively add many months and often several years to total development time, along with millions of dollars in additional costs.

The result is delayed new drug application filings, delayed patient access to novel treatments, and a signal to sponsors that work on related compounds carries added regulatory risk.

Recommendations

We recommend that DEA withdraw the proposed rule and instead:

- **Continue surveillance.** DEA should keep tracking these substances through the National Forensic Laboratory Information System (NFLIS)-Drug and the National Poison Data System (NPDS), and work with federal survey sponsors to add them by name to surveys such as the National Survey on Drug Use and Health and Monitoring the Future. If misuse or harm rises meaningfully, DEA can revisit control with substance-specific evidence.

¹

<https://reunionneuro.com/2026/01/20/reunion-neuroscience-presents-full-data-from-reconnect-phase-2-clinical-trial-of-re104-for-the-treatment-of-postpartum-depression-ppd-at-acnp-annual-meeting/>

² <https://www.mindstate.design/press-releases/topline-study-msd-001-clinical-trial-results-and-lead-fixed-dose-combination-program-announcement>

³ <https://www.biospace.com/press-releases/u-s-fda-grants-reunion-neurosciences-luvesilocin-re104-breakthrough-therapy-designation-status>

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- **Manage risk through FDA at approval.** If FDA approves a product containing any of these substances, it will determine, based on an eight-factor analysis and other considerations, whether CSA control is warranted and, if so, which schedule is most appropriate. In addition, or as an alternative, FDA can require a Risk Evaluation and Mitigation Strategy (REMS) to address potential public safety and health risks.

Thank you for the opportunity to provide these comments. Please contact Dan Wang at Pinney Associates at dwang@pinneyassociates.com or (301) 718-8440 if you have any questions or need further information.

Sincerely,

Daniel Wang, Director, Cannabinoids and New Dietary Ingredients, corresponding author

Contributing authors:

Judy Ashworth, MD, Senior Scientific Advisor

Caitlyn Durgin, MS, Associate

Jack Henningfield, PhD, Vice President, Research, Health Policy, and Abuse Liability

Ryan Lanier, PhD, Senior Director, Clinical Development and Abuse Liability

Steve Pype, Senior Data Manager

Mark Sembower, MS, Director, Data Management and Statistical Analysis

REFERENCES

Comer, S. D., Pravetoni, M., Coop, A., Baumann, M. H., & Cunningham, C. W. (2021). Potential unintended consequences of class-wide drug scheduling based on chemical structure: A cautionary tale for fentanyl-related compounds. *Drug and Alcohol Dependence*, 221, Article 108530. <https://doi.org/10.1016/j.drugalcdep.2021.108530>

Henningfield JE, Coe MA, Griffiths RR, Belouin SJ, Berger A, Coker AR, Comer SD, Heal DJ, Hendricks PS, Nichols CD, Sapienza F, Vocci FJ, Zia FZ. Psychedelic drug abuse potential assessment research for new drug applications and Controlled Substances Act scheduling. *Neuropharmacology*. 2022 Nov 1;218:109220. doi: 10.1016/j.neuropharm.2022.109220. Epub 2022 Aug 17. PMID: 35987353.