UNITED STATES DISTRICT DEPARTMENT OF JUSTICE

Drug Enforcement Administration

In the Matter of **Scheduling 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT**	**Docket No. 22-15**

STATEMENT OF SHANE PENNINGTON, J.D.

My name is Shane Pennington. I am a practicing attorney at Vicente Sederberg LLP. I routinely work with clients in the controlled substances space. In my practice, I advise clients on federal controlled substances law and, in particular, DEA regulations governing registration to handle Schedule I psychedelic substances under the Controlled Substances Act. I also research, publish, and speak publicly on the CSA, its history, and DEA regulations.[1]

I obtained my J.D. from the University of Texas School of Law and served as a law clerk to federal judges on the D.C. Circuit, the Fifth Circuit, and the D.C. District Court.[2]

I offer this testimony as an expert in the history of controlled substances regulation, controlled substances policy, and regulatory alternatives available to DEA. I do not offer a legal opinion on the legal issues in this case, only my experience and observations.

Exhibits

M&TX 27 is a May 7, 1969, memorandum I obtained from Mr. Zorn who had obtained the document from the Nixon Archives. The document is a memorandum from Michael Sonnenreich, the Deputy Chief Counsel of the Bureau of Narcotics and Dangerous Drugs.

[1] *See* https://vicentesederberg.com/people/shane-pennington/.

[2] Because of my law practice, I also qualify as an interested person.

Sonnenreich is widely known as one of the architects of the CSA. In the document, he addresses arguments made in staff papers from the Department of Health, Education, and Welfare (HEW) regarding the draft "Controlled Dangerous Substances Act of 1969." He notes that a "major bone[ ] of contention" between the Justice Department and HEW that had "been discussed with staff members of HEW time and time again" was which department would have ultimate control over drug scheduling. **M&TX 27** at 1. Sonnenreich explains that under the new framework, control of drugs is not "purely a scientific and medical determination." **M&TX 27** at 2. He also explains that abuse potential is a trigger, to be followed by a scientific evaluation from HEW and other scientific bodies to determine potential for abuse. On the law enforcement side, agencies evaluate information from actual street abuse. After all the information is presented, Sonnenreich explains that it is a "policy determination whether or not a drug should be controlled." **M&TX 27** at 2. That policy determination includes, among other things "the practical problems of enforcement." **M&TX 27** at 2.

M&TX 28 is a March 13, 1969, memorandum I obtained from Mr. Zorn who had obtained the document from the Nixon Archives. The document is a memorandum from Will Wilson, the Assistant Attorney General to the Attorney General. This document demonstrates that in 1969, it was recognized that new scientific advances may yield new insights abpit old drugs and that such new scientific developments might warrant revisiting the original classifications. **M&TX 28** at 5.

M&TX 63 are pages from the February 9, 1970 FDC Reports I obtained from Mr. Zorn who had obtained the document from the Nixon Archives. The document discusses and summarizes discussions leading up to the passage of the Controlled Substances Act and concerns over the roles of HEW and the Attorney General in issuing medical and scientific findings in

scheduling proceedings. In particular, I note congressional concerns that a future Attorney General might seek "to build up his [department]… by bringing in a great number of scientists…"

M&TX 26 is a June 4, 1969 memorandum from Patrick Gray to Hugh Durham on HHS letterhead I obtained from Mr. Zorn who had obtained the document from the Nixon Archives. The document discusses HEW's involvement in decisions to subject a substance to control and an objection that such a decision is essentially a medical decision and should rest with HEW, or alternatively, that the Attorney General should be required to obtain the scientific advice and consent of the HEW Secretary in making decisions to control.

Discretion Not to Schedule Drugs that Meet Scheduling Criteria

DEA has exercised discretion not to schedule or to delay the scheduling of drugs that may meet the scheduling criteria, including Schedule I criteria, for policy reasons, such as enforcement difficulties and impact on ongoing medical research.

Take Nutmeg. "Because of its euphoric and hallucinogenic effects, nutmeg has been widely abused as a cheap substitute for narcotic drugs since the 12th century." **M&TX 15** at 2. **M&TX 41** is a 1968 article discussing the use of nutmeg as a psychotropic drug. **M&TX 17** describes nutmeg ingestion calls received by Texas poison centers from 1998 to 2004. The article discusses the constituents of nutmeg, describing them as potentially having effects similar to amphetamine, a Schedule II drug available by prescription, and LSD, a Schedule I drug. **M&TX 17** considered 17 cases of nutmeg intoxication over 7 years to be "extremely rare" and concluded that nutmeg abuse did not result in serious medical outcomes requiring the involvement of health care facilities. **M&TX 17** at 4.

Notably, at the time Congress enacted the CSA, nutmeg was a known drug of abuse, considered to be a narcotic, and believed to be dangerous when consumed in large quantities,

evidenced by **M&TX 13** at 109.[3] Congress did not place nutmeg on the schedules, however. Nor has DEA scheduled nutmeg in the interim, despite it being regarded as a drug having a potential for abuse and no accepted medical use. Indeed, there is evidence that Nutmeg is being abused by America's youth. In 2020, for example, there was a dangerous trend on TikTok called the "nutmeg challenge" that encouraged TikTok users to consume quantities of nutmeg that would cause hallucinations. **M&TX 9, M&TX 22**. *See also* **M&TX 15** at 2 (noting several reports of nutmeg abuse in adolescents to achieve a "euphoric state at low cost" and "widespread use"). By all accounts, nutmeg has been and is currently more abused than each of the five tryptamines.

Despite open and potentially wide-spread abuse by youth, to my knowledge, DEA has never taken any action to schedule nutmeg. Likely this is because, despite a well-documented danger of overdosing and hallucinations surrounding the substance, nutmeg is often a common food item sold in grocery stores nationwide and it takes a high quantity of consumption of nutmeg to cause harm. This underscores a point reflected in the Sonnenreich memorandum introduced above, **M&TX 27**, and consistently repeated in the legislative history[4]: DEA has discretion to evaluate whether scheduling a drug that is actually being abused would be in the public interest.

The case of tiletamine presents an important historical example of this discretion that is directly relevant to this case. **M&TX 35** at 3. On August 11, 1986, the Administrator proposed placing tiletamine and zolazepam into Schedule I and preparations containing equal weights of the drug into Schedule III. The action was in response to a letter from HHS recommending that the

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[3] **M&C 13** is a hearing transcript from the legislative history to the CSA. Pages 93 to 112 of **M&TX13** are parts of the publication entitled "Answers to the Most Frequently Asked Questions About Drug Abuse" read into the record.

[4] For example, **M&TX 13** at 13 explains that "[a]n affirmative decision to control involves more than medical and scientific determination. It has important policy, legal and enforcement implications, as well."

combination product be placed into Schedule III due to a New Animal Drug Application for the combination product.

First, in 1981, the administrator determined that individually neither ingredient was approved for marketing as a therapeutic agent or met the criteria for Schedule III. The Administrator proposed placing tiletamine, a chemical analog of the Schedule II drug, PCP, into Schedule I. That 1981 proposal was met by objection from the American Association of Zoo Veterinarians and Warner-Lambert Company, the pharmaceutical company that made tiletamine and zolezapam, and a request for hearing. In response, the Administrator withdrew the proposed rule, but the combination drug never came to market.

A second pharmaceutical company notified DEA of an intent to market the combination product in 1985. The Administrator ultimately concluded that "[f]inalization of rules applicable to the scheduling of tiletamine and zolazepam as individual entities is not warranted at this time." Despite the fact that tiletamine was a PCP analog, the agency reached this conclusion on grounds that neither substance was "perceived to pose a significant threat to the health and general welfare at this time," "neither had been encountered in the illicit trade," and "neither is available as a commercial product." **M&TX 35** at 3. Importantly, the Administrator also noted that tiletamine was a controlled substance analog having a chemical structure and pharmacological profile substantially similar to PCP, and therefore, persons engaged in activities contrary to the Analogue Act could be prosecuted. With respect to zolazepam, the Administrator did not find the drug was subject to the Analogue Act; however, if it was encountered in the illicit trade and found to be an imminent hazard to public safety, the substance could be emergency scheduled under § 811(h). The Administrator concluded that these legal considerations were taken "so as to accommodate

legitimate industry in the production and marketing of a Food and Drug Administration approved product." **M&TX 35** at 3.

Continuing to regulate the five tryptamines as controlled substance analogues, as was the case with tiletamine, presents an obvious regulatory alternative to avoid derailing ongoing valuable scientific and medical research that would affect numerous small start-up business seeking to develop new medicines to treat disorders such as suicidal depression, treatment resistant depression, post-traumatic stress disorder, and more. My understanding is that at least four small businesses would be affected by the proposed rule, and maybe more.

Ergine or LSA is an example of a hallucinogenic drug without medical uses that is not in Schedule I. Ergine or LSA is the active chemical in morning glory seeds. It was known in 1970 that morning glory seeds were hallucinogens, evidenced by their listing alongside Schedule I hallucinogens such as mescaline, psilocybin, LSD, DOM (STP), and MDA in the legislative history. **M&TX 13** at 101. Yet Congress placed ergine in Schedule III. At no point has ergine been moved to Schedule I, despite its status as a known hallucinogen.

I further note that HHS, in addition to DEA, has discretion not to recommend that drugs be scheduled when presented with newer scientific data. Kratom is a recent example. **M&TX 8** is an October 17, 2017 letter from HHS to then-Acting Administrator Robert Patterson recommending the active constituents in kratom, mitragynine and 7-OH-mitragynine, be placed in Schedule I. The letter concludes that both had pharmacological effects similar to morphine, a Schedule II opiate. **M&TX 8** at 4. The compounds showed activity in opioid receptors and that individuals developed cross-tolerance with morphine. **M&TX 8** at 5. The letter notes kratom is used to achieve a "legal high." **M&TX 8** at 9. Throughout, the letter provides evidence of kratom abuse.

On August 16, 2018, HHS reversed course, instead recommending the substances not be controlled at the time "until scientific research can sufficiently support such an action." **M&TX 21** at 1. The letter noted that the HHS decision was based on "many factors" including "new data" a "lack of evidence," and notably, "unknown and potentially substantial risk to the public health if these chemicals were scheduled at this time." **M&TX 21** at 1. HHS changed its recommendation based on the review of "new scientific data" including an animal study that indicated mitragynine actually reduced morphine intake. **M&TX 21** at 3 (citing **M&TX 18**). One study, **M&TX 19**, for example, was an anonymous online survey which showed 40.9% of individuals used kratom to reduce or stop opioid use, including opioid medications and heroin. Kratom also helped reduce opioid withdrawal symptoms. The study criticized the reasoning behind the Schedule I classification, noting that the 44 possible kratom-related deaths over the previous decade mostly involved other substances or preexisting medical conditions. **M&TX 19** at 7. The paper concludes by noting that "[i]f controlled research in humans finds that kratom exhibits analgesic effects with minimal abuse liability and risk of respiratory depression, this could provide a much-needed avenue towards the development of novel medications for pain management and potentially OUD." **M&TX 19** at 7.

According to the HHS letter, the new data suggested that mitragynine did not satisfy the first of the three statutory requisites for Schedule I, "irrespective of broader considerations of public health." **M&TX 21** at 3. Despite the data presented in the 2017 letter, the 2018 recommendation concluded that "the level of scientific data and analysis presented by the FDA and available literature do not meet the criteria for inclusion of *kratom* or its chemical components in Schedule I of the CSA at this time." **M&TX 21** at 3. A footnote in the letter also expresses concern about the impact of scheduling *kratom* on the ability to conduct research, consistent with

the tiletamine decision discussed above and the policies underlying the CSA. **M&TX 21** at 3 n.1. Despite a recognition that *kratom* may have harmful effects and had no medical use, HHS recommended a wait-and-see approach. **M&TX 21** at 4.

I note that two of the same authors of **M&TX 19** authored a similar observational study involving psychedelic use, **M&TX 18**, concluding, much as **M&TX 19** does, that those who used psychedelics with substance use disorders showed a dramatic decrease in their use of harmful substances. Over 70% reported greatly reducing or quitting a primary substance following a psychedelic experience. **M&TX 18** at 9. Also, most respondents reported no persisting adverse effects from their psychedelic experience. **M&TX 18** at 8. The article concludes that "psychedelic-assisted interventions for addictions may offer an attractive alternative to current treatment models in that they may result in lasting change in substance misuse after only one or a few psychedelic administration sessions." **M&TX 18** at 12.

How Schedule I Hampers Research

It is widely acknowledged and well-documented that Schedule I controls restrict research and hurt innovation in the psychedelic medicine arts. *See, e.g.*, **M&TX 60** at 4. The head of the National Institute of Drug Abuse, Dr. Nora Volkow, has repeatedly testified and explained publicly how Schedule I adversely impacts research. For example, at an appropriations hearing, she testified "the moment that a drug gets a Schedule I, which is done in order to protect the public so that they don't get exposed to it, it makes research much harder.". "This is because [researchers] actually have to through a registration process that is actually lengthy and cumbersome."[5]

I have reviewed, for example, the comments of Matthew Johnson, one of the most published scientists on the human effects of psychedelics. **GX 3** at 174-202. Johnson states that he

[5] https://www.marijuanamoment.net/top-federal-drug-policy-expert-says-marijuanas-schedule-i-status-inhibits-research/ (describing and linking to Volkow's testimony).

is "not convinced by DEA's underlying rationales for proposing to schedule 4-OH-DiPT and by the very serious implications that would befall me and my fellow clinical researchers in the field if the DEA were to actually move forward with its scheduling proposal on 4-OH-DiPT." He notes that placing a compound such as 4-OH-DiPT in Schedule I in the middle of drug development initiatives can effectively bring those efforts to a halt. Johnson notes that it is uniquely important that development of 4-OH-DiPT continue because it has a "novel receptor profile directed at neuro plasticity." He notes the "absence of any current data on its abuse potential." He further contends the 2012 evaluation is outdated and relies on incomplete and erroneous analyses as to the actual or potential for abuse of 4-OH-DiPT. "[I]t could not reasonably be concluded in 2012 -- and it certainly cannot be concluded ten years later in 2022 -- that 4-OH-DiPT is readily available to be abused or actually being illicitly diverted or abused."

The comment of another witness, Anita Clayton, M.D., **GX 3** at 293-347, another extraordinarily accomplished researcher, reinforces Johnson's testimony. She highlights the potential usefulness of 4-OH-DiPT in treating post-partum depression. She comments that placing an investigational medicinal product that is the focus of ongoing research and development erects daunting barriers to the advancement of the biomedical research enterprise and that placing 4-OH-DiPT on Schedule I would curb significant public health advancements that could meaningfully expand treatment of unmet needs in women's health research. She testifies that adding roadblocks to this research would be a "grave disservice to women's health research generally and to the millions of women who are in desperate need of treatments for their medical conditions." She agrees with Johnson that "[m]uch has happened over the ensuing decade" with respect to the medical and scientific understanding of 4-OH-DiPT and there is no evidence of "abuse and diversion."

The comments of these witnesses are consistent with my experience working with small businesses and researchers seeking to research Schedule I substances. To be sure, DEA has made strides in improving its application process for research on Schedule I drugs. In 2018, for example, the agency streamlined the application process by creating a dedicated web portal. In addition, I note that from a legal standpoint, a Schedule I classification does not present an insurmountable barrier to researching a substance. Many researchers I've worked or interacted with have Schedule I licenses.

Nonetheless, a Schedule I classification presents significant hurdles. For example, researchers who need to modify a study of a Schedule I substance—including adjusting the quantity being used—sometimes must re-register with DEA, causing delays. DEA sometimes requires researchers to obtain multiple registrations for every physical site at which they carry out studies into Schedule I drugs. Some researchers report that obtaining a new registration can take more than a year, and that differing interpretations of the Schedule I registration requirements among local DEA field offices, as well as distinct federal and state registration requirements, complicate the process.

DEA's Approach to Scheduling

I note three final historical points related to regulatory practice under the CSA relevant to these proceedings.

First, historically, DEA has looked at *relative* abuse potential. For example, in the Basis for the Recommendation to Schedule Tramadol in Schedule IV of the Controlled Substances Act, DEA considered the relative abuse potential of tramadol.[6] DEA noted more than 10,000 emergency department visits from Tramadol use. DEA then noted that these numbers were less

[6] https://downloads.regulations.gov/DEA-2013-0010-0001/attachment_3.pdf.

than Schedule II opiates such as fentanyl, methadone, morphine, and oxycodone. Based on this and other information (such as limited reinforcing effects), DEA concluded that Tramadol had an abuse potential less than that of Schedule III drugs and similar to that of Schedule IV drugs.

In the carisoprodol scheduling action, **M&TX 46**, the number of non-medical uses of carisoprodol over the period between 2004 and 2007 was estimated to be between 2,525,000 and 2,840,000 million. The Administrator agreed with the Secretary of HHS that assessing the abuse potential of a substance considers multiple factors, data sources and analyses, including the prevalence, frequency, and manner of use in the general public and specific subpopulations, the amount of material that is available for illicit use, as well as evidence relevant to populations that may be of particular risk. **M&TX 46** at 008. DEA placed carisoprodol into Schedule IV because, among other reasons, the abuse frequency suggested that carisoprodol was being abused at a similar rate to a Schedule IV benzodiazepine (diazepam). **M&TX 46** at 028.

The example of synthetic dronabinol is also instructive. In 1998, DEA rescheduled Marinol (THC in sesame oil and encapsulated in soft gelatin capsules) from Schedule II to III of the CSA. **M&TX 45**. The agency concluded that the pharmacological and behavioral effects of dronabinol were comparable to those of THC and marijuana. Nonetheless, there was "little evidence of actual abuse." DEA noted that despite the drug's "THC-like abuse liability" there were several factors that deterred actual abuse and trafficking, including the drug's formulation in sesame oil and the improbability that THC would be extracted from the product. DEA noted that the scientific data reviewed to date and the "minimal evidence of actual abuse and trafficking." Based on this evidence, DEA concluded that Marinol had a potential for abuse less than the drugs or other substances in Schedules I and II and transferred the drug to Schedule III.

Second, as discussed above, Congress listed substances without medical uses, including hallucinogens, in other schedules. For example, as discussed above, ergine or LSA is an LSD precursor. It is psychedelic, a 5-HT2A receptor agonist, and has potential for abuse. Yet it is listed in Schedule III. LSA has never been approved for medical use in treatment.

Third, FDA has recognized in other contexts that drugs in the same class (such as stimulants, opiates, benzodiazepines, or hallucinogens) may have different potentials for abuse. In 1997, the Food and Drug Administration (FDA) in conjunction with other Federal agencies convened a hearing on benzodiazepines and related substances to distinguish among them to address appropriate scheduling under the CSA.[7] At issue were more than a dozen different benzodiazepines. The FDA Federal Register publication noted that between 1983 and 1993, most benzodiazepines were controlled "without differentiation," but recent studies (circa 1997) suggested benzodiazepine substances may be distinguishable by pharmacologic properties that influence their abuse liability characteristics and that a review of the clinical literature reflected differences in "attractiveness" to abusers. That research showed that, based on pharmacokinetic profiles and self-administration studies in animals, lorazepam and diazepam appeared to have high abuse liability, while oxazepam, halazepam, and chlordiazepoxide had less potential for abuse than diazepam. The FDA further stated that "recent research suggests that benzodiazepines may be distinguishable on the basis of their specific potential for abuse."

Regulatory Alternatives

There are regulatory alternatives available to DEA with respect to analogues of Schedule I substances that have shown little signs of abuse: using the Analogue Act. 21 U.S.C. § 813.[8]

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[7] 62 Fed. Reg. 33418 (June 19, 1997).

[8] The proposed rule appears to have an impact on a substantial number of small entities and researchers. In this hearing, the rule appears to impact Mindstate, Tactogen, Panacea Life Sciences, Field Trip, Wallach & Morris, and Nicholas Denomme.

Congress enacted the Analogue Act in 1986 to combat a problem with "designer drugs." Until 1986, the CSA defined controlled substances strictly with regard to the precise chemical makeup of the substances described in the schedules. This allowed underground chemists to make a minor alteration in the molecular structure of a scheduled substance and obtain an unscheduled substance that may produce some or all the effects of a scheduled drug. To deal with this issue, Congress enacted the Analogue Act, which permits the federal government to treat a "controlled substance analog," to the extent intended for human consumption, as a controlled substance in Schedule I.

The drafters of the Analogue Act did not intend for the legislation to interfere with medical research. Then-Senator Joe Biden explained at **M&TX 42** at 3:

> I wish to make clear that this legislation is not aimed at legitimate drug research that unwittingly falls within the designer drug definition. This act specifically exempts substances manufactured, possessed, or distributed in conformance with the new drug approval provision of the Federal Food, Drug, and Cosmetic Act. Early stage, clinical research is also protected by the new drug approval requirement for investigational use. These exemptions were included to prevent interference with legitimate research and development of new pharmaceuticals. Industrial and nonclinical applications are not affected since they are not intended for human consumption.

DEA's approach in this case is troubling for several reasons, most prominently, DEA relying on a 10-year-old evaluation and recommendation. What is equally troubling, however, is how DEA's approach is at odds with how Congress structured the CSA with the Analogue Act. As these remarks show, the Analogue Act balances the need to research analogues of Schedule I substances by including a "human consumption" requirement. It is hard to square DEA's approach in the proposed rulemaking in this case—scheduling five substances with little to no track record of abuse and that have presented no significant risk to the public—with the Analogue Act. In

addition, 21 U.S.C. § 811(h) provides DEA authority to temporarily schedule an analogue in the event one does present significant danger to the public.

According to DEA's method in this case, any Schedule I analogues that could show resemblance to one or more already scheduled drugs in a rat discrimination study should also be put on Schedule I. If that is the case, the Analogue Act serves almost no purpose.

The Analogue Act also presents an obvious regulatory alternative to scheduling the five substances at issue in these proceedings. Certainly, the Analogue Act presents law enforcement difficulties, particularly the need to prove that a substance is a "controlled substance analog" to a jury. But DEA has used the Analogue Act effectively in the past to deal with analogues and designer drugs, such as Operation Web Tryp. **M&TX 56**. Indeed, the successful use of the Analogue Act to stop the unlawful distribution of analogues, commensurate with the level of abuse and without unduly interfering with research, appears to be shown by **GX 5** at Appendix 3, which outlines the successful arrest and prosecution of vendors selling research chemicals that, under the Analogue Act, were not being used for research, were being sold for human consumption, and therefore could be treated as Schedule I substances.

In addition, the Attorney General (and by delegation DEA) has another alternative available. Under the CSA, the agency has authority to promulgate rules, regulations, and procedures that the agency deems necessary and appropriate for the efficient execution of his functions under this subchapter. 21 U.S.C. § 871(b). To the extent the agency believes it is necessary to execute their functions under the CSA, the agency, for example, could require documentation, licensing, or verification to sell analogues "not for human consumption."

I certify under penalty of perjury that the foregoing is true and correct.

Executed on 7/14/22

Shane Pennington, J.D.