UNITED STATES DEPARTMENT OF JUSTICE

Drug Enforcement Administration

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

ORDER MODIFYING ORDER FOR PREHEARING STATEMENTS

On January 14, 2022, the Drug Enforcement Administration (DEA) published a Notice of Proposed Rulemaking (NPRM), with the docket number DEA-623, titled "Schedules 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) in Schedule I." 87 Fed. Reg. 2376 (2022). The NPRM proposes to place the five tryptamine hallucinogens (4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT) in Schedule I of the Controlled Substances Act. *Id.* The NPRM provided a February 14, 2022 deadline for comments and requests for a hearing but did not fix a location for any hearings. *Id*. at 2377.

I am the Administrative Law Judge assigned to hear the above-captioned matter.

On January 31, 2022, Panacea Plant Sciences (Panacea), filed a document titled "Regarding Docket No. DEA-623" regarding the proposed placement of the five tryptamine hallucinogens in Schedule I. In its filing, Panacea: (1) indicated that it is a "Washington State biotech company;" (2) set forth its reasons why it opposes DEA's proposed action; and (3) stated that its filing serves as both a comment and a Request for Hearing (RFH).[1] Panacea RFH at 1, 5.[2] Panacea did not serve its RFH on the DEA Office of the Chief Counsel (Government) but requested that the RFH be shared with: "(1) Drug Enforcement Administration, Attn: Administrator, 8701 Morrissette Drive, Springfield, Virginia 22152; and (2) Drug Enforcement Administration, Attn: Hearing

[1] Panacea's RFH is herein provided to the parties as Attachment A.
[2] Panacea's written submission did not contain page numbers.

Clerk/OALJ, 8701 Morrissette Drive, Springfield, Virginia 22152; and (3) Drug Enforcement Administration, Attn: DEA FR Representative/DPW, 8701 Morrissette Drive, Springfield, Virginia 22152." *Id.* at 5-6.

On February 1, 2022, I issued an Order for Prehearing Statements setting **March 2, 2022** at **2:00 p.m. Eastern Time (ET)** as the deadline for the Government's Prehearing Statement and **March 30, 2022** at **2:00 p.m. ET** as Panacea's deadline to file a Prehearing Statement. Additionally, I scheduled a Prehearing Conference to be conducted by video teleconference (VTC) for **April 5, 2022, at 1:00 p.m. ET.**

On February 14, 2022, Dr. Jason Wallach and Mr. Hamilton Morris jointly filed correspondence under the subject line: "Request for Hearing in the matter of Docket No. DEA-623."[3] Dr. Wallach and Mr. Morris, through counsel, indicated that they are academic scientists who have been studying DiPT and other hallucinogenic compounds. Wallach & Morris RFH at 1. They oppose DEA's proposed scheduling of DiPT in Schedule I and set forth their reasons in their RFH. *Id.* Dr. Wallach and Mr. Morris served their RFH on the Government.

On February 14, 2022, Kykeon Biotechnologies Inc. (Kykeon) and Tactogen Inc. (Tactogen) jointly filed correspondence, dated as February 10, 2022, under the subject line: "Docket No. DEA-623."[4] Kykeon and Tactogen, through counsel, indicated that they are also requesting a hearing regarding the NPRM. Kykeon and Tactogen RFH at 1. Both companies are investigating one or more of the five tryptamines and listed five objections as to why the tryptamines should not be added to Schedule I. *Id*. at 2-8. Kykeon and Tactogen did not indicate whether they served the RFH on the Government.

On February 14, 2022, Amy Rising filed correspondence, dated as February 11, 2022, under the subject line: "Request for Hearing."[5] Ms. Rising indicated that she is requesting a hearing because she believes that putting the five tryptamines in Schedule I would "result in barriers to research and the denial to life-saving healthcare to US patients." Rising RFH at 1. Ms. Rising did not indicate whether she served the RFH on the Government.

Upon consideration of each RFH, it is hereby **ORDERED** that the deadlines set forth in the February 1, 2022 Order for Prehearing Statements are **VACATED** and the Prehearing

[3] Dr. Wallach and Mr. Morris' RFH is herein provided to the parties as Attachment B.
[4] Kykeon and Tactogen's RFH is herein provided to the parties as Attachment C.
[5] Ms. Rising's RFH is herein provided to the parties as Attachment D.

Conference scheduled for **April 5, 2022** is **CANCELED**. It is further **ORDERED** that the Government file a Prehearing Statement no later than **2:00 p.m. ET** on **March 28, 2022**. It is further **ORDERED** that each party requesting a hearing file a Prehearing Statements no later than **2:00 p.m. ET** on **April 27, 2022**.

The parties' Prehearing Statements must be served on each other and contain the following sections:

1. **Issue(s).** Statement of the perceived issues.
2. **Requested Relief.** Statement of the relief requested.
3. **Stipulations.** Proposed stipulations and admissions of fact. Each party is directed to examine available evidence and determine which facts may be the subject of stipulation to narrow the issues to those that will be and should be the subject of contested litigation.
4. **Witnesses.** Names and *current* addresses of all witnesses whose testimony is to be presented.
5. **Summary of testimony.** Brief summary of the testimony of each witness. *The summaries are to state what the testimony will be, rather than merely list the areas to be covered.* The parties are reminded that testimony not disclosed in the Prehearing Statements or pursuant to subsequent rulings is likely to be excluded at the hearing.
6. **Documents.** A list of all documentary evidence, including affidavits and other exhibits to be offered in evidence, specifying the number of pages in each. Each exhibit is to be numbered or lettered ("For Identification") with the designation to be used at the hearing.
7. **Position regarding hearing situs.** Statement of position regarding the location where the hearing will be conducted.[6]
8. **Other matters.** Any other matters that the parties consider relevant.
9. **Best estimate as to time required for presentation of own case.**

It is further **ORDERED** that **a Prehearing Conference in this matter will be conducted by VTC** on **May 4, 2022, at 1:00 p.m. ET**;[7] and it is further **ORDERED** that all proceedings will

[6] The current COVID-19 pandemic may impact the setting of venue in this case, and may result in the hearing being conducted in whole or in part through the use of videoconference (VTC) technology.

[7] Logistical issues (including counsel availability) will be coordinated by Law Clerk Anne Cotter, who can be contacted at (571) 362-7930 and Anne.M.Cotter@dea.gov. To access the VTC Prehearing Conference, the respective counsel will receive an evite to the email addresses of record in this case.

be governed by the provisions of 21 C.F.R. §§ 1316.41-1316.68.[8] Your attention is specifically directed to 21 C.F.R. § 1316.45, which provides, *inter alia*, that "[d]ocuments shall be dated and deemed filed upon receipt by the Hearing Clerk." Documents (other than proposed exhibits) may be filed electronically, by hard copy, or by facsimile with a hard copy follow-up on all facsimiles. Only one method of document filing may be utilized.

Electronic Filing: The preferred method of filing correspondence in these proceedings is as a PDF attachment via email to the DEA Judicial Mailbox (**ECF-DEA@dea.gov**). The forwarding email on all electronically filed correspondence must indicate that it was simultaneously served on the opposing party via email. The parties requesting a hearing must ensure that all documents filed with the DEA Judicial Mailbox are simultaneously served on the Government Mailbox at (**dea.registration.litigation@dea.gov**). Any request(s) to modify email addresses of a party or counsel must be made on notice to this tribunal and the opposing party. The email receipt date reflected by the DEA Judicial Mailbox server shall conclusively control all issues related to the date of service of all filed correspondence, provided however, that correspondence received after 5:00 p.m., local Washington, D.C. time, will be deemed to have been received on the following business day. Note: While email is utilized as the method to forward documents for filing—as attachments—no substantive matter communicated through the body of a forwarding email will be considered. The parties are directed to refrain from including social security numbers or personally identifiable information in electronically-filed documents. Proposed exhibits will not be accepted via electronic filing.

Hard Copy and Facsimile Filing: Alternatively, correspondence may be filed in hard-copy form. Hard-copy filings must be served in triplicate and addressed to my attention at: **The DEA Office of Administrative Law Judges, 8701 Morrissette Drive, Springfield, VA 22152**. Because the DEA Hearing Facility is not physically collocated with the DEA mailing address, hard copy filings must be posted sufficiently in advance of the due date to assure timely receipt by this office. Documents may also be served via facsimile,[9] so long as they are followed up by hard copies consistent with the directions above that are simultaneously placed for delivery. Facsimile filings will be deemed timely if received at this office by the date and time

[8] Additional helpful information regarding DEA administrative proceedings may be found at the OALJ website, https://www.dea.gov/administrative-law-judges.
[9] The facsimile number for this office is (202) 307-8198.

due, and are limited in size to twenty (20) pages, absent prior permission granted by me upon advance request.

It is further **ORDERED** that any requests for extension of time to file must be made by written motion sufficiently in advance of scheduled deadlines to be considered and ruled upon.

Dated: February 15, 2022

TERESA WALLBAUM
Digitally signed by TERESA WALLBAUM
Date: 2022.02.15 08:17:54 -05'00'

TERESA A. WALLBAUM
Administrative Law Judge

CERTIFICATE OF SERVICE

This is to certify that the undersigned, on February 15, 2022, caused a copy of the foregoing to be delivered to the following recipients:

(1) John E. Beerbower, Esq., Counsel for the Government, via email at John.E.Beerbower@dea.gov and to the DEA Government Mailbox at dea.registration.litigation@dea.gov;
(2) David Heldreth, CEO of Panacea Plant Sciences, via email at davidh@panaceaplantsciences.net;
(3) John T. Hunter, Esq., Counsel for Dr. Jason Wallach and Mr. Hamilton Morris, via email at John@hljdefense.com;
(4) Matt Baggott, Tactogen Inc., via email at matt@tactogen.com;
(5) Dillian DiNardo, Kykeon Biotechnologies Inc., via email at dillan@mindstate.design;
(6) Graham Pechenik, Esq., Counsel for Tactogen Inc. and Kykeon Biotechnologies Inc., via email at graham@calyxlaw.com;
(7) Matthew C. Zorn, Esq., Counsel for Tactogen Inc. and Kykeon Biotechnologies Inc., via email at mzorn@yettercoleman.com; and
(8) Amy Rising, via First Class mail at 1266 Oates St. NE, Washington, DC 20002.

ANIAYAH BECKFORD
Digitally signed by ANIAYAH BECKFORD
Date: 2022.02.15 08:11:30 -05'00'

Aniayah S. Beckford,
Secretary to Judge Wallbaum

ATTACHMENT A

Panacea
Plant Sciences

2021 JAN 31 PM 2:58

Regarding Docket No. DEA-623

To Drug Enforcement Administration,

Panacea Plant Sciences is writing in regards to: "Docket No. DEA-623" which is titled "Schedules of Controlled Substances: Placement of 4-hydroxy-N,N-diisopropyltryptamine, 5-methoxy-alpha-methyltryptamine, 5-methoxy-N-methyl-N-isopropyltryptamine, 5-methoxy-N,N-diethyltryptamine, and N,N-diisopropyltryptamine in Schedule I." Panacea Plant Sciences would like to provide comment and information in opposition to the following proposed actions by the DEA.

The DEA is trying to place these items into schedule 1:

- 4-Hydroxy-N,N-diisopropyltryptamine (4-OH-DiPT),
- 5-Methoxy-alphamethyltryptamine (5-MeO-AMT),
- N-Isopropyl-5-Methoxy-N-Methyltryptamine (5-MeO-MiPT),
- N,N-Diethyl-5-methoxytryptamine (5-MeO-DET), and
- N,N-Diisopropyltryptamine (DiPT)

Panacea Plant Sciences is a Washington State biotech company focused on developing foods and medicines from the cannabis plant (hemp) as well as plants/fungi which contain controlled compounds such as psilocybin and DMT more commonly known as psychedelics or hallucinogens. We reached out to the DEA to seek clarification on the status of the above compounds in December regarding medical research and have yet to get a response, but the DEA instead published the above referenced document, "Docket No. DEA-623".

Medical Uses

At the moment hallucinogens/psychedelics are having a revival for their use as medical treatments. This is due to the apparent connection between 5-ht2a agonism and the ability to provide long term relief from and treatment of depression, anxiety, addiction, PTSD and other mental health conditions.-5ht2a receptor agonism has been identified as a primary mechanism of medical benefit. As such it is intriguing to see the DEA document in the docket which is entitled "Five Tryptamines Eight-factor Analysis DEA 082021" where one can see the 5ht2a activity and binding levels used as reasons to make these compounds illegal. This same activity is precisely *why* these compounds do, in fact, have medical uses.

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.

Until recently, psychedelic/5ht2a agonist compounds such as LSD, mescaline, psilocybin and DMT have been ruled schedule 1 and thus having no accepted medical benefit. However, as mentioned above, 5ht2a agonists, including the compounds listed here, have now been established to definitely have medical benefit. The same DEA, FDA and NIH are currently allowing and hosting/funding medical trials which have already shown medical benefits of using LSD, mescaline, DMT and psilocybin.

The FDA has given Compass Pathways breakthrough treatment status for the 5ht2a agonist psilocybin:
https://compasspathways.com/compass-pathways-receives-fda-breakthrough-therapy-designation-for-psilocybin-therapy-for-treatment-resistant-depression/

Another company, mindmed, is working with the FDA for LSD, another 5ht2a agonist, as a medical treatment:
https://www.prnewswire.com/news-releases/mindmed-provides-status-update-on-ind-for-phase-2b-trial-of-lsd-for-the-treatment-of-generalized-anxiety-disorder-301448831.html

Another company is working with the FDA for a DMT IND and medical treatment:
https://www.biospace.com/article/releases/algernon-pharmaceuticals-receives-positive-feedback-from-u-s-fda-for-psychedelic-drug-dmt-clinical-research-program-for-stroke/

Further Field Trip, another biotech company investigating psychedelics, has recently obtained IND status and investigation talks with the FDA for a 4-OH-DIPT drug they refer to as *FT-104,*. https://www.globenewswire.com/news-release/2021/09/09/2294187/0/en/Field-Trip-Health-Ltd-to-Pursue-Treatment-Resistant-Depression-and-Postpartum-Depression-as-Indications-for-FT-104.html

Our understanding is that if a compound specifically is being studied for medical use then it should NOT qualify for schedule 1 status as that is reserved for compounds with no known medical use. Similarly this data would further indicate that no psychedelic compound should be in schedule 1 as the entire class of drugs is being investigated for their method of action being key to providing mental health treatments. It would seem unacceptable and disingenuous for the DEA/FDA to approve medical trials using 5ht2a agonists and even specifically 4-OH-DIPT and then ask for the compounds to be placed in schedule 1, which would ultimately hinder future medical research and clinical applications.

Panacea Plant Sciences and our collaboration partner in Canada, Egret Biosciences/Lexston Life Sciences, have similarly been studying the uses of: DIPT, 4-OH-DIPT, 5-MEO-MIPT, 5-MEO-AMT, 5-MEO-DET along with other similar compounds in order to treat conditions like depression, anxiety, post-traumatic stress disorder (PTSD) and traumatic brain injury (TBI).

Lack of Dangers

Deaths attributed to these compounds have only occured with comorbid use of psychiatric medications along with alcohol and the identified tryptamines. As such it is likely that these deaths have very little to do with the tryptamines alone and are either directly due to the use of alcohol and psychiatric medications which present a known danger or from the combination of those items with the drugs.

Additionally the doses and purity of the drugs used by the affected individuals was unknown. These factors which led to unknown drug dosing and the polydrug use are due to lack of education and transparency associated with the drugs' prohibition for human use under the Federal Analogue Act of 1986. As such the public cannot share information directly and openly about their drug use, which exacerbates unsafe drug use. These compounds have only been encountered a few hundred times by law enforcement vs thousands of daily encounters for other compounds. The attributed risk and dangers are overblown by DEA analysis. Further the risks named, science cited and data used for this process started in 2008 and much of the cited info is outdated. The DEA should conduct a new analysis with newer information as cited in this correspondence and other comments to be made on "Docket No. DEA-623."

Additionally there is little diversion risk from research and development of these compounds. From the DEA document entitled "Five tryptamines Eight-factor analysis DEA 082021" you can find the below selection which directly states the finding that companies conducting research are NOT involved with the diversion into recreational or related markets.

"HHS states in the 2012 reviews that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeODET, 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."

Federal Analogue Act

The DEA is expressing the view that it is necessary to place these items into schedule 1 in order for the DEA in order to reduce the risk to the public and due to lack of medical uses. However, as we describe above these compounds do have medical uses and the risks are actually due to the illegal or unregulated nature of the compounds and due to use of alcohol and other medications with them, NOT due to the compounds themselves. Additionally, any recreational use of the compounds or sales for unregulated human use are ALREADY illegal and already within the jurisdiction of the DEA and law enforcement without need to move them into schedule 1. This is due to the fact that the compounds fall under the definitions included in the analog act.

Under the Federal Analogue Act:

- (A) Except as provided in subparagraph (C), the term controlled substance analogue means a substance -
    - (i) the chemical structure of which is substantially similar to the chemical structure of a controlled substance in schedule I or II;
    - (ii) which has a stimulant, depressant, or hallucinogenic effect on the central nervous system that is substantially similar to or greater than the stimulant, depressant, or hallucinogenic effect on the central nervous system of a controlled substance in schedule I or II; or
    - (iii) with respect to a particular person, which such person represents or intends to have a stimulant, depressant, or hallucinogenic effect on the central nervous system that is substantially similar to or greater than the stimulant, depressant, or hallucinogenic effect on the central nervous system of a controlled substance in schedule I or II.
- (B) The designation of gamma butyrolactone or any other chemical as a listed chemical pursuant to paragraph (34) or (35) does not preclude a finding pursuant to subparagraph (A) of this paragraph that the chemical is a controlled substance analogue.
- (C) Such term does not include -
    - (i) a controlled substance;
    - (ii) any substance for which there is an approved new drug application;
    - (iii) with respect to a particular person any substance, if an exemption is in effect for investigational use, for that person, under section 355 of this title to the extent conduct with respect to such substance is pursuant to such exemption; or

- (iv) any substance to the extent not intended for human consumption before such an exemption takes effect with respect to that substance.

If the compounds are already able to be controlled by the DEA under the Federal Analogue Act and are illegal for recreational use under that act, then there is no reason for the DEA to make the move to place these items in schedule 1 in order to have police powers over them.

Risk of Scheduling

However, the move to schedule 1 WILL make it more complicated for scientists, doctors, researchers and companies to study these compounds in order to find new treatments for mental health or other diseases and conditions. This is due to the fact that schedule 1 compounds are considered as having no medical potential and then require additional licenses which cost additional fees to the DEA, FDA etc in order to research something which is essentially unregulated as a medical product to study now. As such the proposed move to schedule 1 is in antithesis to the fact that these compounds specifically and broadly (~~5ht2a~~) are being shown to have medical use via their 5ht2a activity. LSD, mescaline, DMT and other 5ht2a agonists which are structurally and receptor profile similar are in active trials for medical use. As such there is adequate evidence that these compounds do in fact have medical use and should not be moved to schedule 1.

Currently the DEA, White House and congress are working on and supporting a bill to reduce the restrictions on researching scheduled compounds for medical use. The bill is entitled Halt All Lethal Trafficking of (HALT) Fentanyl Act, which has these policy changes added. The Drug Enforcement Administration (DEA) and National Institute On Drug Abuse (NIDA) say they are in favor of a White House proposal to streamline the process of researching Schedule I drugs like marijuana and certain psychedelics.The agencies testified at a House Energy and Commerce subcommittee hearing recently, expressing support for the Office of National Drug Control Policy (ONDCP) research plan. -
https://www.marijuanamoment.net/bidens-drug-czar-wants-to-make-it-easier-to-research-marijuana-psychedelics-and-other-schedule-i-substances/

Placing these items into schedule 1 seems to be antithesis to the DEA policy move to reduce restrictions for research.

Conclusion

Panacea Plant Sciences as such would like to ask the DEA and federal agencies <u>not</u> to move these items into schedule 1 for the above cited reasons. Additionally we would like to request a public hearing on these issues and the scheduling. As such in addition to serving as public comment on Docket No. DEA-623: , we would also like these comments and statements of fact and request for a hearing shared with:

(1)Drug Enforcement Administration, Attn: Administrator, 8701 Morrissette Drive, Springfield, Virginia 22152; and (2) Drug Enforcement Administration, Attn: Hearing Clerk/OALJ, 8701

Morrissette Drive, Springfield, Virginia 22152; and (3) Drug Enforcement Administration, Attn: DEA FR Representative/DPW, 8701 Morrissette Drive, Springfield, Virginia 22152.

David Heldreth
CEO
Panacea Plant Sciences
davidh@panaceaplantsciences.net
www.panaceaplantsciences.net

Panacea Plant Sciences
14321 SE 49th St
Bellevue WA 98006

SEATTLE WA 980
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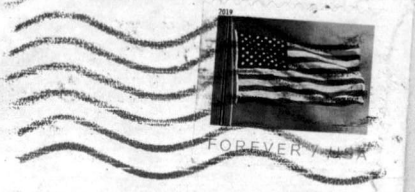


Drug Enforcement Administration (DEA)
ATTN: Hearing Clerk / DEA
8701 Morsette Dr.
Springfield VA 22152

RECEIVED
JAN 31 2022
THIS PARCEL
HAS BEEN X-RAYED

22152-108001

ATTACHMENT B

HUNTER, LANE & JAMPALA
310 S. ST. MARY'S STREET
SUITE 1740 – TOWER LIFE BLDG.
SAN ANTONIO, TEXAS 78205

JOHN T. HUNTER
THOMAS J. LANE
VIVEK JAMPALA

TEL. (210) 202-1076
FAX (210) 880-6162

February 14, 2022

Drug Enforcement Adminstriation,
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 a 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.

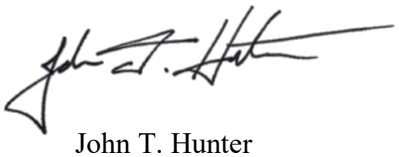
8. There is no known report of DiPT dependence anywhere in forensic or medical literature, nor are their anecdotal reports on sources such as erowid or TiHKAL.

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

Select Journalistic Publications:

"Amfonelic Acid: A structural annotation", *Harper's Magazine*	February 2015
"Gaboxadol", *Harper's Magazine*	August 2013
"Blood Spore", *Harper's Magazine*	July 2013
"Sea DMT" (with Jason Wallach), *Vice Magazine*	March 2013
"Criminal Chlorination", *Vice Magazine*	September 2012
"Pages from the Laboratory Notebook of Alexander Shulgin" (with Paul Daily), *Vice Magazine*	September 2012
"Great Medicinal Chemists of the 20th Century", *Vice Magazine*	September 2012
"Carsten Höller: Artist's Portfolio", *The Brooklyn Rail*	June 2012
"Cracking Cryptocacti", *Vice Magazine*	June 2012
"I Walked With A Zombie", *Harper's Magazine"*	November 2011
"Interview with A Ketamine Chemist", *Vice Magazine*	February 2011
"Psychedelic Maturity", *The Brooklyn Rail*	July 2010
"The Last interview with Alexander Shulgin", *Vice Magazine*	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, *University of Cambridge* February 2021

USciences Honors Spring Colloquium Speaker, *USciences* March 2018

"From PCP to MXE" (with Jason Wallach), *UMASS Amherst* April 2014

"Arylcyclohexylamines: A historical perspective", *Bard University* March 2014

"Pharmacopeia: Meet The Filmmaker", *Brandeis University* February 2013

"The Interplay of Journalism and Gray-Markets", *UPENN* September 2012

Wallach, J. & Morris, H. "N-benzyl-phenethylamines: Pharmacophore approach to receptor binding selectivity" (poster) September 2012

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

Teaching Experience:
“Hypnotic Psychopharmacology”, *USciences,* Introduction to Neuropsychopharmacology (PC340) February 2019
“Science and Filmmaking”, The New School, Documentary Production Workshop March 24, 2021

Jason V. Wallach

600 South 43rd St. Philadelphia PA, 19104
j.wallach@usciences.edu ▪ (c) 267.261.7590

Education

University of the Sciences (USciences) *Philadelphia*, PA
PhD in Pharmacology and Toxicology 2014

Indiana University of Pennsylvania *Indiana*, PA
BS in Cell and Molecular Biology (Honors Thesis Track), *Cum Laude* 2008
Minors: Chemistry, Biochemistry

Awards and Recognitions

PCP Dean's Award 2021
Excellence in Research

First Place Post-Doctoral Division Poster Award 2016
Mid-Atlantic Pharmacology Society (MAPS) Annual Meeting

Basic Science Research Poster of the Year Award 2016
Philadelphia College of Pharmacy, University of the Sciences

Alzheimer's Drug Discovery Foundation Young Investigator Scholarship 2011
Sigma Xi Outstanding Research Poster Award 2008
Indiana University of Pennsylvania

Sigma Tau Gamma Pi Fund Scholarship 2007-2008
Interfraternity Council GPA Award 2007
Indiana University of Pennsylvania

Provost Scholar 2007
Indiana University of Pennsylvania

Research Experience

University of the Sciences (USciences) *Philadelphia*, PA
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} recpetors. 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*-benzylphenalkylamine scaffolds.
- Pharmacological characterizations include radioligand-based competitive binding studies, functional assays and *in vivo* 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 CB_1/CB_2 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. McCorvy, 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. Ephenidine: 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' Diphenidine, Methoxphenidine 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-methoxydiphenidine (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

9. **Wallach, J.** Colestock, T. Cicali, B. Haigh, B. Adejare, A. Uncompetitive NMDA Receptor Antagonist and Monoamine Reuptake Inhibitor Polypharmacology for Treatment of Neuordegenerative Disorders. Poster presented at: Neurodegenerative Diseases: Biology & Therapeutics. December 3-6, 2014. Cold Spring Harbor Laboratory. Cold Spring Harbor, NY

10. **Wallach, J**. Morris, H. The History of Dissociative Drugs. Invited lecture at Psymposia. April 12-14, 2014; University of Massachusetts, Amherst. Amherst, MA

11. **Wallach, J**. Cicali, B. Haigh, B. Sun, S. Adejare, A. Arylbicycloheptylamines: Novel Conformationally Restricted Uncompetitive NMDA Receptor Antagonists. Poster presented at: Mid-Atlantic Pharmacology Society Annual Meeting. October 7, 2013; University of the Sciences, Philadelphia, PA

12. **Wallach, J**. Morris, H. *N*-benzyl-phenethylamines: Pharmacophore approach to receptor binding selectivity. Poster presented at: Psychedemia; September 27-30, 2012; University of Pennsylvania, Philadelphia, PA

13. **Wallach, J**. Haigh, B. Sun, S. Adejare, A. Arylbicycloheptylamines as novel uncompetitive NMDA receptor antagonists. Poster presented at: 244th ACS National Meeting & Exposition; August 19-23, 2012; Philadelphia, PA

14. **Wallach, J**. Sun, S. Adejare, A. Discovery of Novel NMDA Receptor Antagonists with Neuroprotective Properties. Poster presented at: 12th International Conference on Alzheimer's Drug Discovery; September 26-27, 2011; Jersey City, NJ

15. Nguyen, QN. Gaye, BT. Ates-Alagoz, Z. **Wallach, J**. Adejare, A. Antioxidant properties of novel NMDA receptor antagonists and radiosensitizers. Poster presented at: 244th ACS National Meeting & Exposition; August 19-23, 2012; Philadelphia, PA

Patents and Patent Applications

1. Becker, J., Peterson, G. and **Wallach, J.,** Bexson Biomedical Inc, 2021. *Ketamine formulation for subcutaneous injection*. U.S. Patent 10,973,780.

2. Becker, J., Peterson, G. and **Wallach, J.,** Bexson Biomedical Inc, 2020. *Systems, devices, formulations and methods for controlled drug delivery*. U.S. Patent 20200384188A1

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 Koh

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 CSA[1] 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-HT2A receptors in the brain (Nichols, 2006). DIPT binds with low-moderate affinity to 5-HT2A receptors, with an inhibitor constant (Ki) 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-HT1A 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-HT1A receptor (Ki = 687 nM, Toll and Berzetei-Gurske, 2006) or no significant activity for the 5-HT1A receptor (Ki = 2270 nM, Janowsky and Eshleman, 2007). A functional assay evaluating a second messenger system associated with the 5-HT1A receptor (GTP) also shows that DIPT does not have significant activity at the 5-HT1A 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 (Ki = 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-HT2A 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

novel drug produces bar pressing ≥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"

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 $C_{16}H_{24}N_2$, 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.

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[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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ATTACHMENT C

YetterColeman LLP

February 10, 2022

Drug Enforcement Administration
Attn: Hearing Clerk/OALJ
8701 Morrissette Drive
Springfield, VA 22152

Re: *Docket No. DEA-623*

Dear Sir:

Petitioners[1] hereby request a hearing in the matter of: *Schedules 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) in Schedule I.*

Introduction

DEA recently published in the Federal Register a notice of proposed rulemaking proposing to place Five Tryptamine[2] hallucinogens into Schedule I. 87 Fed. Reg. 2376 (Jan. 14, 2022) (the "proposed rule"). Based on an HHS evaluation from 2012, DEA concludes that these compounds meet the criteria for placement in Schedule I.

Petitioners oppose the rule as proposed. The evidence of actual or potential abuse presented in the proposed rule and supporting materials does not justify placement of one or more of the Five Tryptamines into Schedule I. Placing these substances in Schedule I would greatly disturb ongoing research into these Five Tryptamines and other related compounds—research that could transform mental health care at a moment in time when new treatments are desperately needed.

Petitioners encourage DEA to withdraw or delay the proposed rule and continue to regulate the Five Tryptamines under the Federal Analogue Act. Alternatively, if DEA concludes that the law and evidence warrants control of the Five Tryptamines, Petitioners urge DEA to consider alternative placements, such as Schedules II or III.

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1 Mindstate Design Labs (Kykeon Biotechnologies Inc.) and Tactogen Inc.

2 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT.

Comment/Request for Hearing

(A) Statements of Interest

- **Mindstate Design Labs** (Kykeon Biotechnologies Inc.) is a Pennsylvania-based company that develops psychedelic drug therapies for intractable mental health conditions. It is currently investigating one or more of the Five Tryptamines in preclinical research. Its website is at https://www.mindstate.design/.

- **Tactogen Inc** is a California-based public benefit corporation that is developing safer, more effective prescription medicines for mental wellness. It is currently investigating one or more of the Five Tryptamines as part of a program to develop new medicines. Its website is at https://tactogen.com/.

(B) Objections/Issues[3]

1. Whether the proposed rule's reliance on the 2012 HHS evaluation is arbitrary, capricious, or contrary to law; whether DEA failed to observe the procedure required by the CSA; and whether the HHS analyses must be updated before DEA can institute rulemaking.

2. Whether significant aspects of the § 811(b) analyses are arbitrary, capricious, contrary to law, or lack substantial evidence.

3. Whether the proposed rule sets forth subsantial evidence to support actual or potential for abuse.

4. Whether a finding that a substance lacks accepted medical use is dispositive of a classification.

5. Whether DEA complied with the Regulatory Flexibility Act; and whether it must conduct an initial and final regulatory flexibility analysis.

(C) Statement of Positions on Objections/Issues

1. Use of a 2012 HHS Evaluation and Recommendation is Improper.

Scheduling evaluations by HHS and DEA must be based on *current* data. *See, e.g.*, 21 U.S.C. § 811(c)(4) ("history and *current* pattern of abuse"). Because the proposed rule relies on a 2012 HHS evaluation, however, it cannot be based on current data.

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[3] Petitioners request a hearing according to the rulemaking procedures prescribed by subchapter II of chapter 5 of title 5, but do not necessarily require a hearing on all six issues. Consistent with 21 C.F.R. § 1308.42, a hearing is only needed for the purpose of receiving factual evidence and expert opinion regarding the issues involved in the issuance of the rule. Other issues can be addressed in pre-hearing or post-hearing submissions.

After receiving the HHS evaluation, Section 811(b) states that "[i]f the Attorney General determines that these facts and all other relevant data constitute substantial evidence of potential for abuse such as to warrant control ... he *shall* initiate proceedings for control." Here, DEA received the HHS evaluations in 2012. But DEA did not initiate proceedings shortly thereafter. Presumably, it concluded that the facts and relevant data did not constitute substantial evidence of potential for abuse to warrant control. The proposed rule provides no explanation for why, ten years later, DEA changed its mind.

DEA states that in June 2020, it "confirmed with HHS that their 2012 statements are still applicable," but only with respect to medical use. DEA does not explain why it did not ask HHS to update its 2012 evaluation. That is significant considering (1) the 2012 HHS evaluations rely on older research to generalize about hallucinogenic compounds, and (2) a wave of newer research calls into question older research and assumptions about the actual and potential abuse and risks of hallucinogenic compounds. A PubMed search for "hallucinogen" shows that the research surrounding hallucinogens has grown considerably since 2012, including 1,036 papers in 2020.

Indeed, DEA's eight-factor analysis relies on substantial relevant scientific research that post-dates the HHS evaluation, such as Rickli et al., 2016 and Janowsky, 2018a-f.[4] HHS in 2012 did not and could not consider this evidence. Some contradicts or undermines conclusions reached by HHS in its 2012 evaluations. For example, DEA states that drug discrimination studies in rats show that DiPT fully substitutes for DMT (citing Gatch and Forster, 2006d). But Carbonaro et al., 2015 and Carbonaro et al., 2013 explain that while DMT and DiPT are structurally similar hallucinogens, they produce different effects from each other and do not fully cross-substitute for each other. Excluding the HHS evaluations themselves, nearly 1 out of 3 references cited in DEA's analysis post-dates the 2012 HHS evaluation—none of which could have been considered by HHS in its 2012 review.

Section 811(b) requires DEA to request from the Secretary a scientific and medical evaluation "*after* gathering the necessary data." Therefore, DEA must ask HHS for a new or updated evaluation *before* initiating proceedings for control.

2. The Eight Factor § 811(b) Analysis is Fundamentally Flawed.

Several components of the eight-factor § 811(b) analysis are arbitrary, capricious, contrary to law, or lack substantial evidence. The following illustrates some of the deficiencies:

Factor 1(d) should not apply. None of the Five Tryptamines are *new* drugs. In its analysis, HHS states that it relied on the legislative history's definition. But the legislative history explains

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[4] Similarly, it is unclear why the DEA's analysis does not cite Gatch, Michael B et al. "Discriminative Stimulus Effects of Substituted Tryptamines in Rats." *ACS pharmacology & translational science* vol. 4,2 467-471. 29 Dec. 2020, which was research supported by contract 15DDHQ18P00000735 from HHS/DEA and appears to have been awarded prior to August 2019. Gatch et al., 2020 raises further questions about why DEA did not ask HHS for a current medical evaluation as the statute requires.

that the fourth "potential for abuse" factor applies to *new* drugs.[5] The Five Tryptamines, in contrast, have been around for decades. DEA's August 2021 § 811(b) analysis correctly restates the legislative history, but incorporates the flawed HHS analysis. And where, as here, the drugs are not *new*, it is not reasonable to make assumptions flatly contradicted by the available evidence.

Improper generalizations and conclusions. The § 811(b) analyses repeateadly make improper conclusions about the Five Tryptamines, tryptamines, and hallucinogens generally based on unsubstantiated statements and unsound scientific reasoning; for example:

- For factor 6, HHS concludes that "hallucinogen abusers may develop psychological dependence, as evidenced by continued use despite knowledge of potential toxic and adverse effects of the substances." This statement is unsubstantiated. Most hallucinogens are not "habit forming."[6] Hallucinogens are not typically considered to be drugs of dependence. Neither are they reliably self-administered in nonhuman animals, nor associated with a known withdrawal syndrome.[7]

- It is unclear how or why HHS selected certain hallucinogens (DOM, DMT, LSD, and mescaline) as comparators to the Five Tryptamines but not others. Neither DOM nor mescaline are tryptamines, for example. Research since 2012 has shown that the subjective effects of 4-substituted tryptamines such as 4-HO-MiPT are most closely related to psilocybin and its active metabolite psilocin.[8] The agencies should thus consider the detailed eight-factor analysis in light of Johnson, Matthew W et al. "The abuse potential of medical psilocybin according to the 8 factors of the Controlled Substances Act." *Neuropharmacology* vol. 142 (2018).

- For factor 5, DEA's eight-factor analysis states that "[t]ryptamine hallucinogens, both natural and synthetic, have been popular among the attendees of rave parties, music concerts, ... Often these substances are promoted as substitutes for LSD. Synthetic hallucinogens and stimulants are known as 'club drugs.'" Moreover, DEA states that there "has been significant availability, trafficking, and abuse of a number of tryptamines." Generalizations aside, there is little evidence about the Five Tryptamines, for example, that any has ever been regarded as a "club drug."

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5 *See* H.R. Rep. No. 91-1444 91st. Cong., 2d Sess. 47 (1970) (House Report) at 34.

6 *See* House Report at 36 (explaining that "psychic or physiological dependence liability" requires an assessment of the extent to which a drug is "physically addictive or psychologically habit forming").

7 Johnson, Mw et al. "Human hallucinogen research: guidelines for safety." *Journal of psychopharmacology* (Oxford, England) vol. 22,6 (2008): 603-20.

8 Rickli, Anna et al. "Receptor interaction profiles of novel psychoactive tryptamines compared with classic hallucinogens." *European neuropsychopharmacology* vol. 26,8 (2016): 1327-37.

- That two substances may have similar molecular structure or may exhibit affinity over the same receptor is not a sufficient scientific basis to conclude that the two substances exhibit similar pharmacological action. For example, DEA states that "[c]hemically, 5-MeO-MiPT is a synthetic analogue of tryptamine, which is structurally related to other tryptamines, such as DMT. The effects and pharmacological action of 5-MeO-MiPT are therefore similar to that of other Schedule I hallucinogens, such as DMT or LSD, both of which have no accepted medical use and high abuse potential." This syllogism is not sound. For example, analogues of tryptamine include the prescription anti-migraine drug sumatriptan as well as the over-the-counter sleep aid melatonin.

Insufficient and Contrary Evidence. Numerous points and statements in the eight-factor analyses lack sufficient evidence, including but not limited to:

- In factors 1(a) and 6 in the HHS analysis of 5-MeO-MiPT, HHS concludes that individuals are taking 5-MeO-MiPT in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community based on *two* case reports in which a *combination* alleged to be 5-MeO-MiPT and harmala extracts/harmaline were consumed.[9] In one of the two cases, the evaluation notes that it is "unclear from the available information whether 5-MeO-MiPT played a direct role in the death." HHS also notes that there are "23 anecdotal case reports described on the Internet www.erowid.org in which individuals who purported to use 5-MeO-MiPT were treated by medical professionals," but it is unclear which reports on www.erowid.org HHS refers to. Many involve combinations of 5-MeO-MiPT and other substances.

- The HHS evaluation concludes that "[u]se of 5-MeO-MiPT is associated with emergency room admissions." It is unclear what evidence supports an association.

- The HHS evaluation concludes that evidence from law enforcement databases and case reports regarding seizures demonstrate that 4-OH-DiPT has been available as a "street drug" of abuse. But DEA's NFLIS database for drug cases did not report *any* cases involving 4-OH-DiPT, and only *three* cases reported in DEA's STRIDE database from 2003 to 2004. None of those three cases provide evidence to support any scope, duration, or significance of abuse and do not support the conclusion that 4-OH-DiPT's has been available for purchase as a street drug. The conclusion runs "counter to the evidence before the agency." *Motor Vehicle Mfrs. Ass'n of U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983).

Methodology and Standards Used. In making § 811(b) determinations and assessing the research, it is unclear what standards DEA and HHS apply to the evidence. For many items, a handful anecdotal reports reported over a period of years is deemed sufficient in support of abuse

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[9] That a combination of an MAOI and 5-MeO-MiPT may have led to a hospital admission and death says little about whether 5-MeO-MiPT itself is sufficient to create a hazard. The proposed rule does not present evidence suggesting a pattern of combining of these substances.

potential. In contrast, in July 2016, in responding to a petition to reschedule marijuana by the Governors of Washington and Rhode Island, HHS did a searching review of publicly available medical literature; determined that only 11 out of 566 studies met the selection criteria, including placebo and double-blinding; and critically reviewed those 11 studies, concluding that none proved efficacy due to "limitations in the study designs."[10] In short, the agencies appear to be applying wildly different standards in different scheduling actions. This unexplained inconsistency and departure from prior practice renders the proposed rule arbitrary and capricious. *See Encino Motorcars, LLC v. Navarro*, 579 U.S. 211, 221 (2016).

Risk to Public Health. The eight-factor analysis presumes that any drug that induces hallucinogenic effects poses a risk to public health. The available and additional evidence, however, is to the contrary: the harm potential of most hallucinogenic compounds like psilocybin and LSD is less than other Schedule I and II compounds and many Schedule III and IV compounds.

3. The Proposed Rule Provides No Substantial Evidence of Actual or Relative Potential For Abuse.

Neither the proposed rule nor the supporting materials present *substantial* evidence of actual or potential for abuse to warrant control. Actual or potential abuse requires more than isolated or occasional non-therapeutic purposes. To show actual or relative potential abuse, there must exist a *substantial* potential for the occurrence of significant diversion from legitimate channels, *significant use* by individual's contrary to professional advice, or *substantial capability* of creating hazards to the health of the user or the safety of the community. *See Grinspoon v. DEA*, 828 F.2d 881, 893 (1st Cir. 1987); House Report at 35. The House Report further explains:

> In speaking of "substantial" potential the term "substantial" means *more than a scintilla* of *isolated abuse*, but less than a preponderance. Therefore, documentation that, say, several hundred thousand dosage units of a drug have been diverted would be "substantial" evidence of abuse despite the fact that tens of millions of dosage units of that drug are legitimately used in the same time period. The normal way in which such diversion is shown is by accountability audits of the legitimate sources of distribution, such as manufacturers, wholesalers, pharmacies, and doctors

For at least some of the Five Tryptamines, DEA has concluded a potential for abuse based on a scintilla of isolated abuse. Therefore, based on the evidence described above, DEA's conclusion runs "counter to the evidence before the agency." *State Farm*, 463 U.S. at 43. And to the extent DEA relies on "potential for abuse" as a basis to schedule the Five Tryptamines, DEA fails to analyze *relative* potential for abuse as the statute requires. *See, e.g.*, 21 U.S.C. § 812(b)(1)(A) (high potential for abuse); *id.* § 812(b)(3)(A) (has a potential for abuse less than the

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[10] Schedules of Controlled Substances: Maintaining Marijuana in Schedule I of the Controlled Substances Act, Background, Data, and Analysis: Eight Factors Determinative of Control and Findings Pursuant to 21 U.S.C. 812(b) at 36 (DEA July 2016)

drugs or other substances in Schedules I or II); *id.* § 812(b)(4)(A) (has a potential for abuse less than the drugs or other substances in Schedule III).[11]

4. Whether Lack of Medical Use is Dispositive of a Classification.

Currently, DEA treats medical usefulness as the controlling factor in classification decisions. Any drug with a potential for abuse with "no currently accepted medical use" is placed in Schedule I. *See, e.g.*, 86 Fed. Reg. 44271 (Aug. 12, 2021). This approach, however, is contrary to the text and the decision by the D.C. Circuit Court of Appeals in *NORML*. *See Nat'l Org. for Reform of Marijuana L. (NORML) v. DEA*, 559 F.2d 735, 748 (D.C. Cir. 1977) ("placement in Schedule I does not appear to flow inevitably from lack of a currently accepted medical use").

As the *NORML* court explained, DEA has more flexibility and discretion in scheduling substances, and it can place the Five Tryptamines (or any drug lacking a currently accepted medical use) in a schedule other than Schedule I. The CSA "contemplates balancing of medical usefulness along with several other considerations, including potential for abuse and danger of dependence." *Id.* "To treat medical use as the controlling factor in classification decisions is to render irrelevant the other 'findings' required by Section 202(b)." *Id.*

Here, even if the Five Tryptamines lack a currently accepted medical use, one or more of them may be appropriately and reasonably placed in a lower schedule. DEA may conclude, in its reasoned judgment, that (a) the Five Tryptamines do not have the same potential for abuse or harm as drugs currently listed in Schedule II such as cocaine, methamphetamine, fentanyl, and PCP; and (b) abuse of the Five Tryptamines would not lead to "severe psychological or physical dependence" but "may lead to moderate or low physical dependence or high psychological dependence," such that Schedule II or III is a more appropriate placement under the circumstances.

5. Non-compliance with § 603 and 604 of the Regulatory Flexibility Act.

The Administrator's § 605 certification is deficient. Although the certification speculates about the effect the proposed rule may have on 31 *suppliers* of the Five Tryptamines, it makes no attempt to analyze the economic impact on other entities, including small entities that use these drugs in scientific and medical research. Because the Administrator "entirely failed to consider an important aspect of the problem," *State Farm*, 463 U.S. at 43, the certification is invalid.

Petitioners request initial and final regulatory flexibility analyses under § 603 and § 604. Such analyses would include a description of the reasons why action by the agency is being considered and alternatives to the proposed rule which accomplish the stated objectives of applicable statute and which minimize any significant economic impact of the proposed rule on small entities. Petitioners specifically request the agency consider two alternatives aligned with the objectives of the CSA that would permit DEA to control abuse and diversion while minimizing

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[11] *See, e.g.*, Basis for the Recommendation to Schedule Tramadol In Schedule IV of the Controlled Substances Act at 12-13 (HHS Sept. 16, 2010) (performing a *relative* abuse potential analysis and concluding that tramadol produces limited reinforcing effects, consistent with a lower schedule) *available at* https://www.regulations.gov/document/DEA-2013-0010-0005.

the economic impact the proposed rule would have on small entities conducting legitimate research, such as Petitioners:

a. Whether DEA could regulate the Five Tryptamines as analogues under the Federal Analogue Act. *See* 21 U.S.C. § 813 ("A controlled substance analogue shall, to the extent intended for human consumption, be treated, for the purposes of any Federal law as a controlled substance in Schedule I."). According to the HHS evaluations, all Five Tryptamines are analogues of other Schedule I substances and produce substantially similar pharmacological effects to those scheduled substance. It is unclear why continued regulation under the Federal Analogue Act could not obtain the objectives of the CSA.[12]

b. Whether DEA could effectively curb abuse and diversion by placing the Five Tryptamines in a lower schedule, either by recognizing that the Five Tryptamines have a "currently accepted medical use with severe restrictions" in medical and scientific research, or by not treating the lack of a currently accepted medical use as dispositive. Notably, placement of these substances in Schedule II would align with recent public statements from DEA and other agencies in the Biden-Harris Administration made in December 2021 regarding relieving research restrictions into controlled substances.

Conclusion

For the reasons stated herein, Petitioners request DEA withdraw or delay the proposed rule.

Alternatively, Petitioners request that DEA (1) update the 2012 HHS evaluation, (2) conduct a Regulatory Flexibility Analysis, and (3) hold a formal rulemaking hearing. In the event DEA ultimately concludes that the Five Tryptamines should be controlled, Petitioners request DEA place the Five Tryptamines in Schedule II or below.

All notices to be sent pursuant to the proceeding should be addressed to Petitioners:

Matt Baggott Tactogen Inc 3790 El Camino Real Unit #510 Palo Alto, CA 94306 matt@tactogen.com	Dillan DiNardo Kykeon Biotechnologies Inc. 1900 Main Street Suite 241 Canonsburg, PA 15317 dillan@mindstate.design

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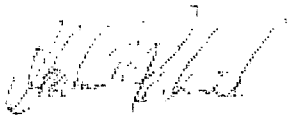
[12] *See, e.g.*, 52 Fed. Reg. 2221 (Jan. 21, 1987) (noting that finalization of rules placing tiletamine into schedule I was not warranted at the time because "persons engaged in activities prohibited by the CSA [could] be prosecuted if those activities involve tiletamine, pursuant to [the Federal Analogue Act]" and delaying scheduling could "accommodate legitimate industry in the production and marketing of a Food and Drug Administration approved drug product").

With copies to:

Graham Pechenik Calyx Law 78 Virgil Street San Francisco, CA 94110 graham@calyxlaw.com	Matthew C. Zorn Yetter Coleman LLP 811 Main St., Ste. 4100 Houston, TX 77002 mzorn@yettercoleman.com

Respectfully yours,

CALYX LAW



Graham Pechenik

YETTER COLEMAN LLP

Matthew C. Zorn

Counsel for Petitioners Tactogen Inc and Mindstate Design Labs (Kykeon Biotechnologies Inc.)

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ATTACHMENT D

Schedules of Controlled Substances: Placement of 4-hydroxy-N,N-diisopropyltryptamine, 5-methoxy-alpha-methyltryptamine, 5-methoxy-N-methyl-N-isopropyltryptamine, 5-methoxy-N,N-diethyltryptamine, and N,N-diisopropyltryptamine in Schedule I

Docket ID DEA-2022-0001

February 11, 2022

Drug Enforcement Administration, Attn: Hearing Clerk/OALJ

8701 Morrissette Drive,

Springfield, Virginia 22152

Subject: Request for Hearing

To whom it may concern:

The undersigned Amy Rising hereby requests a hearing in the matter of: Docket ID DEA-2022-0001, the Schedules of Controlled Substances: Placement of 4-hydroxy-N,N-diisopropyltryptamine, 5-methoxy-alpha-methyltryptamine, 5-methoxy-N-methyl-N-isopropyltryptamine, 5-methoxy-N,N-diethyltryptamine, and N,N-diisopropyltryptamine in Schedule I.

(A) Amy Rising believes that the expected outcome to the scheduling of Controlled Substances: Placement of 4-hydroxy-N,N-diisopropyltryptamine, 5-methoxy-alpha-methyltryptamine, 5-methoxy-N-methyl-N-isopropyltryptamine, 5-methoxy-N,N-diethyltryptamine, and N,N-diisopropyltryptamine in Schedule I would result in barriers to research and the denial to life-saving healthcare to US patients.

(B) In the matters of Controlled Substances, an objection to the placement of 4-hydroxy-N,N-diisopropyltryptamine, 5-methoxy-alpha-methyltryptamine, 5-methoxy-N-methyl-N-isopropyltryptamine, 5-methoxy-N,N-diethyltryptamine, and N,N-diisopropyltryptamine in Schedule I.

(C) All Controlled Substances aforementioned should be placed in Schedule 5.

All notices to be sent pursuant to the proceeding should be addressed to:

Amy Rising

1266 Oates St.

Washington, DC

Respectfully yours,

LJ

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