To the Drug Enforcement Administration and Health and Human Services:

We, the scholars, scientists, social workers, allied healthcare professionals, and activists of Students for Sensible Drug Policy at the University of Michigan, write to oppose the proposed rule outlined in "Docket No. DEA-623," which is titled "Schedules of Controlled Substances: Placement of 4-hydroxy-N,N-diisopropyltryptamine, 5-methoxy-alpha-methyltryptamine, 5-methoxy-N-methyl-N-isopropyltryptamine, 5-methoxy-N,N-diethyltryptamine, and N,N-diisopropyltryptamine in Schedule I." The proposed rule rests on a gross misrepresentation of fact, specifically regarding the medicinal and scientific value of these substances and their purported harms. We also find serious flaws with the reasoning and evidence supplied in the Docket, which will be elaborated below. The DEA and HHS recommendation should be reevaluated in light of broad evidence-based opposition to placing these chemicals, especially DiPT and 4-OH-DiPT, into Schedule I of the 1970 Controlled Substances Act.

The only purpose for this proposed rule is to inhibit medical and scientific research as a rebuke to the psychedelic renaissance; and as such is an inappropriate motivation for federal legislation. Recreational consumption and sales of these substances are already illegal under the Federal Analogues Act. So, the only reason to place these tryptamines in Schedule I is to make the work of psychedelic medical science more costly and difficult. Researchers like Tactogen CEO Matthew Baggott have already stated that they are currently working with these chemicals (5-MeO-MiPT in Tactogen's case) and would cease to do so if these substances are scheduled.[1]

The scientific consensus about psychedelic drugs has dramatically changed since HHS's original 2012 report and their recent affirmation of the original report is a deeply flawed judgment that should be revisited. A tidal wave of research is released daily supporting the promising medicinal value of psychedelics. Psychedelics have demonstrated efficacy for a variety of physical and mental ailments. Based on promising preliminary results, psychedelics are aggressively being investigated further for their value in treating addiction and other compulsive behaviors,[2] depression,[3] anxiety,[4] post-traumatic stress,[5] eating disorders,[6] autism,[7] cluster headaches,[8] migraines,[9] chronic pain,[10] traumatic brain injury,[11] anxiety surrounding old age, grave illness, and impending death;[12] as well as inspiring creative problem solving,[13] occasioning mystical experiences,[14] and serving as bona fide religious sacraments.[15]

These facts indicate that the placement of psychedelic drugs in Schedule I is a substantial error that needs immediate rectification. We endorse Panacea Plant Sciences assessment of the available data, which indicates that no psychedelic compound should be in schedule I "as the entire class of drugs is being investigated for their method of action being key to providing mental health treatments. It would seem unacceptable and disingenuous for the DEA/FDA to approve medical trials using 5ht2a agonists and even specifically 4-OH-DIPT and then ask for the compounds to be placed in schedule 1, which would ultimately hinder future medical research and clinical applications." The proposed rule is misguided and relies on a fundamentally flawed analysis.

"Docket No. DEA-623" shows precisely the opposite of what it purports to show. Namely, these substances are largely benign to users and the public; and, as already argued, they likely have a net positive value to society and individuals. The Docket asserts that "There is evidence that

individuals are taking the drug or other substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community." This is belied by the DEA's own assessment that there has been only one death eighteen years ago associated with one of these compounds, 5-MeO-AMT, which the Docket notes was coadministered with bupropion and alcohol and "it is unclear what role 5-MeO-AMT played in the death." The Docket asserts substantial similarity to LSD; yet in a discrimination study "5-MeO-AMT did not fully substitute for any of the training drugs[,]"[16] one of which was LSD.

The tryptamines the Docket proposes placing in Schedule I have no known cytotoxicity.[17] Taking 5-MeO-MiPT at low doses "did not cause any serious histopathological effects on the liver, kidney, and brain."[18] In fact, a review of the existing research on tryptamines, including the specific substances named in the Docket, explains that "the tryptamine compounds are unlikely to cause life-threatening changes in cardiovascular, renal or hepatic function because of their little or no affinity for relevant biological receptors and targets[.]"[19]

DiPT and 4-OH-DiPT have immense value to the scientific community. DiPT is one of the only chemicals capable of reliably producing auditory hallucinations,[20] and as such is a powerful tool for researchers trying to understand how the brain processes sound. The immense burdens Schedule I would place on researching such a unique chemical is likely to impede research that could lead to breakthrough understanding of the auditory system and the resulting medical applications.

Per the proposed rule and the Federal Analogues Act, each of the compounds' analogues would also become subject to Schedule I. The rule would end up banning over 100 compounds.[21] Notably, the proposed rule could jeopardize Field Trip's Phase I study of F-104, a prodrug of 4-OH-DiPT,[22] which aims to mimic the antidepressant properties of psilocybin[23] and expand the therapeutic potential by inducing a shorter-lasting "high."

The DEA is essentially demanding a perfect safety profile, at all doses and in all polydrug combinations, from psychedelics, which is a standard not applied to other classes of drugs. By this standard, other drugs associated with hospitalizations and any confirmed deaths would also merit inclusion in Schedule I. Yet, we all have acetaminophen in our medicine cabinets, despite the fact that "Acetaminophen overdose is the leading cause for calls to Poison Control Centers (>100,000/year) and accounts for more than 56,000 emergency room visits, 2,600 hospitalizations, and an estimated 458 deaths due to acute liver failure each year."[24]

The DEA reports hundreds of police encounters, a handful of hospitalizations, and single polydrug death in all reported history for all five of the tryptamines in question, compared to alcohol, a drug which is implicated in millions of hospitalizations and tens of thousands of deaths in America every year.[2526] Further: "Evidence from the British Medical Association found that alcohol use is associated with 60-70 per cent of murders, 70 per cent of stabbings, 50 per cent of fights or assaults in the home. For non-violent offences the association is very strong as well: 88 per cent of those arrested for criminal damage, 83 per cent for breach of the peace, 41 per cent for theft and 26 per cent for burglary, had drunk in the four hours prior to their arrest."[27] This intimates that public and individual safety is not the determining factor in this recommendation, but other, unspoken factors are at play in the DEA's proposed rule.

Moreover, the Docket states that there is no significant problem of diversion from legitimate sources for these drugs. Indeed, one group of experts concludes that "there are no examples of a significant diversion of research drugs (Schedule I or otherwise) into recreational use."[28] So, there is no need to place additional costs and barriers on legitimate scientific and medical research by scheduling these five tryptamines, or any other psychedelics.

The Docket unhelpfully conflates repeated use with dependence and harm. Psychedelics are widely demonstrated to have anti-addictive properties. LSD is not addictive;[29] nor is psilocybin;[30] while MDMA has shown effectiveness as a complement to psychotherapy in the treatment of PTSD.[31] It is not factual to claim that the five tryptamines the Docket names pose a threat to public health when the Docket repeatedly argues for the similarities between them and three out of the five least-harmful widely-used drugs.[32] That people return to an experience periodically is no indicator of dependence, which is defined by withdrawal symptoms, something characteristic of long-term use of medications like benzodiazepines or opioids (not Schedule I drugs). People repeat a variety of pleasurable and enriching experiences: swimming, attending church, eating, taking a vacation, and none of these automatically equate to physical dependence or psychological craving, let alone continued use despite negative consequences (addiction).

Additionally, it was disturbing to see the way existing federal law is twisted to support the DEA's overarching mission of promulgating and enforcing prohibition. The DEA notes that proposed rules must comply with the Regulatory Flexibility Act, which mandates that laws not have "significant economic impact on a substantial number of small entities." Substantial is defined by *West's Encyclopedia of American Law* as: "Belonging to substance; actually existing; real; not seeming or imaginary; not illusive; solid; true; veritable."[33] The thirty-one domestic chemical houses identified by the DEA as selling these compounds are dismissed with a rhetorical sleight-of-hand by which their sales don't matter simply because the DEA doesn't like them. These sales are real, true, and verifiable, and thus meet the definition of substantial. Despite not being afoul of existing law, in which instance the DEA would shut them down, the sales of these chemical houses are discounted because they're not registered with the DEA for scientific research. The DEA admits it does not know the volume of sales, meaning it is impossible for regulators to know they're abiding by the RFA. This abuse of existing law results in an Ahab-like pursuit of prohibition at all costs, flying in the face of democratic governance and American free-market capitalism.

We are further distraught at the DEA's lack of citations for referenced research, citing only federal law and the vague gesture to "NFLIS data." If citizens and organizations are supposed to assess the DEA's claims to intelligently provide public comment, then it is incumbent upon the DEA and HHS to share their sources and data. The HHS report does not seem to be available to the public. This is not the way consequential scientific and public health decisions should be made: with the public and stakeholders in the dark.

This proposed rule flies in the face not only of medical science, but also the DEA's own stated support for a White House proposal to ease research restrictions on substances already in Schedule I,[34] as well as the Office of National Drug Control Policy directives to embrace harm

reduction.[35] Embracing psychedelic research amidst the overdose crisis is harm reduction, due to the aforementioned potential to treat addiction.

It is imperative that the DEA finally learn from over a century of failures to achieve a drug-free America (or even a reduction in drug use) and the incalculable harms perpetrated on people both here and abroad. Attempts at interdiction have failed, with more people dying of overdoses during the pandemic than ever before,[36] despite reduced border traffic by land, air, and sea. The war on relatively safe prescription opioids has ravaged chronic pain patients who are now unable to access adequate quantities of prescribed medications, endure provider disruptions, and suffer an epidemic of suicides.[37] Meanwhile, recreational opioid users shifted to heroin, which due to the iron law of prohibition pressured markets to increase potency for smuggling efficiency,[38] leading to the rash of fentanyl and fentalogue overdose deaths. The DEA's increased pressure on illicit fentanyl will soon become an epidemic of nitazene deaths, then when that crackdown begins a more powerful class to evade the increased criminalization. Stop the chemical arms race!

In the strongest possible terms, we urge the DEA and HHS not to pass this proposed rule and to change the broken scheduling system that the Controlled Substances Act has burdened the American people with (along with a broad slice of the rest of the world through our domination of United Nations processes). The scheduling system inhibits legitimate medical and scientific research, fails patients, exposes recreational users to an increasingly volatile and dangerous black market drug supply, and wrongly apportions the relative risks of the substances it classifies. Return the assessment of drugs' utility and the ability to dispense without fear of prosecution to physicians and pharmacists instead of instituting a regime of restriction and fear that leaves Americans sicker, in greater suffering, and more susceptible to death.

To summarize, based on the following reasons these five tryptamines should not be placed in Schedule I: 1. These drugs are already in use in medical research, including FDA-approved studies; 2. Due to proven medical benefits, tryptamines are inappropriately placed in Schedule I as a class ("no currently accepted medical use"); 3. Individuals are not using these substances in sufficient amounts to constitute a broad threat to public health; 4. These substances do not constitute a significant risk to human health, except in high dose or polysubstance combinations, like all drugs; 5. There is no known or claimed problem of diversion of chemicals from legitimate research purposes; 6. Repeated use does not equate to dependence, abuse, or addiction, and these substances likely have limited abuse potential due to tryptamine's fast and powerful development of tolerance; 7. Further, dependence is characteristic of drugs in lower Schedules; 8. This rule abuses the DEA's responsibility under the Regulatory Flexibility Act by disregarding existing sales, which it cannot say do not exceed the financial threshold established by the RFA; 9. The proposed rule is opposed to the DEA's own stated support for the White House's plans to ease research and the ONDCP's directives to embrace harm reduction; 10. Finally, DiPT and 4-OH-DiPT have unique scientific and medical potential that deserve special consideration.

Sincerely,

Students for Sensible Drug Policy at the University of Michigan

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