

ATTACHMENT B

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February 14, 2022

Drug Enforcement Adminstration,
Attn: Hearing Clerk/OALJ
8701 Morissette Drive,
Springfield Virginia 22152

Re: Request for Hearing in the matter of Docket No. DEA-623

Dear Sir,

The undersigned counsel, on behalf of Dr. Jason Wallach and Mr. Hamilton Morris, hereby submit this request for a hearing in the matter of Docket No. DEA-623 (87 Fed. Reg. 2376).

Interest in the Proceedings.

Dr. Wallach and Mr. Morris wish to express their opposition to the proposed scheduling of *N,N*-Diisoproplytryptamine (“DiPT”). These men are academic scientists with over a decade of academic research invested into the study of DiPT and other hallucinogenic compounds. Their curriculum vitae are attached hereto.

Objections to the Scheduling of DiPT.

1. Over the last thirteen years Dr. Wallach and Mr. Morris have conducted extensive laboratory research on DiPT, studying its chemistry and pharmacology. The bulk of their research has not yet been published, and the scheduling of DiPT at this juncture would likely preclude or hamper their abilities to complete their investigative efforts. To date, their research has shown that DiPT can serve as a lead compound in the study of the physiology of auditory processing, local anesthesia, and the treatment of ovarian cancer.

2. Licensure will increase the cost of this research and introduce major obstacles when collaborating with other laboratories who lack the appropriate licensing. The nature of our research requires collaboration with contract research organizations and other academic labs to perform specialized experiments. Many of these labs lack experience in handling scheduled compounds and have little incentive to undertake the involved processes to obtain and maintained licensure.

3. While there is evidence that DiPT causes some of the effects of other tryptamine hallucinogens at high doses, it prominently acts on auditory systems in a way that makes it entirely distinct from related serotonergic tryptamines. The auditory effects of DiPT occur at doses far lower than those required to elicit a hallucinogenic effect. Furthermore, DiPT is unique, there is no other published compound that possesses this effect on auditory processing. Thus, the decision to criminally schedule DiPT would cut off an entire avenue of scientific inquiry and the resulting impact such inquiry could have on medicinal chemistry.
4. No credible abuse potential for DiPT has been demonstrated; there is no documentation of even modest frequency of use, and it has never been implicated in a human death or hospitalization. In the almost ten years since the FDA recommended DiPT be placed in schedule I for concerns of abuse, there is no known seizure, hospitalization, or death discernable from the literature. Such a lengthy window of observation without even the faintest indication of harm countenances that concerns regarding abuse have failed to materialize. Furthermore, the evidence of distribution is limited to a small number of research chemical vendors that were raided during a DEA operation called "Operation Web Tryp" between 2002-2004. These vendors were selling DiPT as a research chemical "not for human consumption" and the impact these vendors had on potential markets for abuse, as well as the role their DiPT itself played in any hypothetical instances of abuse, is dubious at best.
5. Our research into DiPT has itself yielded few if any anecdotal reports of its abuse, the paucity of unconfirmed anecdotal reports – published anonymously online and thus utterly unverifiable – does not firmly demonstrate abuse or even use of DiPT. This substance's unique auditory effects, which are not what one would readily describe as "recreational" or "pleasurable," make it inconceivable that DiPT would be widely abused as a tryptamine hallucinogen. Dr. Alexander Shulgin has authored the only reports on human responses to analytically verified DiPT and observed, "Subjects report little to no euphoria and are curiously neutral when asked whether the experience was unpleasant or pleasant", a statement not likely to be indicative of a substance with a high potential for abuse. Rodent behavioral models have been unable to demonstrate unique pharmacology of DiPT observed in humans for unknown reasons we are actively investigating. This fact tends to suggest a sufficient dissimilarity with other hallucinogens, is not readily demonstrated using current pharmacology assays, making comparisons with other scheduled tryptamine hallucinogens useless as a model for drug policy. Moreover, because DiPT has been used as a tool in pharmacology research since 1959 and was recognized for its unique activity on auditory processing by Alexander Shulgin in 1980, the overwhelming majority of evidence surrounding the pharmacology of DiPT demonstrates its effects are markedly distinct from structurally related tryptamine hallucinogens.
6. We have been unable to identify a single documented diversion of DiPT from legitimate channels.

7. The reports from Erowid that are cited in the FDA letter are unconfirmed anecdotal reports that contain no analytical verification. They cannot serve as evidence of abuse when it remains uncertain that these reports are truthful or genuinely involve the substance in question. In its August 2012 letter, the FDA indicated that “DEA databases and published medical reports” reflect that individuals are taking DiPT in amounts sufficient to create a health hazard. (Page 4 of Exhibit 3, attached hereto.). The quantum of data represented by these allusions in the FDA’s letter cannot be corroborated, and the literature to which it refers is not described in sufficient detail for it to be tested, compared, or otherwise scrutinized by the general public. However, our research into DiPT leads us to the conclusion that DiPT does not represent a serious health hazard and the reliance on anecdotal reports to conclude this, is speculative in nature, amalgamating DiPT reports with existing drugs of abuse, or otherwise fails to paint a meaningful picture of DiPT’s effects on the human body or its availability in recreational markets of abuse.
8. There is no known report of DiPT dependence anywhere in forensic or medical literature, nor are their anecdotal reports on sources such as erowid or TiHKAL.

In light of these objections, it is the position of Dr. Wallach and Mr. Morris that the scheduling of DiPT would do little to protect the public from harm, diversion of chemicals from legitimate channels, or curb abuse. In reality, there is not enough evidence to justify such actions, especially in light of the medically significant information that the continued study of DiPT offers to the scientific community.

We thank you for your kind attention to this important matter. As counsel of record for Dr. Wallach and Mr. Morris, I ask that all notices to be sent pursuant to the proceeding should be addressed to:

John T. Hunter
310 S. St. Mary's Street
Suite 1740 – Tower Life Bldg.
San Antonio, Texas 78205
(210) 202-1076
John@hljdefense.com

Yours Very Truly,



John T. Hunter

HAMILTON MORRIS
318 Grand St. Apt. 4H, Brooklyn, NY, 11211 · (617) 852-1591 ·
hellohamiltonmorris@gmail.com

Education:

The University of Chicago	2006-2007
The New School University (BS)	2007-2020

Professional Experience:

USciences laboratory technician	2021-present
USciences laboratory research	2009-present
Consultant, <i>Mind Cure Pharmaceuticals</i>	2020-present
Science editor, writer, <i>Vice Magazine</i>	2008-2018
Writer, producer, correspondent, <i>VBS.tv</i>	2009-2018
Reviews writer, <i>The Brooklyn Rail</i>	2010-2012
Writer, <i>Harper's Magazine</i>	2011-present
Science editor, <i>Children's Documentary Network</i>	2012-2015
Location Producer, writer, <i>National Geographic</i>	2012-2014
Writer, producer, correspondent, <i>Vice on HBO</i>	2014-2018
Director, Hamilton's Pharmacopeia, <i>Vice TV</i>	2009-2021

Select Journalistic Publications:

“Amfonelic Acid: A structural annotation”, <i>Harper's Magazine</i>	February 2015
“Gaboxadol”, <i>Harper's Magazine</i>	August 2013
“Blood Spore”, <i>Harper's Magazine</i>	July 2013
“Sea DMT” (with Jason Wallach), <i>Vice Magazine</i>	March 2013
“Criminal Chlorination”, <i>Vice Magazine</i>	September 2012
“Pages from the Laboratory Notebook of Alexander Shulgin” (with Paul Daily), <i>Vice Magazine</i>	September 2012
“Great Medicinal Chemists of the 20th Century”, <i>Vice Magazine</i>	September 2012
“Carsten Höller: Artist’s Portfolio”, <i>The Brooklyn Rail</i>	June 2012
“Cracking Cryptocacti”, <i>Vice Magazine</i>	June 2012
“I Walked With A Zombie”, <i>Harper's Magazine</i> ”	November 2011
“Interview with A Ketamine Chemist”, <i>Vice Magazine</i>	February 2011
“Psychedelic Maturity”, <i>The Brooklyn Rail</i>	July 2010
“The Last interview with Alexander Shulgin”, <i>Vice Magazine</i>	May 2010

Scientific Publications:

Morris, H. and Wallach, J., 2014. From PCP to MXE: a comprehensive review of the non-medical use of dissociative drugs. *Drug testing and analysis*, 6(7-8), pp.614-632.

Colestock, T., Wallach, J., Mansi, M., Filemban, N., Morris, H., Elliott, S.P., Westphal, F., Brandt, S.D. and Adejare, A., 2018. Syntheses, analytical and pharmacological characterizations of the ‘legal high’ 4-[1-(3-methoxyphenyl) cyclohexyl] morpholine (3-MeO-PCMo) and analogues. *Drug testing and analysis*, 10(2), pp.272-283.

Wallach, J., Morris, H. and Brandt, S.D., 2017. Is nitrogen mustard contamination responsible for the reported MT-45 toxicity?. *British Journal of Dermatology*.

Elliott, S.P., Brandt, S.D., Wallach, J., Morris, H. and Kavanagh, P.V., 2015. First reported fatalities associated with the ‘research chemical’ 2-methoxydiphenidine. *Journal of Analytical Toxicology*, 39(4), pp.287-293.2015

Wallach, J., Kavanagh, P.V., McLaughlin, G., Morris, N., Power, J.D., Elliott, S.P., Mercier, M.S., Lodge, D., Morris, H., Dempster, N.M. and Brandt, S.D., 2015. Preparation and characterization of the ‘research chemical’ diphenidine, its pyrrolidine analogue, and their 2, 2-diphenylethyl isomers. *Drug testing and analysis*, 7(5), pp.358-367.

Wallach, J., Kang, H., Colestock, T., Morris, H., Bortolotto, Z.A., Collingridge, G.L., Lodge, D., Halberstadt, A.L., Brandt, S.D. and Adejare, A., 2016. Pharmacological investigations of the dissociative ‘legal highs’ diphenidine, methoxphenidine and analogues. *PLoS One*, 11(6), p.e0157021.

McLaughlin, G., Morris, N., Kavanagh, P.V., Power, J.D., O'Brien, J., Talbot, B., Elliott, S.P., Wallach, J., Hoang, K., Morris, H. and Brandt, S.D., 2016. Test purchase, synthesis, and characterization of 2-methoxydiphenidine (MXP) and differentiation from its meta-and para-substituted isomers. *Drug Testing and Analysis*, 8(1), pp.98-109.

Invited Lectures and Conference Presentations:

Chemistry and Filmmaking, <i>University of Cambridge</i>	February 2021
USciences Honors Spring Colloquium Speaker, <i>USciences</i>	March 2018
“From PCP to MXE” (with Jason Wallach), <i>UMASS Amherst</i>	April 2014
“Arylcyclohexylamines: A historical perspective”, <i>Bard University</i>	March 2014
“Pharmacopeia: Meet The Filmmaker”, <i>Brandeis University</i>	February 2013
“The Interplay of Journalism and Gray-Markets”, <i>UPENN</i>	September 2012
Wallach, J. & Morris, H. “N-benzyl-phenethylamines: Pharmacophore approach to receptor binding selectivity” (poster)	September 2012

“Hamilton’s Pharmacopeia”, <i>Columbia School of Journalism</i>	April 2012
“Aphrodisiacs and Pharmacology”, <i>Yerba Buena Center for the Arts</i>	February 2011
“A Brief History of Gray-Market Psychostimulants”, <i>NYU</i>	November 2009

Teaching Experience:

“Hypnotic Psychopharmacology”, <i>USciences</i> , (PC340)	Introduction to Neuropsychopharmacology
	February 2019
“Science and Filmmaking”, The New School, Documentary Production Workshop	March 24, 2021

Jason V. Wallach
600 South 43rd St. Philadelphia PA, 19104
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Education

University of the Sciences (USciences) PhD in Pharmacology and Toxicology	<i>Philadelphia, PA</i> 2014
Indiana University of Pennsylvania BS in Cell and Molecular Biology (Honors Thesis Track), <i>Cum Laude</i> Minors: Chemistry, Biochemistry	<i>Indiana, PA</i> 2008

Awards and Recognitions

PCP Dean's Award Excellence in Research	2021
First Place Post-Doctoral Division Poster Award Mid-Atlantic Pharmacology Society (MAPS) Annual Meeting	2016
Basic Science Research Poster of the Year Award Philadelphia College of Pharmacy, University of the Sciences	2016
Alzheimer's Drug Discovery Foundation Young Investigator Scholarship Sigma Xi Outstanding Research Poster Award Indiana University of Pennsylvania	2011 2008
Sigma Tau Gamma Pi Fund Scholarship Interfraternity Council GPA Award Indiana University of Pennsylvania	2007-2008 2007
Provost Scholar Indiana University of Pennsylvania	2007

Research Experience

University of the Sciences (USciences)	<i>Philadelphia, PA</i> 2009-current
Structure Activity Relationship Studies of Novel 5-HT Receptor Ligands. Project focuses on ligand based drug design to develop ligands for 5-HT _{1A} and 5-HT _{2A} receptors. Project focuses on selective ligands and focuses on improving tolerability through polypharmacology, biased signaling and pharmacokinetics.	
- Design, synthesis and characterization of novel 5-HT receptor ligands including tryptamine, phenylalkylamine, and N-benzylphenylalkylamine scaffolds. - Pharmacological characterizations include radioligand-based competitive binding studies, functional assays and <i>in vivo</i> behavioral studies in rodents - Quantitative structure activity relationship studies	

Structure Activity Relationship and Tolerability Studies of Novel N-methyl-D-aspartate Receptor Antagonists

Project focused on characterizing and improving the clinical tolerability of NMDAR antagonists by modulating binding affinities, receptor interaction kinetics, multi-target polypharmacology and pharmacokinetic profiles.

- Ligand and pharmacophore based design, synthesis and analytical characterizations of novel NMDAR antagonists
- Determine NMDAR radioligand competitive binding studies
- *In vitro* cell culture neuroprotection and toxicity assays
- *In vitro* and *in vivo* studies

Analytical Characterization and Pharmacology of New Psychoactive Substances

Project focused on identifying emerging synthetic psychoactive substances or “legal highs”, particularly dissociative and lysergamide-based classical hallucinogens. These compounds are characterized using analytical chemistry and pharmacological assays.

- Identification, synthesis and analytical characterizations of novel psychoactive substances using synthetic organic chemistry and analytical chemistry techniques including HPLC, GC-MS, LC-MS, HR-MS, NMR, FT-IR and XRD
- Pharmacological characterization of novel psychoactive substances including receptor binding studies, functional assays and *in vivo* characterizations

Indiana University of Pennsylvania

Indiana, PA
2006-2008

Electrophysiological Behavior of Higher Vocal Center (HVC) Neurons in Zebra Finch

- Honors thesis dissertation Investigated effect of social cues on neuronal response of auditory cortex to auditory stimuli
- Animal handling and surgical techniques
- Electrophysiology of neuronal activity

Design and Synthesis of CB₁/CB₂ Cannabinoid Receptor Ligands

2006-2008

Effects of Tamoxifen and Retinoic Acid Derivatives on Phenotypic Behavior in MCF-7 Breast Cancer Cells

2005-2006

International Student Volunteers (ISV)

La Marta Wildlife Refuge, Cartago, Costa Rica

Summer, 2005

- Surveyed wildlife species present in secondary growth rainforest

Professional Experience

Consultant, Pangea Botanica.

2021-present

Scientific Advisor, Mind Cure Health Inc.

2020-present

Consultant, Compass Pathways.

2018-present

Consultant, Bexson Biomedical, Inc.

2017-present

Pharmacology Consultant.

2018-2019

Cannabis and drug testing case.

Pharmacology Consultant and Expert Witness.

2018-2019

Criminal Case, San Antonio Texas.

Assistant Professor

2020-present

Philadelphia College of Pharmacy (PCP), University of the Sciences, Philadelphia, PA.

Instructor, Substance Use Disorders Institute.	2017-present
Philadelphia College of Pharmacy (PCP), University of the Sciences, Philadelphia, PA.	
Instructor, Department of Pharmaceutical Sciences.	2016-2021
Philadelphia College of Pharmacy (PCP), University of the Sciences, Philadelphia, PA.	
Courses: Techniques in Pharmacology and Toxicology; Biomethods in Pharmacology and Toxicology; Virtual Physiology; Principles of Toxicology. Introduction to Neuropsychopharmacology.	
Adjunct Instructor, Cooper Medical School of Rowan University	2016-2021
Camden NJ.	
- UMED Program, Courses: Biochemistry, Pharmacology	
- Post-Bacc Program. Courses: Mechanisms of Disease	
Adjunct Instructor, Immaculata University	May, 2016-2017
Graduate Psychology & Counseling Department, Immaculata, PA	
Course: Clinical Psychopharmacology (PsyD program)	
Adjunct Instructor, Department of Pharmaceutical Sciences	Jan, 2016-Nov, 2016
Philadelphia College of Pharmacy (PCP), University of the Sciences, Philadelphia, PA	
Courses: Pharmacology, Physiology	
Research Technician, Contract Project for Reaction Biology Corporation	2015-2016
Malvern, PA.	
Synthesis of novel histone deacetylase (HDAC) inhibitors as anti-cancer agents	
Instructor, Department of Pharmaceutical Sciences.	Jan, 2015-Aug, 2015
Philadelphia College of Pharmacy (PCP), University of the Sciences, Philadelphia, Pennsylvania.	
Course: Physiology, Pharmacology. Management of graduate and undergraduate laboratory research	
Graduate Student, Department of Pharmaceutical Sciences, Philadelphia College of Pharmacy (PCP), University of the Sciences, Philadelphia, Pennsylvania.	2009-2014
Courses:	
Principles of Medicinal Chemistry and Molecular Pharmacology	2013-2014
Pharmacology	2013
Graduate student instructor, Organic Chemistry	2008-2012
Graduate student instructor, Biomethods in Pharmacology and Toxicology	2009-2013
Graduate student instructor, Research Methods in Drug Delivery	2009-2013
Student Employee, Indiana University of Pennsylvania	2006-2008
Vivarium Manager	2006-2008
Physiology Laboratory Aid	2007-2008
Program Director Assistant, Oxford Summer Study Abroad Program	2007

Research Support and Funding

AWD-0010091, Bexson Biomedical, Inc.

8/9/2019-8/9/2020

Research contract

Role: PI

AWD-00100126, Compass Pathways, Inc.

8/9/2019-8/9/202

Research contract

Role: PI

AWD-00100149, Bexson Biomedical, Inc.

8/9/2019-8/9/2020

Research contract

Role: PI

GR00000229, PA Department of Health

Grant

Role: Collaborator

PCP Faculty Research Award, University of the Sciences

9/1/2019-9/15-2020

Role: PI

PG0157, University of the Sciences

07/01/18-2019

Role: PI

Professional Society Memberships

International Society for Research on Psychedelics

The National Scholars Honors Society

The American Chemical Society

Sigma Tau Gamma National Fraternity

Publications

1. Halberstadt, A.L., Chatha, M., Klein, A.K., **Wallach, J.** and Brandt, S.D., 2020. Correlation between the potency of hallucinogens in the mouse head-twitch response assay and their behavioral and subjective effects in other species. *Neuropharmacology*, p.107933.
2. Ladagu, A.D., Olopade, F.E., Folarin, O.R., Elufioye, T.O., **Wallach, J.V.**, Dybek, M.B., Olopade, J.O. and Adejare, A., 2020. Novel NMDA-receptor antagonists ameliorate vanadium neurotoxicity. *Naunyn-Schmiedeberg's archives of pharmacology*, 393(9), pp.1729-1738.
3. Brandt, S.D., Kavanagh, P.V., Westphal, F., Stratford, A., Odland, A.U., Klein, A.K., Dowling, G., Dempster, N.M., **Wallach, J.**, Passie, T. and Halberstadt, A.L., 2020. Return of the lysergamides. Part VI: Analytical and behavioural characterization of 1-cyclopropanoyl-d-lysergic acid diethylamide (1CP-LSD). *Drug Testing and Analysis*. <https://doi.org/10.1002/dta.2789>
4. **Wallach, J.**, Colestock, T., Agramunt, J., Claydon, M.D., Dybek, M., Filemban, N., Chatha, M., Halberstadt, A.L., Brandt, S.D., Lodge, D., Bortolotto, Z.A., Adejare, A. Pharmacological characterizations of the legal high fluorolintane and isomers. *Eur J Pharmacol*. 2019. p.172427.

5. Dybek, M., **Wallach, J.**, Kavanagh, P.V., Colestock, T., Filbman, N., Dowling, G., Westphal, F., Elliott, S.P., Adejare, A., Brandt, S.D. Syntheses and analytical characterizations of the research chemical 1-[1-(2-fluorophenyl)-2-phenylethyl] pyrrolidine (fluorolintane) and five of its isomers. *Drug Test Anal.* 2019. (Epub ahead of print). <https://doi.org/10.1002/dta.2608>
6. Brandt, S.D., Kavanagh, P.V., Westphal, F., Stratford, A., Elliott, S.P., Dowling, G., **Wallach, J.**, Halberstadt, A.L. Return of the lysergamides. Part V: Analytical and behavioural characterization of 1-butanoyl-d-lysergic acid diethylamide (1B-LSD). *Drug Test Anal.* 2019. (Epub ahead of print)
7. Halberstadt, A.L., Klein, L.M., Chatha, M., Valenzuela, L.B., Stratford, A., **Wallach, J.**, Nichols, D.E., Brandt, S.D. Pharmacological characterization of the LSD analog N-ethyl-N-cyclopropyl lysergamide (ECPLA). *Psychopharmacol.* 2019;236:799-808
8. Colestock, T., **Wallach, J.**, Mansi, M. Filemban, N., Morris, H., Elliott, SP., Westphal, F., Brandt, SD., Adejare, A. Syntheses, analytical and pharmacological characterizations of the 'legal high' 4-[1-(3-methoxyphenyl)cyclohexyl]morpholine (3-MeO-PCMo) and analogues. *Drug Test Anal.* 2017;10:272-283
9. Wang, Y. **Wallach, J.** Duane, S. Wang, Y. Wu, J. Wang, J. Adejare, A. Ma, H. Developing selective histone deacetylases (HDACs) inhibitors through ebselen and analogs. *Drug Des Dev Ther.* 2017;11:1369-82
10. Brandt, SD, Kavanagh, PV. Twamley, B. Westphal, F. Elliott, SP. **Wallach, J.** Stratford, A. Klein, LM. McCory, JD. Nichols, DE. Halberstadt, AL. Return of the lysergamides. Part IV: Analytical and pharmacological characterization of lysergic acid morpholide (LSM-775). *Drug Test Anal.* 2017;20:310-322
11. Brandt, SD. Kavanagh, PV. Westphal, F. Elliott, SP. **Wallach, J.** Stratford, A. Nichols, DE. Halberstadt, AL. Return of the lysergamides. Part III: Analytical characterization of N6 -ethyl-6-norlysergic acid diethylamide (ETH-LAD) and 1-propionyl ETH-LAD (1P-ETH-LAD). *Drug Test Anal.* 2017;9:1641-1649
12. Kang, H. Park, P. Bortolotto, ZA. Brandt, SD. Colestock, T. **Wallach, J.** Collingridge, GL. Lodge, D. Ephedidine: A new psychoactive agent with ketamine-like NMDA receptor antagonist properties. *Neuropharmacol.* 2016;112:144-149
13. **Wallach, J.** Kang, H. Colestock, T. Morris, H. Bortolotto, ZA. Collingridge, GL. Lodge, D. Halberstadt, AL. Brandt, SD. Adejare, A. "Pharmacological Investigations of the Dissociative 'Legal Highs' Diphenidinedine, Methoxphenidinedine and Analogues." *PloS One* 11, no. 6 (2016): e0157021
14. Brandt, SD. Kavanagh, PV. Westphal, F. Elliott, SP. **Wallach, J.** Colestock, T. Burrow, TE. Chapman, SJ. Stratford, A. Nichols, DE. Halberstadt, AL. Return of the lysergamides. Part II: Analytical and behavioural characterization of N6-allyl-6-norlysergic acid diethylamide (AL-LAD) and (2'S, 4'S)-lysergic acid 2, 4-dimethylazetidide (LSZ). *Drug Test Anal.* 2016;9:38-50
15. Brandt, SD. Kavanagh, PV. Westphal, F. Stratford, A. Elliott, SP. Hoang, K. **Wallach, J.** Halberstadt, AL. Return of the lysergamides. Part I: Analytical and behavioural characterization of 1-propionyl-d-lysergic acid diethylamide (1P-LSD). *Drug Test Anal.* 2015;[epub ahead of print]
16. **Wallach, J.** Colestock, T. Cicali, B. Elliott, SP. Kavanagh, PV. Adejare, A. Dempster, NM. Brandt, SD. Syntheses and analytical characterizations of N-alkyl-arylcyclohexylamines. *Drug Test Anal.* 2015;8:801-15
17. McLaughlin G. Morris N. Kavanagh PV. Power J D. O'Brien, J. Talbot B. Elliott SP. **Wallach, J.** Hoang K. Morris H. Brandt SD. Test purchase, synthesis, and characterization of 2-methoxydiphenidinedine (MXP) and differentiation from its *meta*- and *para*-substituted isomers. *Drug Test Anal.* 2015;8:98-109

18. Elliott, SP. Brandt, SD. **Wallach, J.** Morris, H. Kavanagh PV. First Reported Fatalities Associated with the 'Research Chemical' 2-Methoxydiphenidine. *J Anal Toxicol.* 2015;39:287-293
19. **Wallach, J.** Kavanagh, PV. McLaughlin, G. Morris, N. Power, JD. Elliott, SP. Mercier, MS. Lodge, D. Morris, H. Dempster, NM. Brandt, SD. Preparation and characterization of the 'research chemical' diphenidine, its pyrrolidine analogue, and their 2, 2-diphenylethyl isomers. *Drug Test Anal.* 2014;7:358-67
20. Sun, S. **Wallach, J.** Adejare, A. Syntheses and N-methyl-D-aspartate Receptor Antagonist Pharmacology of Fluorinated Arylcycloheptylamines. *Med Chem.* 2014;10(8):843-52
21. Morris, H. **Wallach, J.** From PCP to MXE: a comprehensive review of the non-medical use of dissociative drugs. *Drug Test Anal.* 2014;6:614-632
22. **Wallach, J.** De Paoli, G. Adejare, A. Brandt, SD. Preparation and analytical characterization of 1-(1-phenylcyclohexyl)piperidine (PCP) and 1-(1-phenylcyclohexyl)pyrrolidine (PCPy) analogues. *Drug Test Anal.* 2014;6:633-650
23. De Paoli, G. Brandt, SD. **Wallach, J.** Archer, RP. Pounder, DJ. From the Street to the Laboratory: Analytical Profiles of Methoxetamine, 3-Methoxyeticyclidine and 3-Methoxyphencyclidine and their Determination in Three Biological Matrices. *J Anal Toxicol.* 2013;37:277-283
24. Alagoz, Z. Sun, S. **Wallach, J.** Adejare, A. Synthesis and Pharmacological Evaluation of Novel N-Substituted Bicyclo-Heptane-2-Amines at N-Methyl-D-Aspartate Receptors. *Chem Biol Drug Des.* 2011;78:25-32
25. **Wallach, J.** Endogenous Hallucinogens as Ligands of the Trace Amine Receptors: A Possible Role in Sensory Perception. *Med Hypotheses.* 2009;72:91-94.

Book Chapters

1. **Wallach, J.**, 2021. Medicinal Cannabis: an overview for health-care providers. *Remington*, pp.75-101.
2. Abelian, A., Dybek, M., **Wallach, J.**, Gaye, B. and Adejare, A., 2021. Pharmaceutical chemistry. In *Remington* (pp. 105-128). Academic Press.
3. **Wallach, J.**, Brandt, SD. Phencyclidine-Based New Psychoactive Substances. *Handbook of Experimental Pharmacology*. Springer. 2018. pp 261-303.
4. **Wallach, J.**, Brandt, SD. 1,2-Diarylethylamine- and Ketamine-Based New Psychoactive Substances. *Handbook of Experimental Pharmacology*. Springer. 2018. pp 305-352.
5. **Wallach, J.**, Colestock, T. Adejare, A. Receptor Targets in Alzheimer's Disease Drug Discovery. Chapter 6. *Drug Discovery Approaches for the Treatment of Neurodegenerative Disorders: Alzheimer's Disease*. (Editor: Adejare, A.) Academic Press. London. 2017, pp. 83-109
6. **Wallach, J.**, Gaye, B. Adejare, A. Organic Pharmaceutical Chemistry. Chapter 5. *Remington: An Introduction to Pharmacy*. (Editor: Allen, LV.) Pharmaceutical Press. London. 2013, pp. 79-92
7. **Wallach, J.**, Gaye, B. Adejare, A. Organic Pharmaceutical Chemistry. Chapter 6. In: *Remington* 22nd Edition: *The Science and Practice of Pharmacy*. (Editor: Allen, LV.) Pharmaceutical Press. London. 2012, pp. 71-101

Invited Lectures and Selected Conference Presentations

1. **Wallach J.** Neuroscience and Clinical Pharmacology of Ketamine. Invited lecture at KRIYA Ketamine Conference 2019. KRIYA Ketamine Research Institute. November 10, 2019. Hillsborough, CA
2. **Wallach J.** Pharmacokinetics and Pharmacodynamics of Ketamine (and Related Compounds). Invited lecture at KRIYA Ketamine Conference 2018. KRIYA Ketamine Research Institute. November 3, 2018. Hillsborough, CA
3. **Wallach J.** PCP to DCK: Pharmacology and Toxicology of Dissociative Based Synthetic Psychoactive Drugs. Invited lecture at 7th Annual Philadelphia City-Wide Toxicology Day. October 17, 2018. Philadelphia, PA
4. **Wallach J.** Ketamine Biochemical Mechanisms. Invited lecture at The American Society of Ketamine Practitioners. Sept 21, 2018. Austin Texas
5. **Wallach J.** Dank Science: The Endocannabinoid System and Pharmacology of Phytocannabinoids. Invited lecture at 25th Annual Neuroscience Conference. Penn State College of Medicine. April 26, 2018. Hersey, PA
6. **Wallach J.** Ketamine Pharmacology. Invited lecture at KRIYA Ketamine Conference 2017. KRIYA Ketamine Research Institute. November 4, 2017. Hillsborough, CA
7. **Wallach J.** Improving Tolerabilities of NMDA Receptor Antagonists. Invited lecture at KRIYA Ketamine Conference 2016. KRIYA Ketamine Research Institute. November 13, 2016. Hillsborough, CA
8. **Wallach, J.** Strategies for Improving Tolerabilities of NMDA Receptor Antagonists. Invited lecture at: Philadelphia Drug Discovery Forum. December 10, 2015. The Wistar Institute. Philadelphia, PA
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**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Office of the Secretary

**Office of the Assistant Secretary for Health
Washington, D.C. 20201****AUG 14 2012**

The Honorable Michele M. Leonhart
Administrator
Drug Enforcement Administration
U.S. Department of Justice
8701 Morrissette Drive
Springfield, VA 22152

Dear Ms. Leonhart:

Pursuant to the Controlled Substances Act [CSA, 21 U.S.C. § 811 (b), (c), and (f)], the Department of Health and Human Services is recommending that the substance DIPT and its salts be added to Schedule I of the CSA. DIPT has no known medical use in the United States, does not have an approved new drug application, and is not currently marketed anywhere in the world as an approved drug product. Chemically, DIPT is structurally related to the Schedule I hallucinogen, 5-methoxy-N,N-diisopropyltryptamine (5-MeO-DIPT). The substance elicits pharmacological effects similar to other Schedule I hallucinogens with high abuse potential, including dimethyltryptamine (DMT) and 4-methyl-2,5-dimethoxyphenethylamine (DOM).

The Food and Drug Administration (FDA) and the National Institute on Drug Abuse have also considered the abuse potential and dependence-producing characteristics of DIPT. After reviewing the available information, the agencies conclude that DIPT should be controlled in Schedule I. Enclosed is a document prepared by FDA's Controlled Substance Staff that is the basis for the recommendation.

Should you have any questions regarding this recommendation, please contact Corinne P. Moody, Science Policy Analyst, Controlled Substance Staff, Center for Drug Evaluation and Research, FDA, at (301) 796-3152.

Sincerely yours,

Howard K. Koh, M.D., M.P.H.
Assistant Secretary for Health

Enclosure

**Basis for the Recommendation to Control
N,N-Diisopropyltryptamine (DIPT) and its Salts
in Schedule I of the Controlled Substances Act (CSA)**

A. Background

On December 19, 2008, the Drug Enforcement Administration (DEA) requested that the Department of Health and Human Services (HHS) conduct a medical and scientific evaluation of N,N-diisopropyltryptamine (DIPT) and its salts for control under Schedule I of the Controlled Substances Act (CSA). The substance DIPT, a tryptamine derivative with central nervous system hallucinogenic properties, has no known medical use in the United States, does not have an approved new drug application, and is not currently marketed anywhere in the world as an approved drug product.

Between 2002 and 2004, law enforcement authorities reported the increased abuse of DIPT in the United States, as evidenced by drug seizures involving DIPT.

Chemically, DIPT is structurally related to the Schedule I hallucinogen, 5-methoxy-N,N-diisopropyltryptamine (5-MeO-DIPT). The substance elicits pharmacological effects similar to other Schedule I hallucinogens with high abuse potential including dimethyltryptamine (DMT) and 4-methyl-2,5-dimethoxyphenethylamine (DOM). DIPT and related tryptamine hallucinogens (5-MeO-DIPT, alpha-methyltryptamine (AMT), and lysergic acid diethylamide (LSD), all of which are Schedule I drugs) are highly abusable substances.

Pursuant to 21 U.S.C. § 811(b), the Secretary of HHS is required to consider in a scientific and medical evaluation, eight factors determinative of control under the CSA. The eight factors considered in determining whether a drug or substance should be scheduled are:

1. Its actual or relative potential for abuse;
2. Scientific evidence of its pharmacological effect, if known;
3. The state of current scientific knowledge regarding the drug or other substance;
4. Its history and current pattern of abuse;
5. The scope, duration, and significance of abuse;
6. What, if any, risk there is to the public health;
7. Its psychic or physiological dependence liability; and
8. Whether the substance is an immediate precursor of a substance already controlled under the CSA.

Following consideration of the eight factors, the Secretary must make three findings and a recommendation for scheduling a substance in the CSA. The three required findings relate to a substance's abuse potential, legitimate medical use, and safety or dependence potential.

The medical and scientific evaluation of whether a substance should be recommended for control under the CSA are performed for HHS by the Food and Drug Administration (FDA), with the concurrence of the National Institute on Drug Abuse (NIDA), as described in the Memorandum of Understanding of March 8, 1985 (50 FR 9518-20).

This evaluation discusses the scientific and medical information relative to each of the eight factors, presents findings in the three required areas (abuse potential, legitimate medical use, and safety or dependence liability), and makes a recommendation regarding scheduling. After assessing all available data, FDA recommends that DIPT and its salts be controlled in Schedule I of the CSA. NIDA concurs with this recommendation.

B. Evaluating DIPT Under the Eight Factors

This section evaluates the scientific and medical information about DIPT under the eight factors that must be considered pursuant to 21 U.S.C. § 811(c). Available information that was evaluated included papers on DIPT published in the scientific and medical literature, law enforcement data from seizures and surveillance of DIPT, and anecdotal reports on the human use of DIPT.

1. ITS ACTUAL OR RELATIVE POTENTIAL FOR ABUSE

The term "abuse" is not defined in the CSA. However, the legislative history of the CSA¹ suggests any of the following points in determining whether a particular drug or substance has a potential for abuse:

- a. Individuals are taking the substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community; or
- b. There is significant diversion of the drug or substance from legitimate drug channels; or
- 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
- d. The substance is so related in its action to a substance already listed as having a potential for abuse to make it likely that it will have the same potential for abuse as such substance, thus making it reasonable to assume that there may be significant diversions from legitimate channels, significant use contrary to or without medical advice, or that it has a

¹ Comprehensive Drug Abuse Prevention and 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.

substantial capability of creating hazards to the health of the user or to the safety of the community.

a. Individuals are taking the substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community.

Evidence that individuals are taking DIPT in amounts sufficient to create a health hazard is found in DEA databases and published medical reports (see Factor 2). DIPT has been seized by law enforcement in the United States (see Factor 5), demonstrating the availability of DIPT as a drug of abuse. Additionally, DEA data, case reports in the medical literature, and anecdotal reports document that DIPT is used for its auditory hallucinogenic activity, with threshold responses occurring at oral doses above 16 mg, and common oral doses ranging from 20-50 mg (see Factor 6). Thus, DIPT presents a safety hazard to the health of individuals who consume it due to its hallucinogenic properties.

b. There is significant diversion of the drug or substance from legitimate drug channels.

As DIPT is not an approved drug product in the United States and there appear to be no legitimate drug channels from which DIPT can be diverted, this characteristic of abuse potential is not applicable.

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 substances.

DIPT is not an approved drug product, so a practitioner may not legally prescribe the substance, and it cannot be dispensed to an individual. Therefore, individuals are using DIPT without medical advice. DIPT is available for purchase on the Internet and "on the street" as an illicit substance. According to the DEA and anecdotal reports (see Factor 2), DIPT has effects similar to the Schedule I hallucinogens 4-bromo-2,5-dimethoxyphenethylamine (2C-B), 4-methyl-2,5-dimethoxyphenethylamine (2C-D), and 2,5-Dimethoxy-4-ethylamphetamine (DOET). Thus, individuals may be using the unscheduled drug DIPT on their own initiative, possibly because they are seeking the same hallucinogenic effects as Schedule I substances while avoiding the criminal penalties associated with those substances.

d. The substance is so related in its action to a substance already listed as having a potential for abuse to make it likely that it will have the same potential for abuse as such substance, thus making it reasonable to assume that there may be significant diversions 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.

DIPT is a chemical structural analog of the Schedule I hallucinogen, 5-MeO-DIPT. The pharmacological action of DIPT is similar to that of other Schedule I hallucinogens, such

as DOM and DMT (see Factor 2), both of which have no accepted medical use and have high abuse potential.

Anecdotal reports from humans who have used DIPT describe effects from the drug that are similar to those from Schedule I hallucinogens, such as 2C-B, 2C-D, and DOET (see Factor 2). Data from animal drug discrimination studies demonstrate that DIPT produces full generalization to the Schedule I hallucinogens, DOM and DMT (see Factor 2).

The risks associated with DIPT, as with other Schedule I hallucinogens, are primarily based on perceptual changes in auditory experience (Shulgin and Shulgin, 1997; http://www.erowid.org/experiences/subs/exp_DIPT.shtml). Due to the psychological and cognitive disturbances associated with this response, it is reasonable to assume that DIPT has substantial capability to be a hazard to the health of the user and to the safety of the community.

2. SCIENTIFIC EVIDENCE OF ITS PHARMACOLOGICAL EFFECTS, IF KNOWN

DIPT produces subjective effects that are hallucinogen-like. The scientific evidence of the pharmacological effects of DIPT includes its neurochemistry and central nervous system effects in animals and humans.

Neurochemical Effects

The neurochemical effects of DIPT occur primarily through serotonergic systems in the brain. Hallucinogens are thought to produce their characteristic effects primarily through stimulation of serotonin (5-hydroxytryptamine; 5-HT) 5-HT_{2A} receptors in the brain (Nichols, 2006). DIPT binds with low-moderate affinity to 5-HT_{2A} receptors, with an inhibitor constant (*K_i*) of 910 nanomolar (nM) (Janowsky and Eshleman, 2006). Functional assays evaluating one of the second messenger systems coupled to 5-HT₂ receptors (arachidonic acid) show that DIPT has moderate activity at the 5-HT₂ site (Janowsky and Eshleman, 2006), with a half maximal effective concentration (EC₅₀) value of 450 nM.

Tryptamine hallucinogens often bind with high affinity to another serotonin receptor in the brain, the 5-HT_{1A} receptor. However, although DIPT is a tryptamine hallucinogen, it was shown in a receptor binding assay to have either low-moderate affinity for the 5-HT_{1A} receptor (*K_i* = 687 nM, Toll and Berzetei-Gurske, 2006) or no significant activity for the 5-HT_{1A} receptor (*K_i* = 2270 nM, Janowsky and Eshleman, 2007). A functional assay evaluating a second messenger system associated with the 5-HT_{1A} receptor (GTP) also shows that DIPT does not have significant activity at the 5-HT_{1A} receptor (EC₅₀ = 4570 nM).

The ability of DIPT to bind at the three monoamine transporters (dopamine, norepinephrine, and serotonin) was also evaluated by Janowsky and Eshleman (2006). These studies showed that DIPT had moderate affinity for the serotonin transporter (*K_i* = 265 nM) and moderate activity on uptake at this site (half maximal inhibitory constant

(IC₅₀) = 215 nM). In contrast, DIPT had no significant affinity (Ki values of greater than 1000 nM) at the dopamine and norepinephrine transporters and did not affect uptake at these two sites (IC₅₀ values greater than 7000 nM). Finally, DIPT was shown to have no activity in release of the three monoamines (dopamine, norepinephrine, and serotonin) via their respective transporters (EC₅₀ values were not determined).

Thus, DIPT has a complex pharmacology involving two serotonin sites, one of which (the 5-HT_{2A} receptor) is likely responsible for its hallucinogenic effects.

Central Nervous System Effects

The central nervous system effects of DIPT have been evaluated through animal studies and reported effects in humans. As described below, published studies in animals and humans suggest that the pharmacological effects of DIPT are similar to hallucinogens such as DOM and DMT, both of which are Schedule I drugs.

Animal Studies with DIPT

Animal studies conducted with DIPT include those evaluating elicited behavioral pharmacology and drug discrimination.

Elicited Behavioral Pharmacology

The elicited behavioral pharmacology of DIPT was investigated by administering the drug to animals and observing its acute behavioral effects.

In mice, administration of DIPT (30 mg/kg, intraperitoneal (i.p.)) produced a time-dependent decrease in locomotion compared to saline (Elsken and Forster, 2006). This depression in activity (measured as horizontal activity counts) began within 10 minutes of drug administration and persisted up to 80 minutes. Administration of DIPT at doses above and below 30 mg/kg (1, 3, 10, 56, 100 mg/kg, i.p.) did not produce a statistically significant change in locomotion behavior compared to saline. However, the 56 mg/kg dose of DIPT produced lethality in 2 of 8 mice (25%), and the 100 mg/kg dose of DIPT produced lethality in 8 of 8 mice (100%).

Drug Discrimination

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. In this test method, animals are trained to press one bar in the test cage following administration of a specific known drug of abuse and to press another bar following administration of placebo. A challenge session with the novel drug determines which of the two bars the animal presses more often, as an indicator of whether the test drug is more like the known drug of abuse or more like placebo. The novel drug is said to have "full generalization" to the known drug of abuse when the

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novel drug produces bar pressing $\geq 80\%$ on the bar associated with the known drug of abuse (Doat et al., 2003, Sannerud and Ator, 1995).

Numerous studies were conducted in animals to evaluate whether DIPT has stimulus characteristics that are similar to those of drugs scheduled under the CSA.

In a drug discrimination study with rats trained to recognize the effects of the Schedule I hallucinogen, DOM, DIPT produced full generalization to the DOM cue (Forster et al, 2006; Glennon et al., 1983a, 1983b). Similarly, there was full generalization between DIPT and the discriminative cue produced by the Schedule I hallucinogen, DMT (Gatch and Foster, 2006). However, there was only partial generalization between DIPT and the discriminative cue produced by the Schedule I hallucinogen, LSD (68% generalization; Gatch and Forster, 2006).

In contrast, there was no generalization between DIPT and the Schedule I substance 3,4-methylenedioxymethamphetamine (MDMA) (Rutledge et al., 2006) or the Schedule II stimulants, cocaine (<38% generalization; Forster et al., 2006) and (+) methamphetamine (<20% generalization; Gatch and Forster, 2006b).

These data indicate that DIPT has stimulus-properties that are similar to those of the Schedule I hallucinogens, DOM and DMT, are partially similar to the Schedule I hallucinogen, LSD, but are not similar to the Schedule I substance, MDMA, or the Schedule II stimulants, cocaine and (+) methamphetamine.

Effects of DIPT in Humans

Reports published in the medical literature are based on anecdotal experiential investigations with DIPT that were not conducted under formal clinical protocols in institutional settings. Such sources have limited reliability and the information may not be entirely representative of the effects of DIPT.

In an anecdotal investigation published by Shulgin and Carter (1980), adult volunteers experienced threshold responses to oral doses of DIPT above 16 mg, with more intense experiences occurring at doses ranging from 20-50 mg. Approximately 20-30 minutes after ingestion, most subjects began to experience effects, which peaked approximately 1.5 to 2 hours after ingestion and persisted for longer than 4 hours. The most notable response was an alteration in auditory perception, including changes in awareness of pitch and distortion of music and voice. Additional responses included lethargy, an experience of withdrawal from one's surroundings, nausea, hyperreflexia, and mydriasis. The lack of "intense hallucinogenesis" and profound "modifications of emotional and intellectual processes" was likened by the volunteers to the Schedule I hallucinogens 2C-B, 2C-D, and DOET.

A similar report with DIPT is provided by Shulgin and Shulgin (1997) in which adult volunteers ingested oral doses ranging from 25-100 mg. The only perceptual change reported was in the auditory modality, with sounds taking on a deeper, more "bass"

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tonality. The report specifically states that, "there were no changes in vision, taste, smell, appetite, vital signs, or motor coordination." The effects of the drug diminished by 4 hours after ingestion and were terminated by 8 hours. According to an anecdotal story mentioned in this report, smoking 8 mg of DIPT produced a rapid response within 4-8 minutes, but the effects were again exclusively auditory in nature.

Anecdotal reports on the Erowid website <http://www.erowid.org/experiences/subs/exp_DiPT.shtml> describe hallucinogenic effects resulting from use of DIPT. The Erowid site notes that the first DIPT reports were received by the site in 2000, typically reporting on responses following oral administration. Details of the experiential reports with DIPT are not typically verified in terms of dose, onset and duration of effects, intensity of effects, and most importantly, chemical substance ingested. The responses described in the reports of DIPT use are consistent with the published reports cited above in terms of the drug response being primarily, or exclusively, changes in auditory perception.

One individual who reported that he had consumed approximately 2 grams of DIPT over a year experienced symptoms associated with the King-Kopetzky syndrome, which involves difficulty in hearing speech in the presence of background noise.

**3. THE STATE OF CURRENT SCIENTIFIC KNOWLEDGE REGARDING THE DRUG
OR OTHER SUBSTANCE**

The current scientific knowledge of DIPT includes information about its chemistry, synthesis, and medical applicability.

Chemistry

DIPT is a centrally-acting drug that is known chemically as N,N-diisopropyltryptamine [also known as: indole,3-[2-(diisopropylamino)ethyl; 3-[2-diisopropylamino(ethyl]-indole; CAS 14780-24-6]. DIPT has a molecular weight of 244.4, a molecular formula of C₁₆H₂₄N₂, and occurs as a white crystalline powder. The hydrochloride salt of DIPT (CAS 67292-67-5) has a melting point that ranges from 192-193°C (synthesis from tryptamine) to 198-199°C (synthesis from indole) (Shulgin and Shulgin, 1997). Instructions for the synthesis of DIPT are available on the Internet.

Medical Use of DIPT

DIPT is not an approved human drug product in the United States or in any other country, and no data are available on its medical use in the treatment of any condition.

4. ITS HISTORY AND CURRENT PATTERN OF ABUSE

The history and current pattern of abuse of DIPT is described in law enforcement reports and anecdotal reports of DIPT use by drug abusers.

DEA databases which document seizures of DIPT provide evidence of abuse of the substance in the United States since 2002. Additional information concerning DIPT abuse from DEA sources is described in Factor 5 (below).

As described in Factor 2, anecdotal reports on the Internet indicate that some individuals are using DIPT and report hallucinogenic effects
<http://www.erowid.org/experiences/subs/exp_DiPT.shtml>.

5. THE SCOPE, DURATION AND SIGNIFICANCE OF ABUSE

Evidence from law enforcement databases and case reports regarding seizures provides evidence of the scope, duration, and significance of abuse of DIPT.

The DEA's System to Retrieve Information on Drug Evidence (STRIDE) database compiles drug seizure information as reported by federal law enforcement agencies. The most recently available report from STRIDE regarding DIPT covers the time period from 2002-2004. From 2002-2004, STRIDE reported 5 cases in which DIPT substance was seized or records related to the sales of DIPT were seized. The amount of seized DIPT substance totaled 587.1 grams. With an average dose ranging from 20-50 mg, the amount of DIPT seized is the equivalent of approximately 12,000 to 29,000 individual doses of the drug for abuse purposes. The majority of these reports involved Internet businesses that sold tryptamines for human consumption. Computer records from one such business provided information on the sale of 66 grams of DIPT in 77 orders (the equivalent of approximately 1300 to 3300 individual doses for abuse purposes). No further sales data was provided from investigations of other Internet businesses that allegedly sold DIPT.

Additionally, the DEA's National Forensic Laboratory Information System, a database for drug cases analyzed by federal, state, and local forensic laboratories, reported one case involving one item containing 880 mg of powdered DIPT in 2003 (the equivalent of about 17 to 44 individual doses of the drug for abuse purposes).

Finally, DEA received information from two other sources regarding Internet sales of tryptamines, including DIPT, for abuse purposes. One source involved an individual associated with a company in the Houston, Texas metropolitan area that listed DIPT for sale in 2004. In the other source, computer records of a company based in Asia listed 1,600 transactions from 2004 to 2007 in which hallucinogenic drugs (including but not limited to DIPT) were sold to online customers around the world, predominantly in the United States.

These data demonstrate that DIPT has been available for purchase as a drug of abuse.

6. WHAT, IF ANY, RISK THERE IS TO THE PUBLIC HEALTH

Public health risks resulting from abuse of DIPT relate primarily to its ability to induce auditory and other sensory distortions (Shulgin and Carter, 1980), which may lead to impaired judgment and dangerous behavior.

Anecdotal reports on websites popular with drug abusers (e.g., Erowid and Bluelight) suggest that the hallucinogenic effects of DIPT are primarily, or exclusively, limited to changes in auditory perception. One of these anecdotal self-reports described an individual who experienced symptoms associated with the King-Kopetzky syndrome (difficulty hearing speech in the presence of background noise) following consumption of approximately 2 grams of DIPT over the course of a year.

In addition to the ability of DIPT to induce hallucinogenic effects, the drug is reported to induce lethargy, an experience of withdrawal from one's surroundings, nausea, hyperreflexia, and mydriasis (Shulgin and Carter, 1980).

The rapidity with which the hallucinogenic effects of DIPT are experienced after smoking the substance (4-8 minutes) (Shulgin and Shulgin, 1997), the intensity of the distinct hallucinatory response, and the inability to feel in control of the experience strongly suggest that DIPT is a public health risk. For an individual, there is the risk of psychological distress, especially if abuse of DIPT occurs while alone. If the individual attempts to smoke the substance, there is the risk that the rapidity of the pharmacological response through this route of administration could be overwhelming. The risk to public health involves the general community if an individual uses DIPT and then attempts to operate a motor vehicle or heavy machinery. Alterations of sensory and cognitive functioning from DIPT use can lead to interference with any important daily activity, without the user being aware of the impairment.

Thus, use of DIPT represents a risk to the individual drug abuser, as well as the community.

7. ITS PSYCHIC OR PHYSIOLOGIC DEPENDENCE LIABILITY

The psychic or physiological dependence liability of DIPT in animals or humans is not reported in the scientific and medical literature. Thus, it is not possible at this time to determine whether DIPT produces psychic or physiological dependence following acute or chronic administration.

DIPT and related tryptamine hallucinogens (5-MeO-DIPT, AMT, and LSD, all of which are Schedule I drugs) are highly abusable substances. Experimental data from drug discrimination studies in animals indicate that DIPT fully generalizes to the discriminative stimulus effects of DOM and DMT (see Factor 2). Hallucinogens are not usually associated with physical dependence. However, hallucinogen abusers may develop psychological dependence, as evidenced by continued use despite knowledge of potential toxic and adverse effects of the substances.

**8. WHETHER THE SUBSTANCE IS AN IMMEDIATE PRECURSOR OF A SUBSTANCE
ALREADY CONTROLLED UNDER THE CSA**

DIPT is not a known immediate precursor of any substance already controlled under the CSA.

C. Recommendation

After consideration of the eight factors determinative of control of a substance [21 U.S.C. § 811(c)], FDA recommends that N,N-diisopropyltryptamine (DIPT) and its salts be controlled in Schedule I.² NIDA concurs with this recommendation. DIPT produces effects similar to those of DOM and DMT, both of which are controlled in Schedule I of the CSA.

The necessary criteria for placing a substance into Schedule I of the CSA are set forth in 21 U.S.C. § 812(b)(1), as follows:

(A) The drug or other substance has a high potential for abuse.

DIPT is a tryptamine hallucinogen with a high potential for abuse that is similar to that of the hallucinogens DOM and DMT, both of which are controlled in Schedule I. DIPT elicits pharmacological effects qualitatively similar to these substances and is marked by hallucinations and central nervous system stimulation.

(B) The drug or other substance has no currently accepted medical use in treatment in the United States.

There are no approved new drug applications for DIPT in the United States. There is no known therapeutic application for DIPT. Therefore, DIPT has no currently accepted medical use in the United States.

(C) There is a lack of accepted safety for use of the drug or other substance under medical supervision.

Since DIPT has no approved medical use and has not been thoroughly investigated as a new drug, its safety under medical supervision is not determined. Thus, there is a lack of accepted safety for use of this substance under medical supervision.

FDA therefore recommends that DIPT and its salts be controlled in Schedule I of the CSA.

² FDA notes that there are chemical substances that could potentially fall under DEA's definition of positional isomer for DIPT, set forth in the final rule published by DEA (72 FR 67850). Since these substances are different chemically from DIPT, however, our scientific and medical evaluation and scheduling recommendation for DIPT might not be applicable to those substances.

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