UNITED STATES DEPARTMENT OF JUSTICE

Drug Enforcement Agency

In the Matter of **Scheduling of Controlled Substances: Placement of 2,5-dimethoxy-4- iodoamphetamine (DOI) and 2,5-dimethoxy-4-chloroamphetamine (DOC) in Schedule I.**	**Docket No. 24-24**

JOINT PREHEARING STATEMENT OF SCIENCE POLICY COUNCIL, STUDENTS FOR SENSIBLE DRUG POLICY AND DR. RAUL A. RAMOS

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Petitioners Science Policy Council, Students for a Sensible Drug Policy ("SSDP") and Dr. Raul A. Ramos[1] (collectively, "Petitioners") submit this Joint Prehearing Statement in accordance with the Tribunal's Second Order for Prehearing Statements, dated July 1, 2024.

ISSUES

1. Whether the Drug Enforcement Administration (the "DEA") has met its burden of showing that DOI has a high potential of abuse so as to warrant placement in schedule I of the Controlled Substances Act, where:

(a) the DEA admits that there are no cases in the medical literature of distressing events or death associated with the use of DOI;

(b) the DEA admits that DOI is available for purchase from legitimate chemical companies because it is used in scientific research, and there is no evidence of diversion from these companies;

(c) the DEA admits that clinical studies with DOI have not been conducted in healthy human volunteers, and there is no data available from studies that evaluate the psychoactive and physiological responses produced by DOI in humans;

(d) in support of its claim that there has been significant abuse of DOI, the DEA reports (i) a total of 40 seizures of DOI by federal, state and local law enforcement, and (ii) a total of five submissions of DOI (none more recent than 2009) in the DEA's Microgram Bulletin on the detection and analysis of suspected controlled substances – with no reported evidence whether or how any of the seized DOI was used or abused – in the more than 30 years since the effects and chemical

[1] Two other petitioners, Amelia A. Furbish, PharmD, and Megan Francis wish to withdraw from this proceeding.

composition of DOI were described to the public in PIKHAL: A Chemical Love Story (Shulgin and Shulgin, 1991);

(e) the DEA's assessment of the potential for abuse does not distinguish between use and abuse of DOI;

(f) The Department of Health and Human Services ("HHS") in its scheduling recommendation to DEA relies in large part on drug discrimination studies comparing the effects on animals of DOI with those of drugs that were previously placed in Schedule I, even though the Food and Drug Administration has stated in a guidance document that it regards drug discrimination studies as insufficient to assess the abuse potential of drugs that are the subject of New Drug Applications in the absence of Human Abuse Potential and other studies;

2. Whether the DEA has met its burden of showing that DOI should be placed in Schedule I, where:

(a) Congress has expressed its intent in the Controlled Substances Act that (A) the availability of psychotropic substances to manufacturers, distributors, dispensers, and researchers for useful and legitimate medical and scientific purposes will not be unduly restricted; and (B) nothing should interfere with bona fide research activities;

(b) HHS and the DEA failed to consider the impact that placement of DOI in Schedule I would have on ongoing and future scientific research on DOI;

(c) petitioners have come forward with compelling evidence of the importance of scientific research on DOI, much of which is funded by the U.S. government; and

(d) petitioners have come forward with compelling evidence that the burdens resulting from placement of DOI in Schedule I would significantly impair the ability of researchers to continue to study DOI.

3. Whether the DEA has met its burden of showing that DOC has a high potential of abuse to warrant placement in Schedule I of the Controlled Substances Act.

4. Whether the DEA has met its burden of showing that DOC should be placed in Schedule I.

5. Whether the DEA's broad discretion in scheduling drugs lacks sufficient legislative guidance and oversight and constitutes an unconstitutional delegation of legislative power by Congress.

6. Whether the DEA has engaged in "reasoned decision making" within boundaries of the delegated authority to effectuate the will of Congress.

7. Whether the DEA's interpretation and application of the Controlled Substances Act has engaged in "reasoned decision making" within boundaries of the delegated authority to effectuate the will of Congress and whether this is an unreasonable interpretation of the Controlled Substances Act.

8. Whether the DEA may satisfy the United States' Single Convention obligations by supplementing scheduling decisions with regulatory action and whether anything in the CSA, , states that a drug must be placed into Schedule I or II, or any other particular schedule, to comply with the Single Convention.

9. Whether there is sufficient evidence presented by the Secretary of HHS to reasonably add DOI to Schedule I and if the Secretary's decision was arbitrary and capricious.

10. Whether there is sufficient evidence presented by the Secretary of HHS to reasonably add DOC to Schedule I and if the Secretary's decision was arbitrary and capricious.

11. Whether absolute reliance on the absence of FDA approval outside of limited contexts is inappropriate and contrary to the intent of Congress in enacting the Controlled Substance Act.

12. Whether the DEA's interpretation of "currently accepted medical use" was reasonable.

13. Whether HHS's overall CAMU recommendation is binding on DEA and if HHS's CAMU recommendation are binding, after the initiation of formal rulemaking proceedings.

14. Whether the DEA is deciding based on the whole record and in accordance with the reliable, probative, and supported by substantial evidence.

15.. Whether the CSA requires that the DEA need rely on scheduling decisions alone to comply with the Single Convention.

16. Whether the DEA's action to add DOI to Schedule I is based upon analysis of fact or interpretation of the Controlled Substances Act is arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law.

17. Whether the separation of powers doctrine precludes an administrative agency from being granted the same authority that Congress, empowered through their legislative authority, to schedules a substance, when that same agency has the statutory authority to pursue criminal enforcement regarding that substance.

REQUESTED RELIEF

1. The Tribunal should recommend a finding and conclusion that the DEA has not met its burden of showing that DOI has a high potential for abuse.

2. The Tribunal should recommend a finding, conclusion and decision that the DEA has not met its burden of showing that DOI should be placed in Schedule I.

3. The Tribunal should recommend a finding and conclusion that the DEA has not met its burden of showing that DOC has a high potential for abuse

4. The Tribunal should recommend a finding, conclusion and decision that the DEA has not met its burden of showing that DOC should be placed in Schedule I.

PROPOSED STIPULATIONS

1. There is no documentation in medical literature of the human use of DOI. To date, there are no reports of distressing responses or death associated with DOI in medical literature.

2. According to HHS, the physiological dependence liability of DOI and DOC in animals and humans is not reported in scientific and medical literature.

3. DOI and DOC are available for purchase from legitimate chemical synthesis companies because they are used in scientific research and there is no evidence of diversion from these companies.

4. There is no evidence of the illicit sales of DOI.

5. Anecdotal reports of hallucinogenic experiences with DOI and DOC are based upon unverifiable anonymous reports from online drug forums such as www.erowid.org.

6. It is impossible to know if the street drugs sold to an individual as DOI or DOC on which anecdotal reports are based are in fact the substances they are marketed as in the absence of chemical analysis or evaluation of biological fluids following ingestion.

7. Data from NFLIS-Drug indicating that DOI and DOC were found in samples does not indicate if the sample was intended for human consumption.

8. DOI and DOC are not immediate precursors of any controlled substance of the CSA as defined by 21 U.S.C. 802(23) (https://www.govinfo.gov/link/uscode/21/802).

9. Clinical studies with DOI have not been conducted in healthy human volunteers, and there is no data available from studies that evaluate the psychoactive and physiological responses produced by DOI in humans.

10. The DEA's assessment of the potential for abuse did not distinguish between use and abuse of DOI.

11. The DEA is not aware of encountering of DOI by law enforcement since 2009.

12. It has never been illegal to possess DOI under federal law.

13. Neither HHS nor the DEA has considered the impact that placement of DOI in Schedule I would have on ongoing and future scientific research on DOI.

14. Abuse is not defined within the Controlled Substances Act.

15. Currently accepted medical use is not defined in the Controlled Substances Act.

16. Adding DOI to Schedule I will financially impact and cause irreparable harm to Dr. Ramos.

17. Adding DOI to Schedule I will financially impact and cause irreparable harm to members of SSDP.

18. Possession of DOI and DOC is not demonstrative of intent for consumption.

19. DOI has been used in the scientific study of serotonin receptors for over 35 years.

20. There are published scientific journal articles of DOI's utility in inflammatory disorders.

21. DOI is used as a tritiated ligand in neuroscience research.

22. There are over 900 scientific journal articles published on PubMed mentioning "2,5-Dimethoxy-4-iodoamphetamine" (DOI).

23. Federal agencies including the National Institute on Drug Abuse and the National Institute of Mental Health have awarded grant funding for the scientific study of psychedelics including DOI in the treatment of mental disorders.

24. DOI and DOC have different pharmacokinetic and pharmacodynamic properties compared to other psychedelics like psilocybin and LSD.

25. DOI has been used in the study of acute and chronic pain.

26. DOI has been demonstrated to have analgesic effects in animal models of neuropathic pain.

27. DOI has been demonstrated to produce a decrease in rodent intracranial self-stimulation.

28. DOI does not produce the same levels of self-administration or self-stimulation as morphine, cocaine or amphetamines in rodent models.

29. DOI decreases motivation for fentanyl seeking and decreases low-cost and total fentanyl consumption in a rodent model.

30. DOI reduced ethanol consumption and preference in two separate studies.

31. On March 4, 2020, the United Nations Commission on Narcotic Drugs voted to place DOC in Schedule I of the 1971 Convention on Psychotropic Substances.

32. The United Nations Commission on Narcotic Drugs has never voted to place DOI in Schedule I of the 1971 Convention on Psychotropic Substances.

WITNESSES AND SUMMARY OF TESTIMONY

The Petitioners proposed witness list and summary of testimony is listed in **Appendix A.**

DOCUMENTS

The Petitioner's proposed documents are listed in **Appendix B**.

POSITION REGARDING HEARING SITUS

The most appropriate venue for the hearing is in the Arlington, VA hearing facility. The petitioners request permission to present all non-party witnesses outside a 100-mile radius remotely for convenience and/or necessity. Dr. Nutt lives in England and is 73 years old and may not be able to travel and therefore may only be able to testify remotely. Dr. Nichols is 79 years old and suffering from severe scoliosis and may not be able to travel and therefore, may only be able to testify remotely. Dr. de la Fuente Revenga is residing in Spain for multiple months with an infant son and therefore may only be able to testify remotely.

ESTIMATE AS TO TIME REQUIRED

With written statements, the Petitioners estimate that their case will take no longer than one full day. With live direct testimony, the Petitioners estimate that their case may take up to four days, exclusive of cross examination. The Petitioners estimate that their cross-examination of Dr. Carbonaro will take a full day.

Dated: July 23, 2024

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on this 23rd day of July, 2024, a copy of the foregoing **JOINT PREHEARING STATEMENT OF SCIENCE POLICY COUNCIL, STUDENTS FOR SENSIBLE DRUG POLICY AND DR. RAUL A. RAMOS** was sent via email to the DEA Office of Administrative Law Judges at ECF-DEA@dea.gov and via email to

(1) Government Mailbox at dea.registration.litigation@usdoj.gov,
(2) Francis W. Mann, DEA at Francis.W.Mann@dea.gov,
(3) Kayla L. Kreinheder, DEA at Kayla.L.Kreinheder@dea.gov,
(4) Alexis B. Attanasio, DEA at Alexis.B.Attanasio@dea.gov, and
(5)David Heldreth, CEO of Panacea Plant Sciences, via email at davidh@panaceaplantsciences.net.

/s/ Robert T. Rush
Robert T. Rush, Attorney at Law

Appendix A

PROPOSED WITNESSES[2]

1. Tanner Anderson
   Department of Neuroscience
   University of Kentucky
   741 S. Limestone St. B369
   Lexington, KY 40526-0001

2. Dr. Lindsay P. Cameron
   Department of Psychiatry,
   Stanford University,
   Palo Alto CA, 94305

3. Dr. Clinton Canal
   Department of Pharmaceutical Sciences
   Duvall Building
   3001 Mercer University Drive
   Atlanta, GA 30341

4. Dr. Pasha Davoudian
   77 Avon Street, Apt 2B
   New Haven, CT 06511

5. Dr. Harrison Elder
   Behavioral Pharmacology Research Unit
   Johns Hopkins Bayview Medical Center
   5510 Nathan Shock Dr
   Baltimore, MD 21224

6. Joseph Hennessey
   Medical Scientist Training Program
   Medical College of Wisconsin
   8701 Watertown Plank Rd.
   Milwaukee, WI 53226

7. Dr. Santiago Jaramillo
   Institute of Neuroscience
   University of Oregon
   1425 E 13th Ave Huestis Hall,
   Eugene, OR 97403

8. Dr. Alaina M. Jaster

[2] Petitioners reserve the right to call rebuttal witnesses.

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Tolan Park Research Building
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Detroit MI, 48201

9. Dr. Shawn R. Lockery
305 Huestis Hall
1254 University of Oregon
Eugene, OR 97403

10. Dr. David Nichols
UNC Eshelman School of Pharmacy
2078 Genetic Medicine Building
Chapel Hill, NC 27599-7363

11. Dr. David Nutt
Division of Psychiatry
Imperial College London
Hammersmith Hospital
Du Cane Rd
London
W12 0NN

12. Dr. Raul Ramos
163 Weill Hall
Berkeley CA, 94720

13. Dr. Mario de la Fuente Revenga
Department of Physiology and Biophysics
Virginia Commonwealth University School of Medicine
Richmond VA, 23298

14. Dr. Jason Younkin
Sanger Hall
1101 East Marshall Street
P.O. Box 980551
Richmond, Virginia 23298-0551

15. Dr. Joseph Palamar
Department of Population Health
NYU Langone Health
180 Madison Avenue, Room 1752
New York, New York 10016

SUMMARY OF TESTIMONY

1. Tanner Anderson

Tanner Anderson will testify that he is a doctoral candidate at the University of Kentucky Department of Neuroscience. He will testify that he has over 5 years of experience studying the neurobiology of substance use disorders and psychedelic drugs. Mr. Anderson's research has followed three main projects, the first of which is in review for publication and the latter two will be submitted for scientific publication in late 2024. The first describes the neurophysiological mechanisms by which serotonin and DOI differentially modulate neuronal activity in the claustrum to anterior cingulate cortex circuit, a brain network that is being increasingly implicated in psychiatric diseases such as substance use disorders. The second project observes how DOI induces long-term plasticity in the brain, and the third project studies how DOI may affect cocaine-induced cognitive deficits. DOI has been the most important drug used to study the prime excitatory serotonin receptor (5-HT2AR) for decades. He will testify that DOI is an absolutely vital tool for neuroscientists to continue to learn about the brain, serotonin, and discovery of therapeutic interventions against psychiatric disease, many of which involve the 5-HT2AR in some capacity.

Mr. Anderson will testify that in 2022 he was awarded a NIDA-funded T32 Traineeship (T32DA035200) to study DOI and its therapeutic potential in animal models of substance use. In 2023, Mr. Anderson was awarded an NRSA F31 Fellowship (F31DA055445) from NIDA to research the neurophysiological mechanisms of DOI in claustrocortical signaling paired with models of cocaine use disorder.

Mr. Anderson will testify that there is a lack of evidence for the abuse potential of DOI, and in fact, much of the preclinical research has indicated therapeutic potential in rodent models of psychiatric disease. He will testify that there is a glaring absence of documentation of DOI being abused or DOI use leading to negative medical outcomes, while there are many papers indicating a therapeutic effect of DOI in models of substance use disorder (Oppong-Damoah et al., 2019), cognitive flexibility (Šabanović et al., 2024), anxiety (Pędzich et al., 2022) and more. Furthermore, as mounting evidence in clinical and preclinical research supports potential therapeutic efficacy of other psychedelic drugs, it is important to note that DOI is one of the best research tools to understand the underlying neurobiological mechanisms of action of this drug class. It is virtually the only psychedelic serotonin 2A receptor agonist that has both decades of research and is not in Schedule I. Additionally, he will testify that DOI serves as an ideal psychedelic mechanism research tool due to its streamlined pharmacological profile of high preferential binding to the 5-HT2A and 5-HT2C receptors. Many psychedelics have a much larger array of receptor affinities, making it more difficult to study specific cell signaling pathways.

Mr. Anderson will testify that the decision to place DOI and DOC in Schedule I will have a disastrous impact on his research. The entirety of his NIDA-funded thesis project has surrounded using DOI as the best pharmacological tool to study the 5-HT2A and 5-HT2C receptors. In fact, Mr. Anderson has one paper currently in review for publication that used DOI extensively to characterize the role of serotonin in a novel brain area that may be linked to several psychiatric diseases, showing that DOI had robust effects on claustrum neuron physiology via the 5-HT2C receptor (Anderson et al., 2024). Two more papers from Mr. Anderson that utilize DOI to observe its effects on neuronal plasticity and recovery of cognitive deficits after cocaine self-administration are to be published by the end of 2024. Mr. Anderson will testify that, like many neuroscientists,

the principal investigator that Mr. Anderson studies under does not have a Schedule I license due to the financial and time-investment hurdles it requires. Mr. Anderson will testify that he is one of many scientists that study serotonin receptors that would have their research halted if DOI and DOC were to be placed in Schedule I.

2. Dr. Lindsay P. Cameron

Dr. Lindsay Cameron will testify that she is a researcher at Stanford University in the Department of Psychiatry at the Stanford School of Medicine and was hired to pioneer a large multi-lab collaboration investigating psychedelic action. She will testify that she received her Ph.D. from UC Davis while working under Dr. David Olson.

Dr. Cameron will testify that she has done research using DOI and DOC during her Ph.D., and that these compounds have a reasonable safety profile and significant selectivity for the serotonin 2A (5-HT2A) receptor. She will testify that the 5-HT2A receptor is the most highly expressed serotonin receptor, and is therefore of significant clinical importance, specifically for understanding the circuits involved in mental health.

She will further testify that through her own research using DOI, and in line with other original investigations, that this compound does not have evidence of abuse potential. She will testify that her findings have found that they increase both dendritic and spine growth in cortical neurons (in vitro and in vivo), suggesting a potential for therapeutic use for neuropsychiatric disorders.

Lastly, Dr. Cameron will testify that reclassifying these DOI and DOC as Schedule I compounds would create significant barriers for researchers to obtain and study the drug, significantly hindering basic research on serotonin signaling, and therapeutically relevant research on mental health.

3. Dr. Clinton Canal

Dr. Clinton Canal will testify that, as a neuroscientist and pharmacologist actively engaged in research involving DOI and DOC, scheduling these substances would have a detrimental impact on the scientific community and the progress of medical research. He will testify that DOI and DOC are pivotal in ongoing research efforts to understand the complex mechanisms of the human body and potential therapeutic avenues for treating various health disorders. DOI and DOC are highly selective, high-affinity agonists at serotonin (5-HT) 2 receptors (unlike psilocin and LSD which bind various other receptors). He will testify that their high selectivity at 5-HT2 receptors makes them invaluable tools for studying the physiology of 5-HT2 receptors, which are expressed not only in the brain, but also in the periphery, e.g., in the gastrointestinal tract, liver, smooth muscles, and platelets. He will testify that these receptors regulate cognition, sleep, thermoregulation, muscle contraction, and platelet aggregation, but there is much more to be discovered about how they impact physiology. He will testify that researchers who study their function would be bereft of highly practical research tools should DOI and DOC be scheduled.

Dr. Canal will testify that DOI has been instrumental in more than 1,000 research articles over the past decade, contributing to high-impact journals, advancing knowledge and facilitating drug discovery. He will testify that the head-twitch response in mice that DOI elicits is commonly used in early antipsychotic drug discovery—antipsychotics block the head-twitch response.

He will testify that DOI and DOC are not commonly diverted for abuse; despite being unscheduled for over 50 years, there is not a single case of DOI or DOC addiction of which he is aware. Dr. Canal will testify that according to reports he has read online of anonymous individuals who have taken DOI, the psychoactive effects are extremely long-lasting—upwards of 48 hours—and aversive, inherently occluding abuse potential.

Dr. Canal will testify that the proposed scheduling will severely restrict access to these compounds, hindering ongoing studies and stifling future research initiatives. He will testify that the scheduling of DOI and DOC as Schedule I substances is not supported by substantial scientific evidence. He will testify that the DEA's claim of "high abuse potential" lacks empirical backing, particularly given the absence of reports linking DOI to a substance use disorder and the paucity of self-administration reports. Finally, he will testify that the potential therapeutic benefits that could arise from research with DOI and DOC are vast, with implications for treating a range of human disorders that affect millions worldwide.

4. Dr. Pasha Davoudian

Dr. Pasha Davoudian will testify that he is a medical and graduate trainee at Yale School of Medicine. He will testify that he has been intimately involved with both basic science and clinical research that aims to better understand psychedelics, including DOI, for a variety of conditions from depression and anxiety to post-traumatic stress disorder.

Dr. Davoudian will testify he has received funding from the National Institutes of Mental Health (F30DA059437) to better understand how psychedelics, including DOI and psilocybin, may be able to alter neuronal circuits to aid in treating patients. He will testify that through their own research group, DOI in this capacity has been shown to contribute to an understanding of how psychedelics and serotonin receptors may aid in the treatment of anxiety by collaborating with a neighboring lab that has world-leading expertise in particular neuroscience methods (Tiwaril et al., 2023). He will testify that their group used DOI to understand the involvement of serotonin receptors in anxiety (Tiwaril et al., *in preparation*). Dr. Davoudian will testify that if DOI had been a scheduled drug this critical research would not be possible and would have a tremendous impact on the scientific community and most importantly, many patients living with anxiety and other

mood disorders.

Lastly, Dr. Davoudian will testify that DOI has low records of abuse and lethality. If the agency would like to schedule these substances, more must be known about their abuse liability and toxicity. However, he will testify that evidence to-date suggests that DOI is safe and rarely abused and may be beneficial for those suffering from substance abuse. He will testify the DEA need not schedule DOI as it is a crucial chemical that poses low to zero public health risk—perhaps even a benefit—and is essential for research into psychiatric conditions and the underlying basic neuroscience.

5. Dr. Harrison Elder

Dr. Harrison Elder will testify that he is a postdoctoral researcher at Johns Hopkins University and received a Ph.D. in Pharmacology & Toxicology from Virginia Commonwealth University. Dr. Elder has ten years of experience studying biology, respiratory depression and substance use disorders of which five years were spent studying psychedelics. Part of Dr. Elder's Ph.D. work focused specifically on using monoamines, including psychedelics, as modulators of respiratory depression.

Dr. Elder will testify to and authenticate as learned treatises several scientific publications concerning the chemistry and neuropharmacology, and behavioral pharmacology that have critical bearing on the question of DOI and DOC's safety, medical potential, mechanism of action, and abuse potential. Per his own publications, he will testify about the pharmacological differences between DOI and other psychedelics, as well as their acute effects in humans and rodent models of drug use and respiratory depression (Jaster et al. 2022a, Jaster & Elder 2024 under review).

Dr. Elder will further testify that review of the academic and/or medical literature fails to reveal documented reports of DOI misuse or abuse, nor its role in any adverse medical outcomes.

They will testify that their time studying the molecule has not revealed any instances of DOI's diversion from legitimate channels; that it does not pose any potential public health risks; and that the drug's potential for recreational abuse is extremely unlikely. The overwhelming majority of the substance that is bought and sold in legitimate channels funnels into research institutions for the purpose of conducting precisely the kind of medical research he is conducting.

They will further testify that there are very few, if any, verified documented cases where individuals have taken this substance on their own initiative rather than based on medical advice. He will testify to the given nature of the drug and its pharmacological effects, and how it would be unlikely that someone would do so—the amount of personal research and inquiry required to even appreciate what the substance is and what its pharmacological effects are, is self-limiting in its potential to be consumed in a haphazard fashion. Additionally, he will testify that while DOI is structurally related to mescaline and DOM, two Schedule I compounds, its 36-hour duration of action sets it sufficiently apart from such other drugs as to make abuse-potential comparisons impractical.

As someone with clinical, preclinical and industry experience, they will further testify that the decision to place DOI and DOC in Schedule I will have significant negative impacts on the continuation of their research. From the financial, supply chain, and collaborative perspectives, a Schedule 1 designation creates enough of a disincentive for academics and contract research organizations (CROs) to discontinue funding and supporting critical research.

Dr. Elder will testify that scheduling makes studies that attempt to ascertain the most relevant molecular structures of the drug costly and difficult, as many resulting modifications of the molecule used to test the functions of the molecular structure necessarily must begin from the Scheduled molecule itself.

6. Joseph Hennessey

Joseph Hennessey will testify that as an MD/Ph.D. student at the Medical College of Wisconsin, he has extensive experience working with psychedelics in the laboratory of Dr. John McCorvy. Mr. Hennessey will offer testimony on the pharmacology of DOI and DOC based on his first-hand experience testing these and other psychedelic compounds at a range of serotonin G-protein coupled receptors (Vargas et. al 2023, Wallach et. al 2023).

He will testify that the unique pharmacological profile of DOI makes it an essential research tool for investigating the 5-HT2 subclass of receptors. Having tested this compound and hundreds of other psychedelics at all 12 serotonin G-protein coupled receptors, he will testify that no other compound exists to his knowledge that possesses DOI's exquisite selectivity for the 5-HT2 subclass of receptors. The 5-HT2A receptor, in particular, has garnered a significant amount of attention due to its likely crucial role in mediating the therapeutic effects of psychedelics (Nichols 2016). Given that the promiscuous pharmacology of other psychedelics complicates the scientific study of 5-HT2 receptors—5-HT2A in particular—Mr. Hennessey will testify that the scheduling of DOI will significantly hinder scientific research of this receptor which has shown immense promise for the treatment of various neuropsychiatric diseases including depression and addiction (Griffiths et al. 2016, Carhart-Harris et al. 2021).

He will testify that, based on animal behavioral models of addiction like self-administration paradigms, psychedelics like DOI and DOC do not show reinforcing effects and do not reliably induce self-administration (Fantegrossi et al. 2004). This, combined with the rapid tachyphylaxis induced by psychedelics (de la Fuente Revenga et al. 2022, Wallach et. al 2023), significantly reduces their potential for abuse and makes it highly unlikely that they could produce physiological dependence or lead to addictive-like use recreationally.

Mr. Hennessey will testify that, based on the FDA's format for an 8 Factor Analysis, and previous summary 8-Factor Analyses performed by experts for other psychedelics (Johnson et al. 2018), his view is that DOI and DOC should be scheduled no more restrictively than Schedule IV.

Finally, he will testify that the placement of DOI in Schedule I would severely adversely affect the work he plans to conduct for his dissertation project. With Dr. John McCorvy and Dr. John Manstch, Mr. Hennessey has begun designing and piloting experiments for a dissertation project that he will complete during his graduate years pursuing a Ph.D. in Pharmacology and Toxicology. This project, which will investigate the polypharmacological contributions of psychedelics to their therapeutic effects, will rely heavily on DOI both due to its ease of access as a tool compound and for its unique selectivity for the 5-HT2 subclass of receptors. Since the project aims to characterize the contributions of each serotonin G-protein coupled receptor to the therapeutic effects of psychedelics, it is absolutely essential to have access to selective compounds for these receptors. The placement of DOI into Schedule I would significantly hamper this work, as it would place significant administrative burdens associated with obtaining a DEA Schedule I license on Mr. Hennessey and the principal investigators who plan to conduct this research with him.

7. Dr. Santiago Jaramillo

Dr. Santiago Jaramillo will testify he is an Associate Professor in the Institute of Neuroscience at the University of Oregon. He will testify that for the last ten years he has maintained an active research program in auditory neuroscience supported by the National Institutes of Health and the National Science Foundation that uses DOI for research purposes.

He will testify that his research on how the auditory system functions relies on the study of neuromodulators, such as serotonin, which play key roles in how the brain processes and

interprets sounds, as well as in how the nervous system associates sounds with appropriate behavioral responses. To this end, his research requires compounds that act as highly selective agonists or antagonists of the cell receptors associated with these neuromodulators.

Dr. Jaramillo will testify that DOI is a highly selective agonist of serotonin (5-HT) 2A receptors, making it an extremely useful tool for the study of neuromodulatory effects in neural processing. He will testify that this compound has been essential in his ongoing studies about the relation between the serotonergic system and the processing of sound by the nervous system. He will testify that the proposed scheduling of DOI will severely restrict access to this compound, greatly affecting ongoing studies like his and stifling future research programs. He will testify that the administrative hurdles, and cost, in terms of personnel and time, resulting from this potential scheduling are counterproductive to the advancement of science.

8. Dr. Alaina M. Jaster

Dr. Alaina M. Jaster will testify that they are a postdoctoral researcher at Wayne State University and received a Ph.D. in Pharmacology & Toxicology from Virginia Commonwealth University. Dr. Jaster has nine years of experience studying neuroscience and substance use disorders, of which five years were spent studying psychedelics and opioids. Dr. Jaster will testify that their Ph.D. work focused specifically on DOI and psilocybin differential effects on oxycodone-induced place preference and the molecular targets and circuits involved in these psychedelics' potential therapeutic effects (Jaster Dissertation 2024).

Dr. Jaster will testify to and authenticate as learned treatises several scientific publications concerning the chemistry and neuropharmacology, and behavioral pharmacology that have critical bearing on the question of DOI and DOC's safety, medical potential, mechanism of action, and abuse potential. Per her own publications and work from her Ph.D. lab, she will testify to the

pharmacological differences between DOI and other psychedelics, as well as their acute and post-acute behavioral effects (Vohra et al 2021; Jaster et al. 2022a, 2022b; Jaster & Gonzalez-Maeso 2023; de la Fuente Revenga et al. 2021; de la Fuente Revenga et al. 2022).

Dr. Jaster will testify that the potential for abuse of DOI is negligible, as evidenced by their own research using two rodent models of drug seeking (Jaster et al 2022a; Jaster Dissertation 2024*).* She will further testify that the drug discrimination paradigm is not sufficient to determine abuse potential of a compound.

Dr. Jaster will testify that review of the academic and/or medical literature fails to reveal documented reports of DOI misuse or abuse, nor its role in any adverse medical outcomes. They will testify that their time studying the molecule has not revealed any instances of DOI's diversion from legitimate channels; that it does not pose any potential public health risks; and that the drug's potential for recreational abuse is extremely unlikely. She will testify that the overwhelming majority of the substance that is bought and sold in legitimate channels funnels into research institutions for the purpose of conducting precisely the kind of medical research she is conducting.

They will further testify that there are very few, if any, verified documented cases where individuals have taken this substance on their own initiative rather than based on medical advice. Further the induction of rapid tachyphylaxis and cross-tolerance of psychedelics, including DOI/DOC, makes recreational use, if any, sporadic and limited (de la Fuente Revenga et al. 2022).

They will further testify that the decision to place DOI and DOC in Schedule I will have significant negative impacts on the continuation of their research. Dr. Jaster will testify that not only was her entire graduate work focused on comparing DOI and Psilocybin, but the lab also uses DOI in a myriad of pilot projects and grants that are currently funded by NIDA (F31DA057818; R01MH084894). Dr. Jaster will testify that DOI being unscheduled has also led to fostering several

collaborations across departments and disciplines, allowing for more innovative and novel research on pain, neuropsychiatric disorders, and substance use disorders.

9. Dr. Shawn R. Lockery

Dr. Shawn R. Lockery will testify that he has been Professor of Biology at the University of Oregon's Institute of Neuroscience since 1993, totaling 29 years of service. He was educated a Yale University, University of Oxford, and University of California, San Diego, where he earned his Ph.D. in Biology in 1989. He will testify that his primary research focus has been on the neuronal and genetic underpinnings of behavior, using the nematode worm, *C. elegans*—a model organism extensively supported by the National Institutes of Health (NIH).

Dr. Lockery will testify that he is also the Co-founder and Senior Research Fellow at InVivo Biosystems, a company born out of his academic research. Established in 2011, the company has over 40 employees, $13M in venture capital funding, $8.5M in NIH research grants, and an annual revenue of $2.2M, year-over-year growth of 40%. He has three issued patents, with another pending.

Dr. Lockery will testify to his experience securing extramural funding for his fundamental research, with continuous NIH support since 1994. Notable achievements include a 23-year R01 award, an NIH Career Award, and the distinction of having the top-ranked NIH Challenge Grant application in bioengineering in 2009. Additionally, he has received several prestigious awards from private foundations, such as the John Simon Guggenheim Foundation and the Searle Scholars Program.

Dr. Lockery will testify that he has a pending grant application for a study that utilizes DOI—a model psychedelic and psychoplastogen—to further the development of psychedelic therapies by identifying their genetic mechanisms. He will testify that he also received a seed grant

from the University of Oregon to advance this line of inquiry.

Dr. Lockery will testify that since March 2023 he has focused his studies on psychedelics, demonstrating that DOI has behavioral effects in *C. elegans* comparable to those observed in mice, inducing hyperactivity at moderate doses and hypoactivity at higher doses. Additionally, he will testify that DOI suppresses feeding and accelerates neuronal branching changes, as it does in mice. These findings are pivotal as the three-day life cycle of *C. elegans* makes it an unsurpassed model for genetic analysis of biological functions, including behavior and neuroanatomy.

Dr. Lockery will provide testimony on the prevailing hypothesis that the therapeutic effects of psychedelics in treating conditions like depression, PTSD, and other disorders stem from their psychoplastogenic properties—they purportedly reverse the pathologies of neuronal atrophy by fostering structural and functional neuroplasticity in the brain. He will testify that the major drawback is that psychedelics are also hallucinogenic, necessitating extensive psychological counseling, which drives up the cost of therapy to between $3,000 and $5,000 per session—a price out of reach for many underserved groups, including veterans with PTSD. He will testify that there is an active and robust initiative, encompassing academia and over sixty companies, striving to discover non-hallucinogenic psychoplastogens and that Dr. Lockery's work is contributing to this effort.

Dr. Lockery will testify that the sole reason he could initiate groundbreaking research on psychedelics using *C. elegans* was the availability of substances not restricted by Schedule I status. He will testify that the pioneering nature of his research, with no preceding evidence to suggest efficacy in *C. elegans*, would have made it essentially impossible to justify the resources and time-delay required to obtain a license for such speculative research.

Dr. Lockery will testify about the potential impact of stringent regulatory measures, like

Schedule I classification, on the research community. He will testify that such restrictions are likely to deter many researchers from entering the field with innovative approaches, thereby potentially stifling advancements in making psychedelics available to underserved populations.

He will testify about his concerns that obtaining a Schedule I license is not a certainty, particularly as the University of Oregon would be navigating this process for the first time, lacking the necessary practical and administrative framework to manage such substances. This could lead to the cessation of his trailblazing research.

Finally, Dr. Lockery will testify that dynamic and exploratory research programs, like his, require the ability to pivot rapidly and redirect based on new discoveries with little delay. Such flexibility is at odds with the rigid and time-consuming protocol re-approval process managed by the DEA. Therefore, even with a Schedule I license, the stringent regulations could severely impede the progress of his psychedelic research.

10. Dr. David Nichols

Dr. David Nichols will testify that he was a Professor in the Purdue University School of Pharmacy for thirty-eight years and is currently an Adjunct Professor of Chemical Biology and Medicinal Chemistry in the School of Pharmacy at the University of North Carolina, Chapel Hill. He will testify that starting with his graduate studies in 1969, and then as a major focus of my research at Purdue, was a study of the structure activity relationships of hallucinogenic (psychedelic) agents. Dr. Nichols will testify that during his time at Purdue University, he was funded almost continuously by NIDA for the study of hallucinogenic agents. He will testify that his laboratory developed the original chemical synthesis for optical isomers of hallucinogenic amphetamines, including DOI (Johnson, Hoffman et al. 1987, Mathis 1988, Johnson, Mathis et al. 1990). He will testify that ^{125}I-DOI was first developed as a radioligand for labeling brain

serotonin 5-HT2A receptors (Johnson, Hoffman et al. 1987) and it was used shortly thereafter to label brain 5-HT2 receptors (McKenna, Mathis et al. 1987, McKenna and Saavedra 1987, McKenna, Nazarali et al. 1989, Nazarali, McKenna et al. 1989).

Dr. Nichols will testify that, within about the past decade, the brain serotonin 5-HT2A receptor has become a focus of intense interest as a target for novel psychiatric medications useful for treating depression, anxiety, and various substance use disorders (i.e. alcohol, nicotine, and cocaine) (Nichols, Johnson et al. 2017). To study the physiological role of this receptor, scientists require ligands to activate and label this receptor. He will testify that virtually all drugs that target the 5-HT2A receptor are currently classified as Schedule I controlled substances and that the only unscheduled molecule that is available to characterize effects of serotonin 5-HT2A receptor activation is DOI. Dr. Nichols will testify that placing DOI into schedule I will short circuit many investigations into the physiological role of the 5-HT2A receptor. Importantly, there is no other high potency ligand for that receptor that is not a controlled substance. He will testify that from 1984 to the present there have been more than 839 published scientific studies listed in the National Library of Medicine that employed DOI in some experimental capacity.

Dr. Nichols will testify that the relatively recent discovery of medical significance for drugs such as LSD and psilocybin that primarily target the 5-HT2A receptor illustrates how DEA scheduling of hallucinogens more than fifty years ago significantly hindered discovery of their medical utility. He will testify that he personally knew numerous neuroscientists over the years who were interested in studying the role and importance of the 5-HT2A receptor, but who were disincentivized by the DEA requirements to work with controlled substances.

He will testify to the great difficulty to obtain a license to work with Schedule I substances. The DEA now wants to know exactly what experiments are planned, how much and which drugs

one wishes to employ, and how one plans to store them to prevent diversion, usually requiring a large and expensive safe that most investigators do not have. The investigator must have a separate schedule for each controlled substance that will be used. Thus, although many scientists might be interested in studying the role of the 5-HT2A receptor, once they learn how much work it takes to get a license, they usually follow other interests. He will testify that he had licenses to study fifteen different Schedule I substances because he believed they were important, so he was willing to invest the effort in obtaining a license. Unfortunately, young investigators, or those who are just developing an interest in the field, may not be so inclined. By contrast, if DOI remains legally available, more scientists may work in this increasingly important field.

11. Dr. David Nutt

Dr. David Nutt will testify that he is a psychiatrist and professor of Neuropsychopharmacology at Imperial College London and has worked for almost all my professional life in psychiatry with a particular interest in psychopharmacology. This topic covers the effects, both beneficial and harmful, of drugs on the brain. He will testify that he has extensive clinical and research experience in this field and in 2024 Scholar GPs ranked him as the leading psychopharmacologist in the world. (https://scholargps.com/scholars/73699337611906/david-j-nutt)

He will testify that he is a Fellow of the Royal Colleges of Physicians and of Psychiatrists, the British Pharmacological Society, and the Academy of Medical Sciences of the UK. Dr. Nutt will testify that because of his expertise in drugs of potential abuse he was appointed to chair the UK government's Advisory Council on the Misuse of Drugs (ACMD) Technical sub-committee for the assessment of drug harms from 1999-2008. As a result of his long and effective contribution to drug policy in the UK he was appointed to Chair of the full ACMD Council in

2008.

Dr. Nutt will testify that in 2004-5 he was the medical lead on the UK government's Foresight committee that provided a 25-year future vision of addiction and brain science. This report was so well received that it was published as a book (Nutt et al 2006). He will testify to having published over 500 research papers as well as several hundred specialist reviews and over forty books in this field, largely on the effects of drugs on the brain (see cv). His book on drugs for the general public, Drugs: without the hot air (UIT press) won the UK Transmission prize for science communication in 2014. Since then, he has written a second edition. In 2023 my latest book Psychedelics was published in the UK and in 2024 in the USA. Also in 2023, he published a book on the clinical uses of psychedelics in psychiatry (Nutt and Castle)

Dr. Nutt will testify that several of his research papers relating to drug harms and policy responses using the Multi Criteria Decision Analysis (MCDA) approach (e.g. Nutt et al 2007; Nutt et al 2010, Nutt et al 2014) have been extensively cited and have been used to produce evidence-based changes to national drug policies in several countries including the USA, Finland, Sweden and New Zealand. As a result of this work, he has been asked to speak on comparative drug harms in a number of important locations including at the UN Office of Drugs and Crime, the Houses of Parliament (UK), the European Commission, and in both the Dutch and New Zealand legislatures.

Dr. Nutt will testify that for over twenty-five years he acted as the editor of the Journal of Psychopharmacology, one of the top journals in the world on the effects of drugs and the brain. Now he edits the journal Drug Science Policy and Law. Dr. Nutt will testify that in 2013 he was awarded the Nature/Sense About Science annual John Maddox prize for Standing up for Science for "pursuing research of public interest with perseveration and courage."

Dr. Nutt's expertise has been recognized with a number of prestigious appointments

including Presidencies of the European Brain Council (2013-2017) and of the European College of Neuropsychopharmacology, the British Association of Psychopharmacology and the British Neuroscience Association. He will testify he also served on the MRC Neuroscience board, and for sixteen years he held program grant funding from the MRC for the study of addictions and the effects of drugs on the brain.

He will testify that he has conducted scientific research on the brain actions in humans of a wide range of legal and illegal drugs including psilocybin, alcohol, tobacco, heroin, cocaine, GHB, buprenorphine, antidepressants, benzodiazepines, antipsychotics, methadone, LSD, amphetamines, DMT, cannabis, cannabidiol, ketamine, paracetamol, ibuprofen and caffeine. Dr. Nutt will testify that he has also studied the effects on the brain of the impact of repeated use of a range of illegal drugs including psilocybin, LSD, cocaine, heroin and cannabis and compared them with the harms of alcohol.

Dr. Nutt will testify that over the past decade he has led a research group studying the impact of psychedelic drugs on the human brain using both psychological and neuroimaging measures. His research group has studied psilocybin, LSD, DMT, and is currently studying 5-MEO-DMT. Dr. Nutt will testify that this work led to the development of studies to explore the clinical utility of psilocybin in psychiatric disorders. His group has conducted studies in treatment-resistant depression, OCD, anorexia nervosa, and fibromyalgia. He will testify that currently he is setting up the world's first study of psilocybin in abstinent heroin addicts and in gambling addiction.

Dr. Nutt will testify that some of this work has been supported by the UK government through the Medical Research Council and through the National Institute of Health. This body of research work has led to over 100 peer reviewed published papers making his group the leading

psychedelic research group in the world.

Dr. Nutt will testify that he has no competing interests in that I do not work for any company that makes or sells DOI. He will testify that he does have interests both personal and through my research group in companies developing psychedelic drugs as medicines.

Dr. Nutt will testify that he has led (Nutt et al 2007; Nutt et al 2010) and been involved in (van Amsterdam et al 2014, Bonomo et al 2019, Crossin et al 2023) expert reviews that have assessed all the sixteen possible harms of a range of drugs including psychedelics. These have consistently shown that even when used in non-clinical settings psychedelics have a low propensity for harm. This risk is even lower than when they are used in research settings (Schlag et al 2022).

Dr. Nutt will testify DOI was not specifically assessed in these studies because there was no evidence of diversion and harm but there is no reason to believe from its pharmacology that it would have a significantly different risk profile. He will testify that when he was a UK government advisor on drugs, they had an early-warning system for detecting the misuse of psychoactive drugs and DOI never appeared on this early-warning system. Dr. Nutt will also testify that there is no evidence of diversion of DOI from research settings.

Dr. Nutt will testify that taken together the risks currently posed by DOI seem very small, and the benefits of it as a tool for research on the 5-HT2A receptor are enormous, and likely to grow as the psychedelic research field continues to develop. He will testify that for these reasons, to control DOI under Schedule I is disproportionate to its risks and would in fact produce significant harms to the scientific community.

12. Dr. Raul Ramos

Dr. Raul Ramos will testify that he holds a Ph.D. in Neuroscience from Brandeis University and has over 9+ years of experience performing neuroscience research using molecular genetics,

behavioral, pharmacological, and physiological techniques. Dr. Ramos has studied the plasticity of sensory systems in both the central and peripheral nervous systems. His work has been published in Nature Neuroscience, Current Biology, and Frontiers in Cellular Neuroscience. Dr. Ramos currently holds two appointments, one as a Miller Fellow with the Miller Institute for Basic Research in Science at the University of California, Berkeley, and as a Hanna H. Gray Fellow with the Howard Hughes Medical Institute (HHMI). Both highly competitive research fellowships were awarded to Dr. Ramos to support his research into the effects of psychedelics on somatosensory (touch, itch, and pain) perception. Together, these facts establish Dr. Ramos as an expert in his field. Dr. Ramos will authenticate a copy of his CV.

Dr. Ramos will testify that the study of serotonin and serotonin receptors is fundamental for advancing our understanding of the brain *as well as* the spinal cord and the peripheral nervous system. His testimony will authenticate as learned treatises several scientific publications concerning the spinal cord and peripheral nervous system, where a significant research effort has been undertaken to understand the crucial role of serotonin in modulating acute and chronic pain, as well as itch (Richardson 1990; Loyd, Henry, and Hargreaves 2013; Morita et al. 2015; Courteix et al. 2018; Watson 2022; Heijmans, Mons, and Joosten 2021). He will further testify that this continues to be an active area of significant investigation with many unanswered questions (Ganley et al. 2023; Courteix et al. 2018; Watson 2022). Additionally, he will testify that a critical component necessary for the success of this research effort is tools like the 5-HT2A receptor agonists DOI and DOC. It has been known for some time now that the 5-HT2A receptor is expressed in both spinal cord circuits and within peripheral nociceptors themselves (Heijmans, Mons, and Joosten 2021; Van Steenwinckel et al. 2009; Nicholson et al. 2003; Usoskin et al. 2015). He will testify that in order to understand the role of the 5-HT2A receptor in neuropathic pain,

DOI has been used for behavioral, electrophysiology, and cell/molecular experiments (Abbott, Hong, and Blier 1996; Kjørsvik Bertelsen et al. 2003; Rahman et al. 2011; Tokunaga, Saika, and Senba 1998; Courteix et al. 2018; Obata et al. 2001). To highlight results from one study, Obata and colleagues (2001) found that in a rodent model of neuropathic pain, DOI has dose-dependent analgesic properties (reducing pain sensitization). The results from this study are supported by analogous results using psilocybin & ayahuasca (Kolbman et al. 2023; Lauria et al. 2024). However, a mechanistic understanding into exactly how this occurs and how it can generalize to other pain conditions in Humans requires further research and continued access to DOI.

Dr. Ramos will testify that since the publication of these previous studies, substantial advances have been made in neuroscience techniques that make it possible to perform more mechanistic studies aimed at determining the action of psychedelics like DOI on touch, itch, and pain. Dr. Ramos will testify that he is leveraging this new level of experimental resolution in his ongoing research focused on DOI. Lastly, Dr. Raul Ramos will testify that his research is supported by a $1.5 million grant awarded by the Howard Hughes Medical Institute to Dr. Ramos (see https://www.hhmi.org/scientists/raul-arturo-ramos-garcia). He will testify that if the proposed Schedule 1 classification is passed, Dr. Ramos's research into the understanding of neuropathic pain and its treatment will be significantly stunted.

13. Dr. Mario de la Fuente Revenga

Dr. Mario de la Fuente Revenga will testify that he has over fifteen years of experience studying Medicinal Chemistry and the Neuropharmacology of psychedelics, and the use of DOI has been integral to his research. He will testify that DOI, in part due to its accessibility, offers an advantageous and relatively narrow profile of interactions with serotonin receptors with limited off-targets. He will testify that DOI is a very valuable tool to establish 5-HT2A dependent actions

and to model human exposure in rodents. The drug produces a duration of action of 16-36 hours in humans, but in rodents its exposure lasts for a few hours. Thus, Dr. de la Fuente Revenga will testify, DOI offers a duration of serotonergic stimulation in rodents akin to that of the most common psychedelics in humans (LSD and psilocybin).

Dr. de la Fuente Revenga will testify that DOI provides an entry point for researchers in many different areas–within and beyond preclinical neuroscience–to access a valuable research tool to explore interactions with the serotonergic system. DOI can be obtained from common suppliers and the bibliographic literature on its pharmacology is abundant. He will testify that by placing DOI under Schedule I, the DEA is effectively stripping researchers of the possibility to access a drug that can enable the multidisciplinary angle that nurtures scientific progress. He will testify that researchers willing to expand their research will be extremely discouraged to do so by the current scheduling proposal. He will testify to the discouragement of integrating psychedelics in research; in an environment that mercilessly demands publications and funding, such scientifically unproductive use of time to simply earn the right to use a tool is a luxury most researchers cannot afford.

Dr. de la Fuente Revenga will testify that drug discrimination and head twitch in rodents, as posited by the DEA as models of abuse potential, are insufficient to determine this, and as such cannot serve as the basis for scheduling a drug under the Controlled Substances Act. He will testify that he has written numerous articles regarding head behavior, including a piece of authorship discussing how mouse head twitches might be about as special as yawning in humans.

Further, he will testify that it is not in the best interest of scientific research that the DEA adopts an ad hoc interpretation of animal models for supporting scheduling DOI but ignores therapeutic potential evidence. He will testify that DOI is a promising therapeutic using the same

lens the DEA employs in the interpretation of preclinical data and its projection to abuse potential. He will testify that numerous articles, including some of his own authorship, demonstrate that DOI bears great therapeutic potential; per se or as a structural lead. He will provide testimony about DOI's therapeutic properties in models of depression, cognition, post-traumatic stress disorder and as an atypical anti-inflammatory.

Dr. de la Fuente Revenga will testify that the therapeutic use criterion used by the DEA is limited to whether there is an FDA-approved use in humans, but without a sufficient body of evidence to justify the tedious and costly process to get past the goal line there cannot be FDA approval. He will testify to and allege that by placing DOI under Schedule I, the DEA is effectively impeding evaluating whether there is any possible therapeutic use that can benefit the US population.

He will testify to data showing that unlike opioids, serotonergic psychedelics are not associated with a reward effect and that DOI's accessibility for research might be misconstrued as an enticement to its abuse. As outlined above, DOI produces a very intense and long duration of effects that can span for days resulting in a major inconvenience and increasing the chances of unpleasant experiences within that time frame. He will testify that DOI's pharmacodynamics and pharmacokinetics effectively are the very deterrent to its abuse, yet its high selectivity for the serotonin 2A and 2C receptors make it an exceptional research tool.

The proposition mentions that there is evidence of human use of DOI, however, Dr. de la Fuente Revenga will testify that the DEA's analysis using the CSA's four prong analysis fails to adopt a quantitative approach and is therefore lacking proper depth and contextualization. He will testify to the importance of quantitation, context and relevance in data analysis. In summary, he will testify that as it stands right now, placing DOI under Schedule will do more harm than good:

negatively affecting 100% of active researchers investigating this drug, 100% of all patients that could receive a treatment based on the research that DOI enables, all for a 0% gain in public health risk prevention and abuse mitigation.

14. Dr. Jason Younkin

Dr. Jason Younkin will testify that they are a Postdoctoral Trainee at Virginia Commonwealth University (VCU) and Adjunct Faculty at Virginia State University (VSU). He received his Ph.D. at VCU studying the cross-talk between dopamine and serotonin receptors, then went to teach at VSU where he spent 5 years (3 years as an Instructor and 2 years as an Assistant Professor). Upon returning to VCU, his primary research focus for nearly three years has been psychedelics and their potential as therapeutics. He will testify that he will be returning to VSU in the Fall 2024 semester as an Assistant Professor to start his own research lab focusing on psychedelics as therapeutics. Dr. Younkin will testify that he intends to continue studying psychedelics and related chemicals in collaboration with a medicinal chemist, part of which will involve behavioral testing of psychedelics in zebrafish, using DOI to set up this assay.

Dr. Younkin will testify that DOI is the quintessential compound used in labs to study psychedelics, whether on its own or as a comparison to others. He will testify it is readily available to qualified researchers, inexpensive, and easy to use. Dr. Younkin will further testify that scheduling DOI will greatly impact his ability to start his own independent research lab and obtain funding. VSU is a small historically black college/university and has specific requirements to establish a DEA license along with the DEA's own requirements, therefore scheduling DOI will immediately and drastically limit what he and his colleague can accomplish. He estimates at least a year delay to get all approvals at VSU and the DEA, if the DEA decides to grant him a license, causing major delay, setback, and impact to his research, as there are no viable substitutes for his

research purposes. He will testify that losing DOI availability will greatly slow down the establishment of zebrafish methods and protocols to be used with other compounds.

Dr. Younkin will testify that DOI becoming Schedule 1 potentially inhibits, if not fully stops, the experimental process for a new Junior Investigator like Dr. Younkin, and possibly Senior Investigators who want to establish similar topics and methods in their labs. He will testify that DOI is extremely important in the science research world and should not be placed in Schedule 1 of the CSA.

15. Dr. Joseph Palamar

Dr. Joseph J. Palamar will testify as Associate Professor of Population Health at NYU Langone Health and as Deputy Director of the NIDA-funded National Drug Early Warning System (NDEWS). He earned his Ph.D. in public health from New York University in 2010 and he has been conducting drug epidemiology research for twenty-three years. He will testify that as a leading drug use epidemiologist, he specializes in the epidemiology of use of party drugs, psychedelics, and new and uncommon psychoactive substances. He is currently Principal Investigator or Co-Investigator on multiple NIDA-funded R01 grants, and he has authored over 200 peer-reviewed papers on the epidemiology of drug use with a particular focus on survey data, toxicology and poisonings, and drug seizures.

Dr. Palamar will testify to discuss the recent and current epidemiology of use DOI and DOC, associated effects and poisonings, and seizures of such compounds in the US. He plans to present information received from his NDEWS network regarding use and poisonings/deaths involving DOI and DOC, as well as seizures, throughout the US. He will also testify about trends in drug submissions testing positive for DOI and DOC in the DEA's National Forensic Laboratory Information System (NFLIS) and in High Intensity Drug Trafficking Areas (HIDTA) law

enforcement seizure data. He will also testify about statistics based on both national surveys (the National Survey on Drug Use and Health) and among high-risk nightclub attendees in New York City.

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