U.S. Department of Justice

Drug Enforcement Administration

Schedule of Controlled Substances: Placement of 4-hydroxy-*N*,*N*-diisopropyltryptamine (4-OH-DiPT), 5-methoxy-*alpha*-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) into schedule I

Background, data, and analysis: Eight factors determinative of control and findings pursuant to 21 U.S.C. 812(b)

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I. Background

Hallucinogens are a diverse group of natural and synthetic substances that alter perception, cognition, and mood. The subjective effects of hallucinogens drive their use. The abuse of these substances can lead to a variety of adverse health effects, such as paranoia, agitation, depression, and violent outbursts, towards self and others (Carbonaro et al., 2016).

Tryptamines are a well-defined structural class known as indolealkylamines, where an indole ring structure is joined to an amino group by a two-carbon side chain. Tryptamines are a broad class of hallucinogens that includes schedule I substances in the Controlled Substances Act (CSA) such as *N,N*-dimethyltryptamine (DMT), *alpha*-methyltryptamine (AMT), 5-methoxy-*N,N*-diisopropyltryptamine (5-MeO-DiPT), 5-methoxy-*N,N*-dimethyltryptamine (5-MeO-DMT), *N,N*-diethyltryptamine (DET), and psilocyn (the primary active compound in psychoactive/hallucinogenic *Psilocybe* mushrooms). Tryptamine hallucinogens generally produce effects similar to those from lysergic acid diethylamide (LSD), 4-methyl-2,5-dimethoxy-amphetamine (DOM), and other schedule I hallucinogens, including profound alterations in sensory perceptions (e.g. visual, auditory, and gustatory), mood, and thought in humans. Reports of intoxication and deaths associated with the use of tryptamines have been described.

The Drug Enforcement Administration (DEA) and international bodies continue to monitor law enforcement and public health data pertaining to the trafficking and use of tryptamines. Tryptamine hallucinogens, both natural and synthetic substances, are readily available over the Internet and are sold through illicit channels. Their abuse has been associated with both acute and long-term public health and safety problems, including emergency room admissions and deaths. This class of substances is generally encountered in tablet, capsule, or powder forms.

4-Hydroxy-*N,N*-diisopropyltryptamine (4-OH-DiPT), 5-methoxy-*alpha*-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) are tryptamine hallucinogens.

These five tryptamines have no known medical use in the United States (U.S.) and are not marketed internationally as approved drug products. They have all been reported as drugs of abuse in the U.S. by law enforcement authorities and identified in seizures. In response to reports of abuse and trafficking, DEA gathered and reviewed the available information regarding the pharmacology, chemistry, trafficking, actual abuse, pattern of abuse, and the relative potential for abuse and dependence of these hallucinogens. On December 19, 2008, DEA sent this data review document to the Assistant Secretary for Health of the Department of Health and

Human Services (HHS)[1] with a request to provide scientific and medical evaluations and scheduling recommendations for these five tryptamines (pursuant to 21 U.S.C. 811(b) of the Controlled Substances Act (CSA)).

On March 29, 2012, May 17, 2012, and August 14, 2012, HHS provided to DEA five separate scientific and medical evaluations and scheduling recommendations for the above mentioned five tryptamines. The scientific and medical evaluations were entitled: 1) "Basis for the Recommendation to Control 4-Hydroxy-N,N-diisopropyltryptamine (4-OH-DIPT) and its Salts in Schedule I of the Controlled Substances Act (CSA);" 2) "Basis for the Recommendation to Control 5-Methoxy-alphamethyltryptamine (5-MeO-AMT) and its Salts in Schedule I of the Controlled Substances Act (CSA);" 3) "Basis for the Recommendation to Control N-Isopropyl-5-Methoxy-N-Methyltryptamine (5-MeO-MIPT) and its Salts in Schedule I of the Controlled Substances Act (CSA);" 4) "Basis for the Recommendation to Control N,N-Diethyl-5-methoxytryptamine (5-MeO-DET) and its Salts in Schedule I of the Controlled Substances Act (CSA);" and 5) "Basis for the Recommendation to Control N,N-Diisopropyltryptamine (DIPT) and its Salts in Schedule I of the Controlled Substances Act (CSA)." Following consideration of the eight factors and findings related to each of the substances' abuse potential, lack of legitimate medical use, and lack of accepted safety for use under medical supervision, HHS recommended that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT and their respective salts be controlled in schedule I of the CSA under 21 U.S.C. 812(b).

The CSA requires the Administrator of DEA, as delegated by the Attorney General,[2] to determine whether HHS's scientific and medical evaluation, scheduling recommendation, and all other relevant data constitute substantial evidence that a substance should be scheduled. 21 U.S.C. 811(b). This document contains an explanation of DEA's determination to place 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT in schedule I of the CSA.

II. Eight Factors Determinative of Control

Pursuant to 21 U.S.C. 811(c), DEA must consider eight factors in making any findings of substantial evidence of potential for abuse, including the data from law enforcement information relevant thereto.

[1] As discussed in a memorandum of understanding entered into by the Food and Drug Administration (FDA) and the National Institute on Drug Abuse (NIDA), FDA acts as the lead agency within HHS in carrying out the Secretary's scheduling responsibilities under the CSA, with the concurrence of NIDA. 50 FR 9518, Mar. 8, 1985. The Secretary of HHS has delegated to the Assistant Secretary for Health of HHS the authority to make domestic drug scheduling recommendations. 58 FR 35460, July 1, 1993.

[2] 28 CFR 0.100(b).

Factor 1: The Substances' Actual or Relative Potential for Abuse

In addition to the information HHS provided in its scientific and medical evaluation documents (HHS, 2012a-e), DEA considers all other relevant data regarding the actual or relative potential of abuse of 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT. The term "abuse" is not defined in the CSA, however the legislative history of the CSA suggests the following four prongs in determining whether a particular drug or substance has a potential for abuse[3]:

a) *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; or*

Data show that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT have been encountered by law enforcement (Factor 5). Based on published case reports in the medical literature and anecdotal reports (Factor 2), HHS states that these substances are being abused for their hallucinogenic properties (HHS reviews, 2012a-e). HHS has determined that consumption of these five tryptamines due to their hallucinogenic properties poses a safety hazard to the public health. Abuse of 5-MeO-AMT and 5-MeO-MiPT has been associated with hospital emergency room admissions. A death of a 19-year old woman, who abused 5-MeO-AMT in combination with alcohol and the antidepressant bupropion, occurred in 2004.

b) *There is significant diversion of the drug or substance from legitimate drug channels; or*

HHS states in the 2012 reviews that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT are not Food and Drug Administration (FDA)-approved drug products for treatment in the United States and is unaware of any country in which its use is legal. As of June 2020, DEA remains unaware of any country approving these drugs for medical use. There appear to be no legitimate sources for 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT as marketed drugs (HHS reviews, 2012a-e). The DEA notes that these five tryptamines are available for purchase from legitimate chemical companies because they are used in scientific research. No evidence of diversion is apparent from these companies. As such, this characteristic of abuse potential is not applicable.

[3] Comprehensive Drug Abuse Prevention Control Act of 1970, H.R. Rep. No. 91-1444, 91st Cong., Sess. 1 (1970), reprinted in U.S.C.C.A.N. 4566, 4603.

c) Individuals are taking the substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such substance; or

According to HHS, 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT are not approved for medical use and practitioners may not legally prescribe these substances. In June 2020, DEA has confirmed with HHS that their 2012 statements are still applicable. Therefore, individuals are taking 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT on their own initiative, rather than based on medical advice from a practitioner licensed by law to administer drugs. This is consistent with the data from law enforcement seizures and case reports indicating that individuals are taking 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT on their own initiative rather than on the medical advice of a licensed practitioner, possibly for the similar hallucinogenic effects produced by LSD and DET while simultaneously circumventing criminal prosecution since these are not scheduled substances (HHS reviews, 2012a-e)(see Factor 5 for more detailed information).

d) The drug is a new drug so related in its action to a drug or other substance already listed as having a potential for abuse to make it likely that the drug substance will have the same potential for abuse as such drugs, thus making it reasonable to assume that there may be significant diversion from legitimate channels, significant use contrary to or without medical advice, or that it has a substantial capability of creating hazards to the health of the user or to the safety of the community.[4]

As stated by HHS (HHS reviews, 2012a-e), 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT are structurally related to schedule I hallucinogens of the tryptamine class and produce similar pharmacological effects to other natural and synthetic schedule I hallucinogens.

4-OH-DiPT

According to HHS, 4-OH-DiPT elicits pharmacological responses similar to the schedule I substances DOM and LSD, which have no accepted medical use and have high abuse potential (HHS review, 2012a). In drug discrimination studies (an *in vivo* test to assess drug abuse liability of test drugs in comparison to known drugs of abuse) in rats, 4-OH-DiPT fully generalizes for the discriminative stimulus effects of DOM (Forster et al., 2006a) and LSD (Gatch and Forster 2006f). Additionally, 4-OH-DiPT produces classic hallucinogenic effects such as perceptual distortions and pleasurable physical effects.

[4] Comprehensive Drug Abuse Prevention Control Act of 1970, H.R. Rep. No. 91-1444, 91st Cong., sess. 2 (1970); 1970 U.S.C.C.A.N. 4566, 4601.

HHS lists the risks and effects of 4-OH-DiPT consumption as follows: hallucinations, euphoria, fatigue, headache, gastrointestinal distress, insomnia, and anxiety. HHS states that these effects are like those of schedule I hallucinogens. HHS also ascertains that based on the psychological and cognitive disturbances associated with effects of 4-OH-DiPT, it is reasonable to assume that this substance has a substantial capability to cause a hazard to public health, both to the user and to the community.

5-MeO-AMT

According to HHS, 5-MeO-AMT elicits pharmacological responses similar to the schedule I substances LSD and DET, which have no accepted medical use and have high abuse potential (HHS review, 2012b). Drug discrimination data demonstrate that 5-MeO-AMT produces partial generalization for the discriminative stimulus effects of LSD in rats (Gatch and Forster, 2006g). In humans, 5-MeO-AMT produces hallucinogenic effects similar to those produced by LSD and DET, including visual and auditory hallucinations. In addition to visual and auditory hallucinations, 5-MeO-AMT, similar to these schedule I hallucinogens, produces other adverse effects including fatigue, headache, gastrointestinal distress, insomnia, and anxiety. Euphoria has also been reported by 5-MeO-AMT users. Based on the hallucinogenic and other effects caused by 5-MeO-AMT, HHS states that it is reasonable to assume that this substance has substantial capability to cause a hazard to public health, both to the user and to the community.

5-MeO-MiPT

According to HHS, 5-MeO-MiPT elicits pharmacological responses similar to the schedule I substances LSD and DMT, which have no accepted medical use and have high abuse potential (HHS review, 2012c). Drug discrimination studies showed that 5-MeO-MiPT fully generalizes to the discriminative stimulus effects of DOM in rats, but partially generalizes to the discrimination stimulus effects of LSD (Gatch and Forster 2006i), DMT (Gatch and Forster 2006e) and 3,4-methylenedioxy-methamphetamine (MDMA, schedule I) (Rutledge et al., 2007b). HHS also states that 5-MeO-MiPT is 15-fold more potent than DMT in producing hallucinogenic effects in humans (Jacob and Shulgin, 1984). Thus, HHS concluded that it is reasonable to assume that 5-MeO-MiPT has substantial capability to cause a hazard to public health, both to the user and to the community.

5-MeO-DET

According to HHS, 5-MeO-DET elicits pharmacological responses similar to the schedule I substances DMT and DOM, which have no accepted medical use and have high abuse potential (HHS review, 2012d). In animal drug discrimination studies, 5-MeO-DET fully generalizes for the discriminative stimulus effect of DMT in rats (Gatch and Forster 2006c). 5-MeO-DET partially generalizes to the discriminative stimulus cues of DOM (Rutledge et al 2006c) and MDMA (Forster et al., 2006c). The reports from users describe the effects of 5-MeO-DET as being similar to those produced by DMT and LSD. HHS mentions that 5-MeO-

DET use, similar to some schedule I hallucinogens, is associated with adverse health risks such as bizarre behavior, hallucinations, and sympathomimetic effects (increased heart rate). HHS ascertains that based on this information, it is reasonable to assume that 5-MeO-DET has substantial capability to cause a hazard to public health, both to the user and to the community.

DiPT

According to HHS, DiPT elicits pharmacological responses similar to the schedule I substances DOM and DMT, which have no accepted medical use and have high abuse potential (HHS review, 2012e). Drug discrimination studies showed that DiPT fully substitutes for the discriminative stimulus effects of DOM (Rutledge et al., 2006e) and DMT (Gatch and Forster 2006d) in rats. The reports from users describe the effects of DiPT as being similar to those produced by the schedule I hallucinogens 4-bromo-2,5-dimethoxyphenethylamine (2C-B), 2-(2,5-dimethoxy-4-methylphenyl)ethanamine (2C-D), and 2,5-dimethoxy-4-ethylamphetamine (DOET). HHS indicates that the risks associated with DiPT use are based on the perceptual changes in the auditory experience. In addition, HHS states that like schedule I hallucinogens, DiPT produces adverse effects such as auditory and other sensory distortions, lethargy, nausea, hyperreflexia, and mydriasis. HHS ascertains that based on the adverse effects associated with DiPT, it is reasonable to assume that this substance has substantial capability to cause a hazard to public health, both to the user and to the community.

Factor 2: Scientific Evidence of the Substances' Pharmacological Effects

As stated by HHS (HHS reviews, 2012a-e), the neurochemical effects of 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT mainly involve the serotonergic system in the central nervous system (CNS). Tryptamine hallucinogens are believed to produce their characteristic effects primarily through stimulation of the 2A subtype of serotonin (5-HT) receptors (5-HT_{2A}; Rickli et al., 2016; Gatch et al., 2011; Nichols 2004; Rabin et al., 2002; Hill and Thomas, 2011; Nichols and Nichols, 2008; HHS review, 2012a-e). DEA further notes that the 5-HT_{2A} receptor has also been shown to mediate the *in vivo* behavioral effects and discriminative stimulus effects of the three classes of classic hallucinogens, ergotamines (e.g., LSD), phenethylamines (e.g., DOM), and tryptamines (e.g., DMT) (e.g., Nichols, 2016; Carbonaro et al., 2015; Gatch et al, 2011; Rabin et al., 2002).

In Vitro Studies

Data from *in vitro* receptor binding and functional studies can be used to assess the pharmacological effects related to abuse of tryptamine hallucinogens. As noted by HHS (HHS reviews, 2012a-e), 4-OH-DiPT (K_i = 229 ± 5.6 nM), 5-MeO-AMT (K_i = 33 ± 5.5 nM), 5-MeO-MiPT (K_i = 42 ± 11 nM), 5-MeO-DET (K_i = 251 ± 92.0 nM), and DiPT (K_i = 910 ± 120 nM), similar to schedule I serotonergic hallucinogens (e.g., DMT, DET, DOM, LSD), have binding

affinity for the 5-HT_{2A} receptor as evaluated using [^{125}I]DOI as the radioligand to measure binding to 5-HT_{2A} receptor. Using arachidonic acid release to measure cellular function, 5-MeO-AMT, 4-OH-DiPT, 5-MeO-DET, 5-MeO-MiPT, and DiPT, like many schedule I hallucinogens, act as agonists at the 5-HT_{2A} receptor and produce 87, 108, 115, 106, and 88% maximal LSD effect, respectively (Janowsky and Eshleman 2006a-e; Gatch et al., 2011). DEA notes that a study by Rickli et al. (2016) showed similar results for 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, and DiPT. 5-MeO-DET was not tested in that study. DEA further notes that recent *in vitro* 5-HT_{2A} receptor binding (using [^{3}H]5-HT as the radioligand) and functional (as measured by inositol phosphate-1 (IP-1) production) studies also reported similar findings for these five tryptamines (Table 1; Janowsky, 2018a-f, 2019a-c).

Table 1: *In vitro* 5-HT_{2A} receptor binding and functional results for 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, DiPT, and select schedule I hallucinogens.

	Binding		Function (IP-1 formation)	
Drug	K_i (nM)	Hill Coefficient	EC_{50} (nM)	% of 5-HT maximal effect
4-OH-DiPT	335 ± 69	-1.14 ± 0.31	633 ± 97	102.7 ± 4.5
5-MeO-AMT	15 ± 2.8	-0.95 ± 0.13	8 ± 4.4	102.0 ± 11
5-MeO-MiPT	113 ± 31	-1.21 ± 0.05	290 ± 62	89.1 ± 0.7
5-MeO-DET	138 ± 5	-1.16 ± 0.03	280 ± 120	84.2 ± 8.7
DiPT	320 ± 120	-0.96 ± 0.11	420 ± 140	81.4 ± 3.9
DPT	374 ± 97	-1.10 ± 0.11	943 ± 88	85.2 ± 5.1
5-MeO-DiPT	162 ± 32	-1.00 ± 0.14	84 ± 20	99.7 ± 2.7
DMT	267 ± 30	-1.2 ± 0.03	628 ± 94	34.8 ± 1.9
DET	530 ± 120	-1.05 ± 0.06	612 ± 97	46.1 ± 6.7
Psilocyn	79 ± 23	-1.05 ± 0.13	69 ± 22	48.3 ± 6.9
DOM	18.4 ± 2.3	-1.03 ± 0.05	56 ± 16	93.4 ± 3.4
LSD	0.59 ± 0.13	-1.27 ± 0.23	1.73 ± 0.21	67.4 ± 1.9

Source: Janowsky, 2018a-f, 2019a-c. Radioligand used was [^{3}H]5-HT.

HHS notes (HHS reviews, 2012 a-e) tryptamine hallucinogens often also bind to 5-HT_{1A} receptors in the brain. There have been reports of partial involvement of 5-HT_{1A} receptors in tryptamine-induced hallucinations (Hill and Thomas, 2011; Nichols and Sanders-Bush, 2001). 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, similar to some schedule I hallucinogens, bound to and functioned as agonists at 5-HT_{1A} receptors. DiPT and 4-OH-DiPT showed weaker effects at this receptor, as determined by evaluating a second messenger system associated with GTP (guanosine-5'-triphosphate) (Table 2).

Table 2: *In vitro* 5-HT$_{1A}$ receptor binding and functional results for 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, DiPT, and select schedule I hallucinogens.

	Binding		Function ([^{35}S]GTPγS binding)	
Drug	K_i (nM)	Hill Coefficient	EC_{50} (nM)	% of 5-HT maximal effect
4-OH-DiPT	8400 ± 2000	-0.71 ± 0.08	3900 ± 1100	36.1 ± 9.9
5-MeO-AMT	207 ± 56	-0.82 ± 0.03	680 ± 250	100.6 ± 7.9
5-MeO-MiPT	108 ± 21	-0.85 ± 0.05	560 ± 230	116.2 ± 4.2
5-MeO-DET	24 ± 8	-0.84 ± 0.07	380 ± 110	103.0 ± 6.2
DiPT	2270 ± 600	-1.01 ± 0.15	4570 ± 640	58.1 ± 9.8
DPT	186 ± 31	-1.04 ± 0.09	274 ± 55	98.5 ± 7.5
5-MeO-DiPT	149 ± 7	-0.76 ± 0.02	56 ± 20	93.8 ± 6.7
DMT	368 ± 50	-0.92 ± 0.01	340 ± 120	103.5 ± 3.9
DET	370 ± 25	-0.93 ± 0.06	270 ± 90	102.9 ± 1.5
Psilocyn	374 ± 25	-0.83 ± 0.02	138 ± 25	97.9 ± 5.6
DOM	10700 ± 1700	-0.84 ± 0.08	6500 ± 1700	83.2 ± 7.4
LSD	2.77 ± 0.65	-1.04 ± 0.07	1.81 ± 0.52	100.6 ± 4.2

Source: Janowsky, 2018a-f, 2019a-c. Radioligand used was [^{3}H]8-OH-DPAT.

As stated by HHS, 5-MeO-AMT, 5-MeO-MiPT, and 5-MeO-DET had weak (K_i values > 1000 nM) or no significant affinity at the three monoamine transporters: serotonin transporter (SERT) (Table 3), norepinephrine (NE) transporter (NET) and dopamine (DA) transporter (DAT) and do not induce the release of NE, 5-HT, or DA, in studies that used human epithelial kidney (HEK) cells which expressed human DAT, SERT, or NET (HHS, 2012a-e; Janowsky and Eshleman 2007a-e; Gatch et al., 2011). However, 4-OH-DiPT and DiPT had greater affinity for SERT (K_i values = 219 and 265 nM, respectively; Table 3), but not significant affinity for DAT or NET. Similar results were published in 2016 for 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT (Rickli et al., 2016), and DiPT (Rickli et al., 2016; Cozzi et al., 2009). DEA further notes, in rat synaptosomes, DiPT (Blough et al., 2014) had reasonable affinity for SERT, whereas 5-MeO-AMT (Nagai et al. 2007; Nonaka et al., 2007), 5-MeO-MiPT (Blough et al., 2014; Nagai et al., 2007; Nonaka et al., 2007), and 5-MeO-DET (Blough et al., 2014), at best, weakly blocked reuptake of monoamines IC_{50} values greater 1000 nM (i.e., 3 μM – 37 μM). Nagai et al. (2011) also observed that in rat synaptosomes, 5-MeO-AMT induced release of DA, 5-HT, and NE with EC_{50} values of 1.5 μM, 460 nM, and 8.9 μM, respectively.

SERT binding and function data for 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT and select schedule I serotonergic hallucinogens are presented in Table 3.

Table 3: *In vitro* SERT binding and functional results for 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, DiPT, and select schedule I hallucinogens.

	Binding		Function (Inhibition of 5-HT uptake)
Drug	**K_i (nM)**	**Hill Coefficient**	**IC_{50} (nM)**
4-OH-DiPT	219 ± 53	-0.66 ± 0.09	131 ± 16
5-MeO-AMT	8270 ± 350	-1.96 ± 0.20	1980 ± 530
5-MeO-MiPT	4040 ± 500	-1.04 ± 0.14	2680 ± 460
5-MeO-DET	3520 ± 190	-1.29 ± 0.03	2990 ± 680
DiPT	265 ± 21	-0.82 ± 0.04	215 ± 72
DPT	480 ± 34	-1.12 ± 0.07	172 ± 35
5-MeO-DiPT	874 ± 71	-1.07 ± 0.03	239 ± 39
DMT	5300 ± 1200	-1.19 ± 0.06	366 ± 81
DET	1200 ± 170	-1.01 ± 0.08	254 ± 29
Psilocyn	3650 ± 270	-1.00 ± 0.11	1140 ± 210
DOM	45300 ± 1700	-1.30 ± 0.07	45700 ± 2400
LSD	> 10 µM	> 10 µM	> 10 µM

Source: Janowsky, 2018a-f, 2019a-c. Radioligand used was [^{125}I]RTI-55.

As concluded by HHS, the complex pharmacology of 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT involve two serotonin sites, one of which (5-HT_{2A} receptor) is likely to mediate their hallucinogenic effects.

CNS Effects

HHS evaluated the CNS effects of 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT using data from animal studies and reported effects in humans, and concluded that pharmacological effects of these tryptamines are similar to those of several schedule I hallucinogens.

Preclinical Studies

According to HHS reviews (HHS, 2012a-e), 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT have been assessed in some psychopharmacological assays including drug discrimination, and locomotor activity.

Locomotor Effects

HHS (HHS reviews, 2012a-e) reported that in mice intraperitoneal (i.p.) administration of 4-OH-DiPT (10 and 30 milligram/kilogram [mg/kg]), 5-MeO-AMT (3 and 10 mg/kg), 5-MeO-MiPT (10 and 30 mg/kg), and DiPT (30 mg/kg) decreased locomotor activity, whereas 5-MeO-MiPT (10 mg/kg) and 5-MeO-DET (10 mg/kg) increased locomotor activity, compared to effects observed after saline administration at the same time periods. Locomotor effects generally occurred by 10 minutes and lasted 30-80 minutes. The stimulatory effects of 5-MeO-MiPT occurred at 50 minutes and lasted 110 minutes. These results indicate that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT have CNS effects and can change behavior. DEA further notes that the half effective dose (ED_{50}) that produced the changes in locomotor activity were 15.8, 2.3, 9.6, 0.24, and 26.3 mg/kg (i.p.) for 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT, respectively (Gatch et al., 2011; Elsken and Forster, 2006a-e).

4-OH-DiPT (30 mg/kg) produced ataxia in two out of eight mice tested. 5-MeO-MiPT at 100 mg/kg (i.p.) dose caused death of all eight mice tested. DiPT at 56 mg/kg (two out of eight mice) and 100 mg/kg (i.p.) (all eight mice tested) doses also caused death.

Discriminative Stimulus Effects

As mentioned by HHS (HHS, 2012a-e), drug discrimination is an experimental method used to determine whether an animal experiences the physiological or behavioral effects of a particular drug as similar to the physiological or behavioral effects of another drug (or class of drugs) to which the animal was previously exposed. DEA further notes that drugs that have discriminative stimulus effects in common with a known drug of abuse are also likely to be abused. Generally, there is strong correspondence between the discriminative effects of drugs of abuse in animals and their effects in humans (Solinas et al., 2006). Thus, drug discrimination is widely used to determine whether or not a drug or substance is pharmacologically similar to a known drug of abuse.

In the preclinical drug discrimination model, a laboratory animal, often a rodent, is trained to press two separate levers based on different stimulus effects of drug versus its vehicle such as saline (or the absence of a drug stimulus cue). After the animals reliably learn the discriminative stimulus effect of the trained drug (e.g., reliably discriminate between the effects of the training drug and vehicle), a test drug with unknown effects is administered. The animals' lever selection indicates whether the novel or test drug is or is not similar to the learned training drug-associated effects. If the novel drug produces ≥ 80% drug-appropriate responding, then the drug is said to have full substitution for the trained drug. Data from drug discrimination studies conducted by a NIDA contract researcher are summarized in Table 4.

Table 4: Summary of drug discrimination study results for 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT tested in separate groups of rats trained on various hallucinogen and stimulant drugs.

Training drug / Test drug	LSD	DMT	DOM	MDMA	Methamphetamine	Cocaine
4-OH-DiPT	Full	Partial 67%	Full	Partial 65%	Partial 52%	Partial 55%
5-MeO-AMT	Partial 67%	Partial 43%	None <40%	None <40%	None <5%	None <20%
5-MeO-MiPT	Partial 67%	Partial <40%	Full	Partial 59%	None <5%	None <40%
5-MeO-DET	None <20%	Full	Partial 40%	Partial 59%	None ~20%	None <40%
DiPT	Partial 68%	Full	Full	None ~20%	Partial 52%	None <40%

Source: Forster et al., 2006a-h; Gatch and Forster 2006a-o; Rutledge et al., 2006a-e; Rutledge et al., 2007a,b.

DEA adds that Carbonaro et al. (2013) conducted a drug discrimination study in rats to determine if hallucinogens and stimulants substituted for the stimulus characteristics of DiPT in DiPT-trained rats. The substances studied were LSD, DOM, DMT, MDMA, and (+)-methamphetamine. LSD, DOM, and MDMA fully substituted, DMT partially substituted, and methamphetamine failed to substitute for DiPT-discriminative stimulus effects.

Based on the drug discrimination data, HHS concluded (HHS reviews, 2012a-e) that stimulus properties of: 4-OH-DiPT are similar to DOM and LSD, and partially similar to DMT; 5-MeO-AMT substantially overlaps with LSD; 5-MeO-MiPT substantially overlaps with DOM, LSD, and MDMA; 5-MeO-DMT are similar to DMT, DOM, and MDMA; and DiPT are similar to DOM and DMT, and are partially similar to LSD.

DEA notes that adverse effects were observed during these drug discrimination tests including vocalization when held (5-MeO-MiPT and 5-MeO-DET), delayed righting reflex (4-OH-DiPT and 5-MeO-AMT), decreased food consumption after testing (4-OH-DiPT, 5-MeO-AMT, and 5-MeO-MiPT), convulsions (DiPT), rear leg paralysis (4-OH-DiPT and 5-MeO-MiPT), and tremors (5-MeO-MiPT). One rat had to be euthanized 48 hours after 5-MeO-MiPT administration due to adverse effects. The more serious adverse effects were observed after i.p. administrations of 5, 10, and 25 mg/kg of the respective drugs. Further testing of some drugs was limited due to adverse effects.

Head Twitch Response

DEA further notes that hallucinogenic drugs that are 5-HT_{2A} receptor agonists have been shown to produce head twitch response (HTR) characterized as a high-frequency and rapidly repeating head rotation in rats and mice (Fantegrossi et al., 2008; Halberstedt and Geyer, 2014, 2018; Canal and Morgan, 2012), but not by non-hallucinogenic 5-HT_{2A} receptor agonists such as lisuride and ergotamine (Hanks and Gonzalez-Maeso, 2013). HTR in rodent models is considered to be predictive of hallucinogenic potential in humans.

DiPT has been shown to produce a HTR (Carbonaro et al., 2015; Smith et al., 2014). A 5-HT_{2A} receptor inverse agonist blocked the dose-dependent (2.5 – 10 mg/kg, i.p.) HTR produced by DiPT in mice (Carbonaro et al., 2015).

Clinical Reports

As stated by HHS, clinical studies to evaluate the effects of 4-OH-DiPT, 5-MeO-DET, and DiPT using formal clinical protocols under institutional settings have not been reported in the published scientific literature. However, subjective effects in humans for these three tryptamines have been reported through individual case reports or summaries of anecdotal reports usually on Internet forums. Because these anecdotal reports were not conducted under formal clinical protocols in institutional settings (HHS reviews, 2012a-e), HHS notes that these sources have limited reliability and the information may not be entirely representative of the effects of the respective drugs. There are limited published clinical studies for 5-MeO-AMT and 5-MeO-DiPT.

4-OH-DiPT

According to HHS (2012a), there have been no published clinical studies on the effects of 4-OH-DiPT in humans. HHS cited a book publication that described the effects of oral ingestion of 15-20 mg of 4-OH-DiPT on adult volunteers (Shulgin and Shulgin, 1997). Changes in muscle tension and the perception of their body temperature were reported after ingesting 15 mg. After ingesting 20 mg, effects including very mild visual and perceptual distortions, followed by philosophical musings, locomotor alterations, and sexual feelings were reported. Onset of effects for both doses were rapid (15 minutes) and these effects lasted 2 to 3 hours.

HHS also cites anecdotal reports, starting in 2003, on drug user websites. According to these reports, 4-OH-DiPT is typically used orally for hallucinogenic effects. Adverse psychological or physiological effects that were frightening or disturbing to the user were also reported.

5-MeO-AMT

Based on clinical studies evaluating the effects of 5-MeO-AMT conducted in healthy adults in the early 1960s, HHS (2012b) stated that the subjective effects of 5-MeO-AMT were similar to those produced by LSD and DET in humans. HHS cited an anecdotal/observational/experimental study by Kantor et al. (1980) in which six adult volunteers orally ingested 2 to 4 mg of 5-MeO-AMT and reported experiencing perceptual alterations such as enhanced color awareness, visual distortions, a sensation of time expansion, insomnia, and "considerable" analgesia that did not affect fine motor coordination. Maximum intensity occurred 2-4 hours after ingestion. The volunteers also reported adverse effects such as "extensive retinal activity," nausea, and gastrointestinal disturbances.

HHS cited information from Shulgin and Shulgin (1997) which summarized anecdotal reports by users on the effects of orally ingested 2.5 to 4.5 mg of 5-MeO-AMT. Early adverse effects reported were gastrointestinal disturbances, such as nausea, vomiting, and diarrhea. A full hallucinogenic response was reported at higher doses, which lasted up to 18 hours. Smoking 5 mg resulted in similar effects.

According to HHS's summary of some anecdotal reports posted on the Erowid website, with first reports in 2000, individuals are using doses less than 5 mg of 5-MeO-AMT. Some effects of 5-MeO-AMT mentioned include euphoria, levity, visual and auditory hallucinations, fatigue, headache, gastrointestinal distress, insomnia, and anxiety. This substance is purchased either as a liquid or tablet.

The death of a 19-year old woman in 2004 was associated with the use of 5-MeO-AMT. According to a report by the Spokane Medical Examiner's Office in Spokane, Washington, 5-MeO-AMT was identified in the urine, blood, and serum of the deceased, along with alcohol and a metabolite of bupropion (an antidepressant) in the urine. The medical examiner concluded on the report that the woman died of toxic encephalopathy. However, it is not clear from this report whether 5-MeO-AMT had a direct role in causing this death.

5-MeO-MiPT

HHS (2012d) cited a clinical study in which orally administered 5-MeO-MiPT (5 mg/kg) produced hallucinogenic effects. Onset of the effects occurred 9-16 minutes after administration and lasted 3-3.2 hours. HHS summarized that 5-MeO-MiPT produces general heightening of awareness along with amphetamine-like stimulation. HHS also cited a paper by Jacob and Shulgin (1984) which reported that 5-MeO-MiPT was 15-fold more potent than DMT when comparing doses that produce hallucinogenic effects.

HHS summarized some anecdotal reports on the effects of 5-MeO-MiPT posted on the Erowid website. Oral consumption (4-6 mg) was the primary route of administration; however,

smoking (10-15 mg) was also reported. The hallucinogenic effects of 5-MeO-DiPT were fairly rapid (15-20 minutes) and long lasting (4-7 hours). A wide range of effects were reported including, but not limited to: euphoria, mood elevation, intensification of tactile sensations and smell, sexual interest, relaxation, feeling of body and muscle energy, visual distortions, and color intensification. Adverse effects included tremor, emotional lability, muscle tension and discomfort, and difficulty sleeping.

5-MeO-DET

According to HHS (2012c), there have been no published clinical studies on the effects of 5-MeO-DET in humans. HHS cited a book publication containing anecdotal information on effects of 5-MeO-DET in humans (Shulgin and Shulgin, 1997). According to these reports, 1 to 3 mg (oral) 5-MeO-DET produced psychoactive effects lasting for 3 to 4 hours. Hallucinogenic effects were also produced after smoking 10 mg of 5-MeO-DET. Reported adverse effects included: dizziness, trembling, anxiety, restlessness, cold sweats, and visual alteration.

HHS also cited anecdotal reports on drug user websites. The reports noted that 5-MeO-DET was typically taken orally or smoked. The effects reported were euphoria, levity, visual and auditory hallucinations, fatigue, headache, gastrointestinal distress, insomnia, and anxiety. Users also reported that 5-MeO-DET caused psychological or physiological effects that are frightening or disturbing to the user.

DiPT

HHS (2012e) cited a published report by Shulgin and Carter (1980) which summarized anecdotal reports by users on the effects of DiPT ingested orally. Threshold doses were above 16 mg, with more intense experiences occurring between 20-50 mg. The experiences began 20-30 minutes after ingestion, peaked around 1.5 to 2 hours, and persisted for longer than 4 hours. The most prominent response was auditory distortions. Adverse effects reported were lethargy, lack of perception of environment, nausea, hyperreflexia, and mydriasis. The users reported that the lack of "intense hallucinogenesis" yet profound "modifications of emotional and intellectual process" was similar to schedule I hallucinogens 2C-B, 2C-D, and DOET. DEA notes that tinnitus has been noted as an adverse effect (Hill and Thomas, 2011).

HHS cited a book publication that described effects of oral doses ranging from 25 to 100 mg of DiPT in adult volunteers (Shulgin and Shulgin, 1997). HHS (2012e) notes that the only perceptual change reported were auditory effects, with sounds generally taking on a deeper or more "bass" tonality. The effects diminished within 4 hours and completely disappeared within 8 hours. A rapid onset (4-8 minutes) of effects were reported after smoking 8 mg DiPT, with exclusively auditory effects. HHS also summarized anecdotal reports on the effects of DiPT posted on the Erowid website, with first reports in 2000, to be primarily or exclusively changes in auditory perception. The effects reported by users were consistent with the two anecdotal

reports cited by HHS. One user reportedly consumed 2 grams of DiPT over one year and experienced symptoms associated with the King-Kopetzky syndrome, which involves difficulty in hearing speech in the presence of background noise.

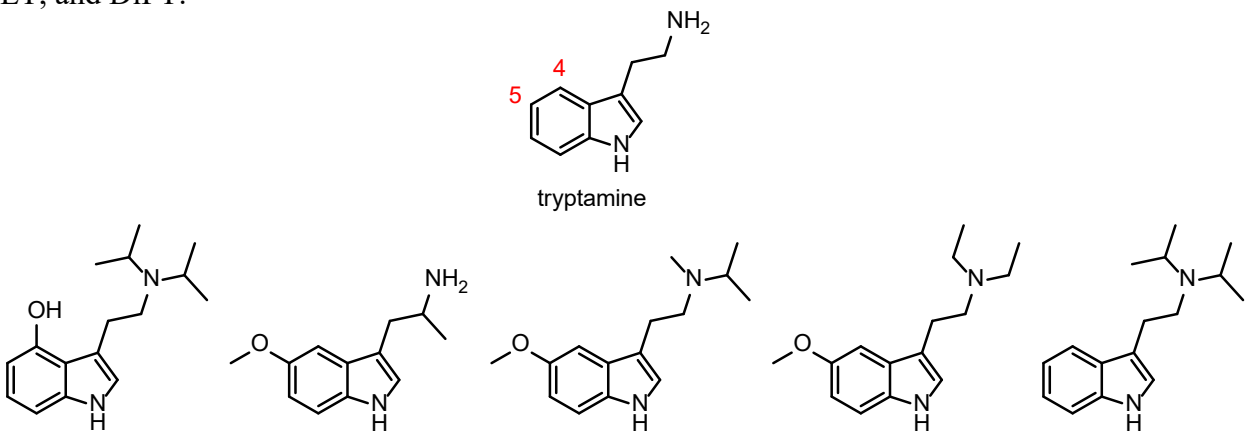
Summary

In summary, 5-MeO-AMT, 4-OH-DiPT, 5-MeO-DET, 5-MeO-MiPT, and DiPT produce similar psychopharmacological effects (e.g., discriminative stimulus effects) produced by other controlled hallucinogens (i.e., LSD, DOM) and tryptamine hallucinogens (i.e., psilocyn, DMT, DET, 5-MeO-DiPT).

Factor 3: The State of Current Scientific Knowledge Regarding the Substance

4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT are part of the tryptamine family and share the core tryptamine structure with substitutions at the α-position, 4-position, 5-position, and on the nitrogen (N) atom (**Error! Reference source not found.**). All of these substances contain an indole ring with a substituted ethylamino sidechain. 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT share structural similarities with schedule I tryptamine hallucinogens such as DMT, DET, AMT, and psilocyn (Figure 2).

Figure 1: Chemical structures of tryptamine, 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT.

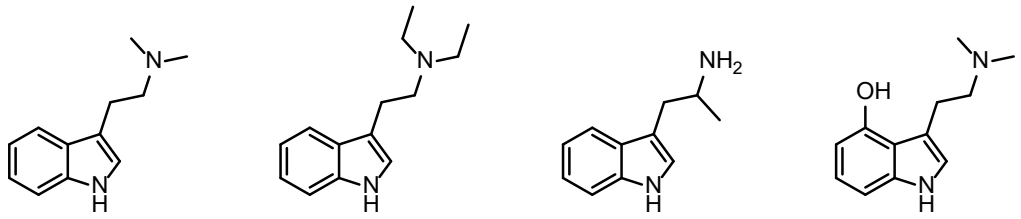


Synonyms include:

1. 4-OH-DiPT – 4-hydroxy-*N*,*N*-diisopropyltryptamine; 3-(2-(diisopropylamino)ethyl)-1*H*-indol-4-ol; iprocin
2. 5-MeO-AMT – 5-methoxy-*alpha*-methyltryptamine; 5-methoxy-α-methyltryptamine; 1-(5-methoxy-1*H*-indol-3-yl)propan-2-amine
3. 5-MeO-MiPT – 5-methoxy-*N*-methyl-*N*-isopropyltryptamine; *N*-(2-(5-methoxy-1*H*-indol-3-yl)ethyl)-*N*-methylpropan-2-amine

4. 5-MeO-DET – 5-methoxy-*N*,*N*-diethyltryptamine; *N*,*N*-diethyl-2-(5-methoxy-1*H*-indol-3-yl)ethanamine
5. DiPT – *N*,*N*-diisopropyltryptamine; *N*-(2-(1*H*-indol-3-yl)ethyl)-*N*-isopropylpropan-2-amine

Figure 2: Chemical structures of schedule I tryptamine hallucinogens: DMT, DET, AMT, and psilocyn.



Metabolism and Pharmacokinetics

Metabolism studies have not been conducted for 4-OH-DiPT, 5-MeO-AMT, 5-MeO-DET, and DiPT. However, metabolism has been reported for 5-MeO-MiPT (Fabregat-Safont et al., 2017; Grafinger et al., 2018). Similar to other structurally related tryptamines, 5-MeO-MiPT has been reported to undergo metabolism through oxidative deamination, *N*-demethylation, *O*-demethylation, and *N*-oxidation with *N*-oxides as major metabolites (Barker et al., 1984; Sitaram et al., 1987a, 1987b, 1987c; Sitaram and McLeod, 1990, Caspar et al., 2018). Thus, it is highly likely that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-DET, and DiPT will be metabolized in a similar manner.

Medical Use

According to HHS, there are no approved new drug applications (NDAs) for 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT and these five tryptamines have no known medical use in the U.S.

Factor 4: History and Current Pattern of Abuse

In the U.S., law enforcement entities initially encountered 5-MeO-AMT and DiPT in 2003, 5-MeO-MiPT in 2004, 5-MeO-DET in 2006, and 4-OH-DiPT in 2009, according to the National Forensic Laboratory Information System (NFLIS). Each of these tryptamines is encountered in various forms (e.g., powder, tablets, capsules, liquid, or on blotter paper). The abuser population of these substances is commonly comprised of young adults. These substances are generally purchased from Internet-based companies in addition to being purchased from dealers. These tryptamines are often misrepresented as LSD to users due to their similarities in producing hallucinogenic effects.

Published and anecdotal evidence indicate that these tryptamines are commonly administered orally at doses ranging from 15 to 20 mg for 4-OH-DiPT, 2.0 to 4.5 mg for 5-MeO-AMT, 4 to 6 mg for 5-MeO-MiPT, 1 to 3 mg for 5-MeO-DET, and 25 to 100 mg for DiPT. Other routes of administration mentioned included smoking at doses ranging from 12 to 20 mg for 5-MeO-MiPT, 10 mg for 5-MeO-DET, and 8 mg for DiPT (Shulgin and Shulgin, 1997).

4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT do not have an approved medical indication in the U.S. and therefore have no legitimate medical use in the U.S. Anecdotal reports from users of these substances indicate that these substances produce classical hallucinogenic properties, such as perceptual distortions and pleasurable physical effects. Users report oral administration as the most common route of administration. Other routes of administration such as insufflation, smoking, and rectal administration have been reported. 5-MeO-MiPT has been mentioned to cause a wide range of effects including: euphoria, mood lift, intensification of tactile sensations, smell, sexual interest, emotional opening, relaxation, powerful "rushing" sensation (smoked), immersive experiences (smoked), feelings of body and muscle energy, buzzing, visual distortions, color intensification, disorientation, and sometimes dissociation, tremor, emotional lability, possible stomach discomfort, gas and vomiting, anxious stimulation muscle tension/discomfort, and difficulty sleeping for 4 to 8 hours after peak effects in some people.

Factor 5: The Scope, Duration, and Significance of Abuse

Tryptamine hallucinogens, both natural and synthetic, have been popular among the attendees of rave parties, music concerts, other large or social venues, as well as in intimate and smaller settings since the 1990s in the U.S. and Europe. Often these substances are promoted as substitutes for LSD. Synthetic hallucinogens and stimulants are known as "club drugs." In addition to sales in raves and nightclubs, Internet sales have become one of the main outlets for the sale and distribution of tryptamine hallucinogens.

According to NFLIS, in the U.S. there has been significant availability, trafficking, and abuse of a number of tryptamines including 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT. This is evidenced by large numbers of encounters of one or more of these tryptamines by U.S. law enforcement in a number of states and the District of Columbia, see Table 5.

Table 5: Summary of NFLIS[5,6] drug encounters in the United States for 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT.

Drug	Year First Reported	Total Reports	Where encountered
4-OH-DiPT	2009	5	CA, TX, TN
5-MeO-AMT	2003	92	CA, CO, CT, FL, IL, IN, KS, ME, MN, MO, NC, ND, NJ, NV, NY, OH, OK, TX, UT, VA, WA, WI
5-MeO-MiPT	2004	348	AL, AR, AZ, CA, CO, CT, DC, FL, GA, HI, ID, IL, IN, KS, KY, LA, MA, MI, MN, MO, NC, ND, NJ, NV, NY, OH, OK, OR, PA, SC, TN, TX, UT, VA, WI, WV, WY
5-MeO-DET	2006	17	CA, CT, ND, NY, OK, TX, WA
DiPT	2003	25	CA, ME, TX, WA

Factor 6: What, If Any, Risk to the Public Health

HHS indicates that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT pose a risk to public health due to their hallucinogenic properties that usually occur quickly after drug administration (often between 5-15 minutes, dependent on the route of administration) and may cause impairing effects on the user's judgment and lead to dangerous behavior. The risks could be to the individual user or to the community, especially when the user is operating a motor vehicle (HHS review, 2012a-e). Several adverse effects were reported in animal studies and in humans from Internet forums for all five tryptamines (see Factor 2). HHS also cited published and anecdotal reports that described the adverse effects of these five hallucinogens including agitation, confusion, psychological distress, and one death in the case of 5-MeO-AMT in 2004 (HHS review, 2012a-e). It is unclear what role 5-MeO-AMT played in the death. The toxicology report also reported alcohol and the presence of an antidepressant, bupropion. Some users of 4-OH-DiPT reported that the hallucinations were intense and the psychological and physiological effects were frightening or disturbing. A non-lethal poisoning was reported in 2005 of an adolescent after ingesting an alleged combination of 5-MeO-MiPT and harmaline, a CNS stimulant (HHS review, 2012c).

[5] NFLIS is a DEA program and a national forensic laboratory reporting system that systematically collects results from drug chemistry analyses conducted by federal, state, and local forensic laboratories in the U.S.
[6] NFLIS data were queried February 18, 2020, by date of submission.

Factor 7: Psychic or Physiological Dependence Liability

According to HHS, hallucinogens are not usually associated with physical dependence and the physiological dependence liability in animals or humans has not been reported in scientific and medical literature for these five substances. Thus, it is not possible at this time to determine whether 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT produce physiological dependence following acute or chronic administration. However, hallucinogen abusers may develop psychological dependence to these substances as evidenced by the continued use of these substances despite knowledge of the potential toxic and adverse effects (HHS review, 2012a-e).

The data on the drug discrimination studies conducted through a NIDA contract, cited in HHS reviews (2012a-e), show that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT share discriminative stimulus effects with schedule I hallucinogens: 4-OH-DiPT fully substitutes for DOM and LSD; 5-MeO-AMT partially substitutes for LSD and DMT; 5-MeO-MiPT fully substitutes for DOM; 5-MeO-DET fully substitutes for DMT; and DiPT fully substitutes for DOM and DMT. DEA adds that Carbonaro et al. (2013) showed that LSD, DOM, and MDMA fully substitute for DiPT-trained discriminative stimulus effects, confirming that DiPT has hallucinogenic effects similar to schedule I hallucinogens.

Factor 8: Whether the Substance Is an Immediate Precursor of a Substance Already Controlled

4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT are not immediate precursors of a substance already controlled under the CSA as defined by 21 U.S.C. 802(23).

III. Findings for Schedule Placement Pursuant to 21 U.S.C. 812(b)

21 U.S.C. 812(b) requires the evaluation of a substance's abuse potential, accepted medical use, and safety for use under medical supervision for placement in the CSA as a controlled substance. After consideration of the above eight factors determinative of control of a substance (21 U.S.C. 811(c)), and a review of the scientific and medical evaluations and scheduling recommendations provided by HHS, DEA finds that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT meet the following criteria for placement in schedule I of the CSA, under 21 U.S.C. 812(b)(1).

1) The drug has a high potential for abuse.

HHS mentions that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT elicit pharmacological effects qualitatively similar to those of schedule I hallucinogens,

discussed below. These effects are marked by hallucinations and CNS stimulation. Law enforcement reported a number of encounters of these substances. Law enforcement first encountered 5-MeO-AMT and DiPT in 2003, 5-MeO-MiPT in 2004, 5-MeO-DET in 2006, and 4-OH-DiPT in 2009.

The available data indicate that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT have high potential for abuse that is similar to that of schedule I tryptamine hallucinogens DET (5-MeO-AMT) and DMT (5-MeO-DET, 5-MeO-MiPT, and DiPT), the phenethylamine hallucinogen DOM (4-OH-DiPT, 5-MeO-DET, 5-MeO-MiPT, and DiPT), and the ergotamine hallucinogen LSD (5-MeO-AMT, 4-OH-DiPT, 5-MeO-DET, 5-MeO-MiPT; HHS reviews, 2012a-e).

2) The drug has no currently accepted medical use in treatment in the United States.

According to HHS, there are no approved New Drug Applications for 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT. In addition, DEA notes that there are no therapeutic applications for these five tryptamines accepted by qualified experts, nor are there adequate and well-controlled studies proving safety or efficacy for any medical use. Therefore, 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT have no currently accepted medical use in treatment in the United States.

3) There is a lack of accepted safety for use of the drug under medical supervision.

Because 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT have no approved medical use and have not been thoroughly investigated as new drugs, their safety for use under medical supervision is not determined. Thus, there is a lack of accepted safety for use of these substances under medical supervision.

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