

# **ATTACHMENT A**



2021 JAN 31 PM 2:58

## Regarding Docket No. DEA-623

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DEPARTMENT OF ADMINISTRATION  
2021 JAN 31 PM 2:58

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. 5-HT2A 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<sub>2A</sub> receptor binding and functional results for 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, DiPT, and select schedule I hallucinogens.**

Drug	Binding		Function (IP-1 formation)	
	K <sub>i</sub> (nM)	Hill Coefficient	EC <sub>50</sub> (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 [<sup>3</sup>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 occurred 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.marijuananamoment.net/bidens-drug-czar-wants-to-make-it-easier-to-research-marijuana-pschedelics-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 not 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

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

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