UNITED STATES DEPARTMENT OF JUSTICE

Drug Enforcement Administration

In the Matter of **Schedules 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**

RECOMMENDED RULINGS, FINDINGS OF FACT, CONCLUSIONS OF LAW, AND DECISION OF THE ADMINISTRATIVE LAW JUDGE

Paul E. Soeffing
U.S. Administrative Law Judge

June 20, 2025

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PROCEDURAL HISTORY

On December 13, 2023, the Drug Enforcement Administration ("DEA") published a Notice of Proposed Rulemaking with docket number DEA1156 and titled "Schedules of Controlled Substances: Placement of 2,5-dimethoxy-4-iodoamphetamine (DOI) and 2,5-dimethoxy-4-chloroamphetamine (DOC) in Schedule I" ("Notice of Proposed Rulemaking" or "NPRM").[1] 88 Fed. Reg. 86,278 (2023); ALJ Ex. 1. The Notice of Proposed Rulemaking provided a January 12, 2024 deadline for requests for a hearing. *Id.* at 86,278-79. The Notice of Proposed Rulemaking further states that "[i]n accordance with 21 U.S.C. 811 and 812, the purpose of a hearing would be to determine whether DOI and/or DOC meet the statutory criteria for placement in schedule I, as proposed in this rule." *Id.* at 86,280.

In response to the proposed placement of DOI and DOC in Schedule I of the Controlled Substances Act, Panacea Plant Sciences ("Panacea" or "PPS"), the Science Policy Council, Students for Sensible Drug Policy ("SSDP"), and Dr. Raul A. Ramos ("Dr. Ramos"),[2] (collectively, "the Petitioners") each timely filed requests for hearing ("RFH"). *See* ALJ Exs. 2, 3, 4. A hearing was conducted in a hybrid hearing format on November 12, 13, 14, 15, 18 and 19, 2024, at the DEA Hearing Facility in Arlington, Virginia, with the Government and its representative, the counsel and representatives for SSDP and two of its non-party witnesses, and Dr. Raul A. Ramos and his counsel appearing in person at the DEA Hearing Facility, and one witness for the Government and the remaining joint witnesses for SSDP and Dr. Ramos ("SSDP/Ramos") appearing via video teleconference ("VTC") technology.[3]

After carefully considering the testimony elicited at the hearing, the admitted exhibits, the

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[1] ALJ Ex. 1; Gov't Ex. 2.

[2] On October 9, 2024, the tribunal issued an Order Granting Amelia A. Furbish, PharmD and Megan Francis' Unopposed Motion to Withdraw finding that Ms. Furbish and Ms. Francis had waived their opportunity to participate in the hearing on the merits in these proceedings. ALJ Ex. 58 at 1-2.

[3] On November 12, 2024, Panacea filed Panacea Plant Sciences' Motion for Written Testimony notifying the tribunal that its representative and sole witness, David Heldreth, was ill and unable to travel to attend the hearing, and requesting that it be allowed to provide its opening statement, its testimony, and its closing statement in written form. ALJ Ex. 74 at 1-2. On November 13, 2024, the tribunal issued an Order Granting Panacea Plant Sciences' Motion for Written Testimony, acknowledging Mr. Heldreth's stated inability to travel and granting Panacea's request to submit written testimony. ALJ Ex. 75 at 1. On November 15, 2024, Panacea filed Panacea Plant Sciences' Opening Statement and Testimony of David Heldreth. *See* ALJ Ex. 77.

arguments of counsel, and the record as a whole, I have set forth my recommended findings of fact and conclusions of law below.

ISSUE

The issue in these proceedings is whether 2,5-dimethoxy-4-iodoamphetamine (DOI) should be listed in Schedule I of the Controlled Substances Act, pursuant to 21 U.S.C. §§ 811 & 812(b)(1), and whether 2,5-dimethoxy-4-chloroamphetamine (DOC) should be listed in Schedule I of the Controlled Substances Act, pursuant to 21 U.S.C. §§ 811 & 812(b)(1).

THE EVIDENCE

STIPULATIONS OF FACT

The parties agreed to the following stipulations, which I recommend be accepted as fact in these proceedings:[4]

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. 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.

4. 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).

5. 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.

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

GOVERNMENT'S CASE

The Government presented its case-in-chief through the testimony of two witnesses: (1) Heather Achbach; and (2) Theresa M. Carbonaro, Ph.D.

[4] ALJ Ex. 53 at 3.

Heather Achbach [5]

Background

Ms. Achbach is the Acting Section Chief of the Diversion Regulatory Drafting & Policy Support Section ("DPW") of DEA's Diversion Control Division. Tr. 32; Gov't Ex. 1 at 1. She has worked at the DEA since 2012, and prior to her current position worked as a Diversion Investigator ("DI"), Lead Staff Coordinator, and Policy Analyst. Tr. 32, 45.

Ms. Achbach testified that the Regulatory Drafting and Policy Support Section "is in charge of drafting all of the non-scheduling rulemaking that DEA does for [the] Diversion Section or Diversion Office." Tr. 32-33. Ms. Achbach is also "responsible for [liaising] with The Federal Register, ensuring that documents from DEA that need to be published for public view get published, and then comments are appropriately managed."[6] Tr. 33. Ms. Achbach testified that she "was one of two Federal Register Liaisons" during the time the NPRM was published. Tr. 36.

Publishing of NPRM and Receipt of Comments

The Government submitted a Declaration of Heather E. Achbach, which was signed by Ms. Achbach on August 12, 2024, and admitted into the record as Government's Exhibit 1. Tr. 35-36. In the Declaration, Ms. Achbach provides that she is "authorized to sign and submit documents to the Office of the Federal Register as official documents of DEA." Gov't Ex. 1 at 1. Ms. Achbach further attests to the publication of the NPRM and subsequent receipt of comments. Specifically, Ms. Achbach states that:

[5] Government Exhibits 1-3 were offered and admitted through Ms. Achbach.

[6] Ms. Achbach testified that the responsibilities of a Federal Register Liaison include "review and ensure [any documents signed by the Administrator and approved for publication do not] have any track changes," and "add a Federal Register Liaison statement to the Word document, electronically sign it in Word, and submit it to the Federal Register through their online portal." Tr. 33. Once a document is scheduled and published by the Federal Register, Federal Register Liaisons are "responsible in the back-end system, which is called the Federal Docket Management System . . . [and] are responsible for managing all of the comments that come in and ensuring that they are posted to public view, and then, at the end of the comment period, download[ing] and transfer[ring] [the comments] to whomever is responsible for that specific rulemaking." Tr. 34.

> On December 13, 2023, a Notice of Proposed Rulemaking (NPRM) was published in the Federal Register, on behalf of DEA, proposing to place 2,5-Dimethoxy-4-chloroamphetamine and 2,5-Dimethoxy-4-iodoamphetamine into Schedule I of the Controlled Substances Act. The NPRM permitted interested persons to file written comments on the proposed rulemaking. Such comments could be submitted electronically through the Federal eRulemaking portal . . . or in paper directly to DEA. The deadline to file written comments was January 12, 2024.

Gov't Ex. 1 at 1.

Ms. Achbach testified that she "was not involved in the actual publication [of the NPRM], although [she] was copied on all of the transmittals" and received the NPRM draft "cleared for publication and signed from the Administrator." Tr. 36-37. Her predecessor "is the one who validated everything and signed as the liaison and submit[ted] [the NPRM]."[7] Tr. 37. Ms. Achbach additionally "received a copy of [the NPRM] from the Federal Register" after its publication on December 13, 2023. Tr. 38.

Ms. Achbach states in her Declaration that "[t]here were approximately 151 electronic comments submitted through the Federal eRulemaking Portal in response to the NPRM," and one comment "submitted through the mail." Gov't Ex. 1 at 2. DPW "downloaded the electronic comments received through the Federal eRulemaking Portal in response to the NPRM . . . in 'agency view,' which includes confidential business information provided by the commenter." *Id.* Ms. Achbach further states that "comments serve an important role in informing the agency of potential issues and of information the agency may lack,"[8] and that although "the agency does not provide any responses to comments at any interim stage of the rulemaking . . . [t]he agency provides its responses to comments in the final rule."[9] *Id.*

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[7] Ms. Achbach testified that Scott Brinks "is the former Section Chief of the Regulatory Drafting and Policy Support Section and was the second of the two Federal Liaisons" who signed the NPRM on behalf of the DEA. Tr. 37.

[8] Ms. Achbach testified that "comments serve to help the Agency receive additional information during a rulemaking session that they may not otherwise have . . . at the time that the rule was published, which is why it is a Notice of Proposed Rulemaking." Tr. 40-41. The notice and comment period serves as "an opportunity for the public to not only be notified of what the Agency is planning, but also to let the Agency know if there are any concerns or if they are in agreement with the Agency." Tr. 41.

[9] Responses to submitted comments in the final rule "express the agency's official views as the final rule is signed by the Administrator or her designee." Gov't Ex. 1 at 2. Ms. Achbach testified that DEA does not "respond individually to commenters," but responds "in a final rule, which is the opportunity for the Agency to respond to the comments en masse and to the themes

Regarding the receipt of comments, Ms. Achbach testified that "comments are to be submitted either via paper or electronically . . . where they will receive a comment tracking number."[10] Tr. 40. The electronic comments are received "through the Federal Docket Management System . . . through the docket for the rule, at which point they are not yet posted on public view."[11] Tr. 41. In reviewing the comments, Ms. Achbach testified that DPW is "looking for . . . whether anybody had information in there that they requested to be redacted."[12] Tr. 41. Upon closure of the comment period,[13] Ms. Achbach testified that she "downloaded all of the comments . . . into a file, and transmitted them to the Drug and Chemical Evaluation Section's representative" with no alterations made to the submitted comments.[14] Tr. 42.

Ms. Achbach's testimony was primarily focused on introduction of the NPRM, the procedures for publication of the NPRM, and the receipt of comments associated with the NPRM. Her testimony was consistent and sufficient to establish her personal knowledge of the publication of the NPRM and subsequent receipt and management of comments by DEA. I fully credit her testimony and will give it significant weight in regards to the notice and comment procedures associated with the December 13, 2023 NPRM.

Theresa M. Carbonaro, Ph.D.[15]

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that were received during the comments." Tr. 44. Ms. Achbach further testified that this procedure of responding to comments broadly in the final rule "is the federal government procedure overall . . . not limited to DEA." Tr. 49. As the Agency has reserved for itself the responsibility to respond to the comments in the final rule, this tribunal will not consider the comments for purposes of this Recommended Decision.

[10] Pursuant to the NPRM, "[t]he comments were to be submitted to DEA between December 13th . . . and January 12." Tr. 40; ALJ Ex. 1 at 1.

[11] Ms. Achbach testified that the Government posts the comments for public view "within 48 to 72 hours, unless there are weekends or holidays in play." Tr. 41.

[12] On cross-examination, Ms. Achbach testified that "the only extent of review [of the comments] that [she] did was to ensure that there was no personal identifiable information or confidential business information that needed to be redacted," and thus she did not "read [the comments] for content, only for personal information." Tr. 47.

[13] Ms. Achbach testified that to her knowledge, no comments were received after the comment period. Tr. 42.

[14] *See* Gov't Ex. 3.

[15] Government Exhibits 4, 5, 6, 7, 7A, 8, 9, 10, 11, 12, 13, 14, 15, and 16 were offered and admitted through Dr. Carbonaro.

Background

The Government called Theresa M. Carbonaro, Ph.D., as an expert witness in pharmacology with a special emphasis in hallucinogenic substances, and, in the absence of any objection by the Petitioners, the tribunal accepted Dr. Carbonaro as an expert in the stated subject matter.[16] Tr. 69, 73-74; ALJ Exs. 37 at 3, 54 at 43. Dr. Carbonaro is a pharmacologist currently employed by the DEA, where she has worked since 2018. Tr. 54-55; Gov't Ex. 4 at 1-2. She holds a bachelor of arts in psychology[17] and a Ph.D. in biomedical sciences with a specialization[18] in neuroscience and pharmacology.[19] Tr. 55; Gov't Ex. 4 at 1. Prior to working for the DEA, Dr. Carbonaro worked at the Food and Drug Administration ("FDA") from January 2017 through September 2018, as a pharmacologist at the Center for Tobacco Products, Office of Science, Clinical and Behavior Pharmacology Branch. Tr. 63; Gov't Ex. 4 at 2.

Regarding postdoctoral training, Dr. Carbonaro testified that it is "traditional, to go through the academic pathway, to do a postdoctoral training position that can last one to three years or longer." Tr. 61. Dr. Carbonaro testified that she did two postdoctoral training programs: "[o]ne at the University of Texas Medical Branch in Galveston, Texas,[20] and then

[16] Dr. Carbonaro testified that she has served as an expert witness in other proceedings, including proceedings related to the Analogue Act. Tr. 67.

[17] Dr. Carbonaro testified that her B.A. "focused in psychology classes, but also [involved] pharmacology and drugs of abuse," and "included other science classes like chemistry, biochemistry, and other arts and required criteria." Tr. 56. Dr. Carbonaro testified that she "started focusing more on drugs of abuse during the end of [her] time, because [she] decided [she] was going to go for a [Ph.D.] in pharmacology. So [she] started taking more classes related to psychology related to drugs of abuse." Tr. 59.

[18] Dr. Carbonaro testified that this specialization involved investigation into "mechanisms of action of two hallucinogens . . . N,N-dimethyltryptamine [("DMT")], a Schedule I substance, and another one, N,N-diisopropyltryptamine [("DiPT")], which is not a controlled substance." Tr. 59-60.

[19] Dr. Carbonaro testified that she received her Ph.D. in December of 2012. Tr. 56; Gov't Ex. 4 at 1. To acquire her Ph.D., Dr. Carbonaro testified that she "had two years of additional classes specific to pharmacology and neuroscience and biomedical science, and then, an additional period of classes that overlapped with a dissertation project, and then, focused on [her] dissertation project for the last year and a half." Tr. 56.

[20] Dr. Carbonaro testified that the UT postdoctoral training was a one-year program "where [she was] looking at the effects of lorcaserin, which is a weight-loss drug that was approved at that time, looking at mechanisms of actions related to that, to maybe use it for drug treatment. And then, also . . . working with a chemist that was making new molecules to see if they could be used for drug abuse dependence treatment" in animals and cells. Tr. 61. Dr. Carbonaro testified that this program involved hallucinogens "to some degree . . . because lorcaserin has some

another one in Johns Hopkins University School of Medicine,[21] for about three years." Tr. 61; Gov't Ex. 4 at 1.

Regarding her current position with the DEA, Dr. Carbonaro testified that her section "deals largely with controlled substances' analogues," which involves "case support for drugs that might be considered an analogue under the analogue provision." Tr. 64. Dr. Carbonaro testified that her section also does "scheduling actions," wherein she has "written a number of Notice of Proposed Rulemakings" for placement of drugs in various schedules. Tr. 64. Her section also "monitor[s] drugs to assess if they should be controlled," by "monitor[ing] . . . reports of [drugs] in different databases" to determine if the drugs are "causing harm." Tr. 64-65. This monitoring involves "work with . . . interagency partners to monitor what's going on internationally, as well." Tr. 65. In this capacity, Dr. Carbonaro "worked as a point of contact for the UN . . . working on . . . treaty drugs and processes that are entailed with that." Tr. 65. Dr. Carbonaro acknowledged that she would be considered DEA's "go-to person" for matters involving hallucinogens.[22] Tr. 65.

Overview of Dr. Carbonaro's Analysis of DOI and DOC

Dr. Carbonaro acknowledged that she was asked to do an "Eight Factor Analysis"[23] regarding DOI and DOC, and to render her expert opinion on each factor. Tr. 68. In addition to the Eight Factor Analysis, Dr. Carbonaro also did an analysis to determine whether DOI and/or

activity at some of the same receptors" and she otherwise "did do some hallucinogen work there." Tr. 62.

[21] Dr. Carbonaro testified that at Johns Hopkins, she "started working under the direction of Roland Griffiths, who was researching psilocybin and dextromethorphan in clinical populations, specifically those that have experience using hallucinogens." Tr. 62. This research involved "a trial with 20 participants looking at different abuse liability for psilocybin, dextromethorphan," and Dr. Carbonaro's duties were related to the "[c]ognitive effects and subjective effects" of these substances. Tr. 62. Dr. Carbonaro testified that dextromethorphan "is the active ingredient in cough medicine, but at high doses it can produce hallucinogenic effects." Tr. 62-63. On cross-examination, Dr. Carbonaro testified that dextromethorphan can cause delirium, violent outburst, and psychotic effects, but acknowledged that it is not scheduled. Tr. 199-201.

[22] Dr. Carbonaro testified that she has "given briefings to the field and to other parties within DEA about hallucinogens." Tr. 65. Dr. Carbonaro additionally identified approximately 11 publications with which she was involved that were related to hallucinogens. Tr. 65-66; Gov't Ex. 4 at 3-4.

[23] *See* 21 U.S.C. § 811(c)(1)-(8).

DOC should be placed in Schedule I under 21 U.S.C. § 812(b)(1). Tr. 68. Her analysis also considered whether DOI and/or DOC had a currently accepted medical use in the United States. Tr. 68-69. In preparing her Eight Factor Analysis, Dr. Carbonaro consulted "[a]ny data . . . related to . . . NFLIS-Drug[24] and encounters . . . recorded in that and scientific published papers about DOI and DOC and prior knowledge that [she has] about DOI and DOC." Tr. 86. Regarding the NFLIS data, Dr. Carbonaro testified that DEA "can use that data to assess drug trends." Tr. 87.

Dr. Carbonaro testified that "[g]enerally speaking" the controlled substance scheduling process involves the DEA asking HHS for its recommended decision prior to issuing a notice of proposed rulemaking. Tr. 79. Dr. Carbonaro thus testified that prior to receiving the HHS recommendation, DEA sent HHS a letter[25] "asking for a scientific and medical evaluation of DOI and DOC and a scheduling recommendation" which contained an Eight Factor Analysis that another member of Dr. Carbonaro's section wrote "to help them in their evaluation."[26] Tr. 75. Regarding the relationship between HHS and DEA in reaching scheduling decisions, Dr. Carbonaro testified that "HHS defers to [DEA] on law enforcement encounter data." Tr. 94.

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[24] Dr. Carbonaro testified that "NFLIS" stands for the "National Forensic Laboratory Information System." Tr. 86. She further testified that "it is a DEA system that collects data about drugs specific to law enforcement seizures and encounters from state, local, and federal labs . . . confirmed positive for that drug." Tr. 86. Dr. Carbonaro testified that this is a "voluntary system," wherein "laboratories can put information into NFLIS-drug . . . relating to the seizures . . . where [the seizures are] found and other information, that is collected." Tr. 86-87. Regarding the voluntary nature of these submissions, Dr. Carbonaro acknowledged that every single encounter with these drugs is not required to be submitted by labs to NFLIS. Tr. 87. Non-controlled substances may be reported to NFLIS and DEA has "many reports of non-controlled substances," but it depends "on a lab having a standard for that drug." Tr. 87-88. Dr. Carbonaro testified that "[n]ot all labs have a standard," and that there are "different priorities based on the region or the state or different law enforcement." Tr. 87. Dr. Carbonaro additionally testified that labs may test for "known cutters," which may be non-controlled substances "that can be used in combination with [other] drugs." Tr. 87-88.

[25] *See* Gov't Ex. 5.

[26] Dr. Carbonaro testified that she reviewed the initial letter issued by DEA to HHS seeking an evaluation of DOI and DOC. Tr. 328-29. Dr. Carbonaro testified that she "read through [the letter] to see what content was in [there], [and] what information was provided to HHS that helped them do their analysis." Tr. 329. Dr. Carbonaro testified that she did not verify any of the claims contained within the letter because it was a "pre-decisional document." Tr. 329. Dr. Carbonaro further testified that she believed that HHS "makes their own evaluation independent of" DEA's initial letter. Tr. 345. Dr. Carbonaro indicated that the DEA's initial letter is just a "component[] [she] would consider." Tr. 372.

Dr. Carbonaro testified that "when [she] was assigned to [analyze DOI and DOC], [DEA] had already received an Eight Factor Analysis from HHS, which is their letter of recommendation and scientific and medical evaluation of the substances."[27] Tr. 74. Accordingly, Dr. Carbonaro "reviewed HHS's documents, as well as previous documents that went to HHS, and then reviewed any literature that [she] could find related to DOI and DOC."[28] Tr. 74-75. Dr. Carbonaro testified that the HHS scientific and medical evaluation, issued by the Assistant Secretary of Health with concurrence between FDA and NIDA, recommended placement of DOI and DOC into Schedule I of the Controlled Substances Act ("CSA"). Tr. 78-79.

Dr. Carbonaro testified that she drafted two Eight Factor Analyses related to control of DOI and DOC that were published with the NPRM.[29] Tr. 81, 83; Gov't Exs. 7, 7A. Dr. Carbonaro testified that the initial Eight Factor Analysis was prepared in August of 2021[30] and the second Eight Factor Analysis was prepared in October of 2023.[31] Tr. 81-83. Dr. Carbonaro further testified that the October 2023 Eight Factor Analysis was "updated very slightly" from the August 2021 Analysis prior to its publication in the NPRM.[32] Tr. 83. The October 2023 Eight Factor Analysis serves as the current document being used in the December 13, 2024 NPRM. Tr. 85.

Background of DOI and DOC

Dr. Carbonaro testified that DOI and DOC are synthetic "hallucinogenic substances . . . similar [in molecular structure] to 2,5-dimethoxy-4-methylamphetamine or DOM . . . and 2,5-

[27] *See* Gov't Ex. 6.
[28] Dr. Carbonaro testified that she reviewed Center for Disease Control ("CDC") data for DOI and DOC, but determined that neither drug was "mentioned as one of the drugs that . . . is specifically asked for" in surveys related to lifetime use and thus did not focus on that data. Tr. 376-77.
[29] Dr. Carbonaro testified that the first Eight Factor Analysis was part of an NPRM that was "withdrawn" in 2022. Tr. 83.
[30] *See* Gov't Ex. 7.
[31] *See* Gov't Ex. 7A.
[32] Dr. Carbonaro testified that the "only differences" between the two Eight Factor Analyses was "the National Forensic Laboratory Information System-Drug database . . . where [she] did an updated query for DOI and DOC," and added "five additional encounters of DOC and one additional state . . . Indiana . . . [a]nd then one additional state was noted for DOI which [she] believe[s] was Nevada." Tr. 85; *Compare* Gov't Ex. 7 at 10, *with* Gov't Ex. 7A at 10.

dimethoxy-4-bromoamphetamine, DOB." Tr. 88-89. In addition to molecular structure, Dr. Carbonaro testified that DOI and DOC are also similar to DOM and DOB in how "they work through the Serotonin 2A receptors specifically." Tr. 89. Dr. Carbonaro explained that "serotonin is one of the neurotransmitters in the body . . . [and] has 17 different receptors throughout the body." Tr. 89. Dr. Carbonaro indicated that "[i]t is believed that binding and activity through the specific receptor Serotonin 2A is necessary but not sufficient to cause hallucinogenic effects." Tr. 89.

Dr. Carbonaro testified that this group of hallucinogens, including DOI, DOC, DOM, and DOB, are known to cause adverse health effects, most commonly through "psychological" effects that "can have very profound effects on . . . fear, anxiety, [and] depression."[33] Tr. 89-90. These substances can also "have a very intense challenging experience that can lead to these kinds of effects," in addition to "physiological effects that can happen . . . particularly related to the cardiovascular system." Tr. 90.

Dr. Carbonaro further testified that she believes DOI and DOC are "controlled in Florida," as well as Canada and the United Kingdom. Tr. 90-91. Specifically for DOC, Dr. Carbonaro testified that "it is now a UN Treaty Drug" through the 1971 Convention on Psychotropic Substances where "it was voted on to be controlled." Tr. 91. Dr. Carbonaro testified that DEA received a letter from the Secretary General of the United Nations[34] in which the UN Commission "decided to include DOC in Schedule I of the 1971 Convention." Tr. 91-92. Dr. Carbonaro testified that pursuant to this vote, "a member of the treaty . . . must regulate [DOC] in a way that would meet the [standards of the] 1971 Convention." Tr. 92. Dr. Carbonaro indicated that the U.S. is thus obligated to schedule DOC in some capacity to meet its treaty obligations. Tr. 92.

21 U.S.C. § 811(c)(1); Actual or Relative Potential for Abuse

The Eight Factor Analysis related to a substance's actual or relative potential for abuse notes that "[t]he term 'abuse' is not defined in the CSA," but states that "the legislative history of the CSA suggests . . . four prongs in determining whether a particular drug or substance has a

[33] Dr. Carbonaro additionally acknowledged that these substances could cause paranoia and violent outbursts. Tr. 90.
[34] *See* Gov't Ex. 9.

potential for abuse." Gov't Ex. 7A at 3.

The first prong relates to "evidence that individuals are taking the drug or other substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community" ("Abuse Prong A"). *Id.* DEA found that "[d]ata show that DOI and DOC have been encountered by law enforcement in the U.S. . . . indicating DOI and DOC availability for abuse." *Id.* Additionally, based on anecdotal reports, HHS found that "individuals are using [DOI and DOC] in amounts sufficient to create a health hazard and are being used for their hallucinogenic activity." *Id.* at 3-4.

The second prong focuses on whether "[t]here is significant diversion of the drug or substance from legitimate drug channels" ("Abuse Prong B"). *Id.* at 4. As DOI and DOC "are not approved drug products in the U.S." according to HHS, DEA determined that there "appears to be no legitimate drug channels for which DOI and DOC can be diverted." *Id.* Although DOI and DOC "are available for purchase from legitimate chemical companies" for use in scientific research, DEA found "[n]o evidence of diversion . . . apparent from these companies." *Id.* Accordingly, DEA concluded that "this characteristic of abuse potential is not applicable." *Id.*

The third prong considers whether "[i]ndividuals 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" ("Abuse Prong C"). *Id.* As HHS determined that "DOI and DOC are not found in Food and Drug Administration (FDA)-approved drug products and practitioners may not legally prescribe these substances, nor dispense them to an individual" DEA concluded that "individuals are taking DOI and DOC on their own initiative, rather than based on medical advice from a practitioner licensed by law to administer drugs." *Id.* The determination that individuals were taking DOI and DOC is based on "law enforcement seizures and anecdotal reports" which indicate that DOI and DOC are available as illicit substances "on the street." *Id.* Because DOI and DOC have "effects similar to schedule I substances LSD and . . . DOB," DEA concluded that individuals are taking these substances "on their own initiative rather than on the medical advice of a licensed practitioner, possibly because they are seeking hallucinogenic effects similar to those produced by schedule I substances while simultaneously avoiding criminal penalties associated with those substances." *Id.*

The fourth and final prong asks whether:

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

Gov't Ex. 7A at 4. HHS determined that "chemically, DOI and DOC are analogs of the schedule I hallucinogen DOM," and "[t]he effects and pharmacological action of DOI and DOC are similar to those of other schedule I hallucinogens, such as DOM and LSD." *Id.* at 5. These similarities were determined based on "drug discrimination studies" conducted on animals *in vivo*[35] where "DOI and DOC produce full substitution for the discriminative stimulus effects of DOM, LSD, and . . . DMT." *Id.* Regarding the effects of DOI and DOC in humans, HHS and DEA relied on "anecdotal reports" suggesting that these substances "produce classic hallucinogenic effects that are similar to DOM, including visual and auditory hallucinations, fatigue, headache, gastrointestinal distress, insomnia and anxiety." *Id.* HHS further noted that "use of DOC in combination with other drugs is associated with emergency department admissions and one death." *Id.* Accordingly, "due to the psychological and cognitive disturbances associated with DOI and DOC, as with other schedule I hallucinogens," DEA concluded that "it is reasonable to assume that DOI and DOC have substantial capability to be a hazard to the health of the user and to the safety of the community." *Id.*

Dr. Carbonaro testified that "actual or relative potential for abuse" means "a substance's relative potential for abuse using metrics that are established in scientific literature to assess abuse liability and the four factors." Tr. 95; Gov't Ex. 7A at 3-4. Dr. Carbonaro indicated that the four prongs described above are used to determine "abuse," as abuse is not specifically defined in the CSA.[36] Tr. 95. Dr. Carbonaro further testified that the four-prong test for abuse "was included in the 1970 bill for the Controlled Substance Act," which references "this definition . . . from the Federal Food, Drug, and Cosmetic Act for [the] definition of abuse potential . . .." Tr. 398. Dr. Carbonaro testified that in her opinion, there is substantial evidence of DOI and DOC's relative potential for abuse. Tr. 142-43.

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[35] Dr. Carbonaro testified that "*in vivo*" means "[i]n life," and involves study of the whole body system through animals rather than cells. Tr. 102.

[36] Dr. Carbonaro additionally testified that these four prongs go "back to the initiation of the CSA and what was outlined there." Tr. 95.

On cross-examination, Dr. Carbonaro testified that although there "may be other definitions" of abuse, DEA's four-prong test "is the one that has been used previously in legislative history." Tr. 157. Dr. Carbonaro testified that in her role as a researcher prior to joining DEA, DEA's definition of abuse "would still mirror [her] definition of abuse." Tr. 157.

Abuse Prong A

Regarding Abuse Prong A, Dr. Carbonaro testified that there is evidence that individuals are taking DOI and DOC in amounts sufficient to create a hazard to their health or to the safety of other individuals or in the community. Tr. 96. Dr. Carbonaro testified that "[b]ased on HHS's evaluation and law enforcement seizure data . . . there is evidence that people are using [DOI and DOC]." Tr. 96. Dr. Carbonaro testified that determining a "sufficient amount" depends on "any evidence that produces a psychological or a psychoactive effect that the drug induces. And if there's evidence to show that there are harms associated with it." Tr. 159. She further testified that "DOI and DOC are very potent," and dosages of one to three milligrams can produce hallucinogenic effects. Tr. 159-60. Dr. Carbonaro testified that there is evidence discussing dosage amounts "[i]n the public forums and in . . . the PiHKAL[37] by Shulgin" in addition to amounts referenced in law enforcement data, although the law enforcement data does not necessarily specify "how much any one person is using."[38] Tr. 160.

Dr. Carbonaro acknowledged that for Abuse Prong A, she "relied on HHS's evaluation" which indicated that DOI and DOC are used "in sufficient amounts." Tr. 161. She testified that she also considered "public forums," which provide evidence that people "are using [DOI and DOC] in a way that would cause hallucinogenic effects."[39] Tr. 161. Dr. Carbonaro further testified that this prong does not focus on "a specific dose," but rather considers "evidence that people are using" the substances. Tr. 162.

[37] Dr. Carbonaro testified that "PiHKAL" is Alexander Shulgin's publication "Phenethylamines I Have Known and Loved." Tr. 114-15.

[38] Dr. Carbonaro indicated that the amounts referenced in law enforcement data relate to the amount of drugs tested and encountered by law enforcement, and acknowledged that this does not provide information on the amount of the drugs actually consumed by an individual. Tr. 160-61.

[39] Dr. Carbonaro testified that she believed that HHS's analysis was also based on the same anecdotal reports she reviewed. Tr. 161.

Abuse Prong B

Regarding Abuse Prong B, Dr. Carbonaro testified that this prong "generally applies to a drug that has medical use." Tr. 96. Accordingly, "since there is no approved medical use for [DOI and DOC]," Dr. Carbonaro indicated that there "is no diversion because it's not approved for anything." Tr. 96-97. Dr. Carbonaro testified that she is aware that DOI and DOC are "used in research," but stated that "there's been no evidence of it being diverted from legitimate scientific research."[40] Tr. 97. Dr. Carbonaro acknowledged that DOI and DOC are currently being manufactured, are available for sale, and are being distributed, but the CSA does not control that system since DOI and DOC are not currently scheduled. Tr. 97.

Dr. Carbonaro confirmed on cross-examination that DEA "could not find any evidence" of diversion of DOI and DOC from legitimate channels, but testified that this does not "mean that there is no evidence." Tr. 162. Dr. Carbonaro indicated that DEA's evaluation for diversion from legitimate channels was "very limited" to "what's available online and through . . . court prosecutions."[41] Tr. 162-63. However, Dr. Carbonaro reiterated that "this characteristic of abuse potential is not applicable." Tr. 163.

Abuse Prong C

Regarding Abuse Prong C, Dr. Carbonaro testified that this prong concerns "if people are using [DOI or DOC], are they using it under . . . the advice of a medical practitioner . . . [o]r . . . using it under their own volition." Tr. 98. Dr. Carbonaro determined that "because [DOI and DOC] are not in substances that have been approved by the FDA and . . . there is evidence people are using them, then [DOI and DOC] have to be used not by the medical advice of a practitioner."[42] Tr. 98. Dr. Carbonaro testified that there is no evidence medical practitioners are using, recommending, or prescribing DOI or DOC to any patients. Tr. 98. In reaching the conclusion that individuals are using DOI and DOC recreationally, Dr. Carbonaro indicated that these substances "can be purchased online for people to use recreationally." Tr. 98-99. Additionally, Dr. Carbonaro testified that DEA uses "relative abuse potential compared to other

[40] Dr. Carbonaro testified that this lack of evidence of diversion from scientific evidence does not mean it does not occur, but she is "just not aware of it." Tr. 97.
[41] Dr. Carbonaro was unaware of any criminal prosecutions related to DOI or DOC. Tr. 163.
[42] Dr. Carbonaro testified that "there have been no clinical trials to suggest that [DOI and DOC] have medical utility." Tr. 98.

substances in the same class" as a means to measure the potential for recreational use. Tr. 99. Dr. Carbonaro testified that based on the similarities between DOI and DOC and controlled substances like DOB and LSD, there is abuse potential for DOI and DOC. Tr. 99.

On cross-examination, Dr. Carbonaro reiterated that her research made it apparent that individuals were purchasing DOI and DOC online for recreational use. Tr. 163. She testified that she was aware of "many websites where [an individual] can purchase DOI and DOC and other chemicals online" for recreational purposes.[43] Tr. 164. However, Dr. Carbonaro acknowledged that DEA did not have any evidence of sales of DOI and DOC online, and thus her testimony regarding individuals purchasing these substances for recreational use was speculative. Tr. 164. Dr. Carbonaro testified that "there is evidence of people using [DOI and DOC] and reporting online about their effects," and encounters with DOI and DOC "on the street in blotter[44] paper," which provide evidence that individuals are obtaining and using DOI and DOC recreationally,[45] despite DEA being unable to specifically identify sale of DOI and DOC online. Tr. 164-65.

Dr. Carbonaro testified that the NFLIS-Drug data, which covers law enforcement encounters with substances, indicates that law enforcement encountered DOI forty times between 2005 and 2023, and did not report any encounters since 2019. Tr. 165-67. Dr. Carbonaro reiterated that NFLIS-Drug is "a voluntary database," and that "[w]hat drugs are tested for and confirmed for and reported back to DEA can vary for different reasons, based on priorities of

[43] Dr. Carbonaro specifically testified that there are websites "on the Clearnet and Darknet where" substances can be purchased for recreational use. Tr. 164. Dr. Carbonaro testified that certain companies sell DOI for research purposes, "but also there are other online websites that can be purchased from." Tr. 224. Dr. Carbonaro acknowledged that she was not an expert in DEA's registration requirements for chemical suppliers, but testified that these companies "[i]n theory" could provide non-controlled substances to individuals for recreational use. Tr. 225-26. Regarding the websites on which DOI is available for purchase recreationally, Dr. Carbonaro testified that she did not "feel comfortable giving names of those companies" available through these websites, but stated that they are "internationally recognized." Tr. 227.

[44] Dr. Carbonaro testified that "blotter paper" is "paper [that] has been saturated with a drug that's been dissolved in saline or some solvent . . . and then impregnated into the paper so that a small piece of paper could be put on the tongue or put in the mouth and . . . the drug could be administered that way." Tr. 131. Dr. Carbonaro further testified that she has not seen any drugs approved for human use provided in blotter paper form. Tr. 131-32.

[45] When reviewing the Microgram Bulletins, Dr. Carbonaro testified that most of the reported encounters with DOI and/or DOC related to blotter paper, which she does not "believe would be studied in legitimate research." Tr. 419.

labs and other caveats."[46] Tr. 167. Accordingly, Dr. Carbonaro testified that "[j]ust because . . . there are no reports between 2019 and 2024, it doesn't mean that they're not there," but instead "means [the encounters] were not recorded into NFLIS."[47] Tr. 167. Dr. Carbonaro further testified that "these numbers for . . . non-controlled drugs, tend to be lower than" the numbers for controlled substances. Tr. 168. Once a substance is controlled, Dr. Carbonaro testified that "labs will start testing them" and the numbers will increase as the numbers for non-controlled substances are "very likely . . . under-reported."[48] Tr. 168. Dr. Carbonaro indicated that the NFLIS-Drug data serves as "evidence that [DOI and DOC] are being encountered in seizures." Tr. 168-69.

Regarding anecdotal reports of DOI and DOC usage, Dr. Carbonaro testified that she relied on HHS's evaluation which focused on reports from Erowid.com ("Erowid")[49] and PiKHAL.[50] Tr. 169. Dr. Carbonaro further testified that sites like Erowid and Reddit.com ("Reddit")[51] are routinely reviewed to determine "what effects a drug might have on a person." Tr. 170. She testified that because it is "unethical to give [the substances] to humans in a clinical trial to assess abuse liability without the right parameters," anecdotal reports are relied upon "to some degree" to assess effects. Tr. 170. According to Dr. Carbonaro, the anecdotal reports indicate that the effects of DOI and DOC "lasted a long time," which is different from LSD or other hallucinogenic substances.[52] Tr. 170. Dr. Carbonaro testified that she "relied on HHS's

[46] On cross-examination, Dr. Carbonaro testified that each lab has varying standard operating procedures for testing, and acknowledged that she has not reviewed the standard operating procedures for all labs reporting to NFLIS-Drug. Tr. 207-08. She further testified that "it's likely that not all labs" have DOI or DOC "in the laboratory to confirm" toxicology reports, as DOI and DOC are "not . . . controlled substance[s]." Tr. 209.

[47] Dr. Carbonaro indicated that another potential reporting issue occurs when individuals believe they are taking a substance different than the one they actually consume. Tr. 333. Dr. Carbonaro testified that the Microgram Bulletins show at least one instance where blotter paper was believed to be LSD but turned out to be DOI. Tr. 334; *see, e.g.*, Gov't Ex. 13 at 4.

[48] Dr. Carbonaro acknowledged that reported encounters for MDMA are higher than DOI specifically, but indicated that she would "expect MDMA, LSD, and psilocybin to all be higher" in terms of reporting than non-controlled substances. Tr. 168.

[49] Dr. Carbonaro testified that Erowid is "[a]n online website where users of drugs and chemicals can post the effects of those drugs." Tr. 342.

[50] Dr. Carbonaro testified that she also personally reviewed the Erowid posts. Tr. 169.

[51] Dr. Carbonaro testified that Reddit is an "online website where . . . users of Reddit can post on any topic," including drug use. Tr. 346.

[52] Dr. Carbonaro acknowledged that any individual who read Shulgin's PiHKAL would be aware

evaluation" pertaining to anecdotal evidence, and indicated that such evidence is "one of their prongs when they assess post-market surveillance information."[53] Tr. 171. Dr. Carbonaro further testified that HHS understands "that there are issues with relying on anecdotal evidence." Tr. 171. Dr. Carbonaro acknowledged that she could not confirm whether the anecdotal reports were even posted by humans, but she ultimately concurred with HHS based on her own review of the posts[54] and otherwise gave credence to HHS's medical and scientific evaluation. Tr. 171-72.

Dr. Carbonaro testified that evidence that an individual is self-administering a drug that lacks an accepted medical use is potential evidence of abuse, and reiterated that finding drugs in forms consistent with self-administration, such as blotter paper, is relevant to determine potential abuse. Tr. 397.

Abuse Prong D

Regarding Abuse Prong D, Dr. Carbonaro testified that this prong allows DEA "to compare the known effects of DOI and DOC compared to substances that are in a similar class and assess[] if they have abuse potential based on those findings." Tr. 100. Dr. Carbonaro testified that DOI and DOC are analogues of DOM, a Schedule I hallucinogen, based on their "similar mechanism of action."[55] Tr. 100. She further testified that DOI and DOC "can produce hallucinations and hallucinogenic activity and have the same potential for the psychological effects that [she] noted before and some of the cardiovascular effects." Tr. 100-01.

Dr. Carbonaro testified that she did not believe there is "an operational definition" of the

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of the long-lasting effects of DOI and DOC. Tr. 170.

[53] On redirect examination, Dr. Carbonaro indicated that FDA guidance provides that abuse-related information obtained from internet forums and social media websites may be included in post-marketing data. Tr. 402-03.

[54] Dr. Carbonaro testified that she personally viewed a post on Reddit about DOI and the use of DOI. Tr. 172. The post indicated that DOI was used in "some sort of large group gathering . . . by some two or three hundred people." Tr. 172; *see* Gov't Ex. 10. Dr. Carbonaro testified that these types of posts provide "some indication that people are seeking [DOI] for one thing or another" and "evidence that people are seeking out DOI." Tr. 173. Dr. Carbonaro reiterated that she had no way to confirm the veracity of these posts, but indicated that anecdotal evidence "is often used to assess abuse liability to see what people are saying about" the substances. Tr. 174.

[55] On cross-examination, Dr. Carbonaro acknowledged that to her knowledge, DOI and DOC have never been prosecuted under the Analogue Act. Tr. 183.

term "new drug." Tr. 178. She testified that "new drugs" could "just be a drug that's not controlled and it's being evaluated for that," or "a drug that has been around for a while but is now going through" the scheduling process. Tr. 178-79. Dr. Carbonaro indicated that "new" is a relative term, and DEA typically uses the designation to refer to "a new drug of concern." Tr. 179.

Abuse Potential: Drug Discrimination Studies

Dr. Carbonaro testified that the abuse potential studies are based in part upon discrimination studies, which are "studies that can be done in rodents, mice, and rats, nonhuman primates, and humans," although the use of rodents is most common. Tr. 101. In discrimination studies using rodents, Dr. Carbonaro testified that the test subject "can receive a drug[56] and then learn to press a lever for a food reinforcer based on the effects of those drugs. And then on another day, they are given saline" to produce a non-drug effect. Tr. 101. Dr. Carbonaro testified that the rodents "learn to press the other lever" when they receive the non-drug effect from the saline, and that "with several sessions, [the test subjects are] able to discriminate whether they got the drug that they're used to getting." Tr. 101. Once the subject is "able to discriminate," Dr. Carbonaro testified that researchers "can do other doses or other drugs of varying doses to see if [the drug] has similar effects relative to that known drug of abuse." Tr. 101-02.

Specifically for DOI, Dr. Carbonaro testified that "groups of rats [were] trained to learn to discriminate DOM . . . LSD . . . and N,N-dimethyltryptamine, DMT, from saline." Tr. 102. Dr. Carbonaro testified that "in all three of those cases," DOI "fully substituted for the discriminative stimulus effects of those three hallucinogens."[57] Tr. 102. Dr. Carbonaro explained that essentially the rodents felt as if DOI was the same as DOM and LSD in terms of effects. Tr. 103. For DOC, Dr. Carbonaro testified that DOC "also fully substituted for DOM, LSD, and DMT-trained rats." Tr. 103.

On cross-examination, Dr. Carbonaro reiterated that drug discrimination studies are a

[56] Dr. Carbonaro testified that each of the drug discrimination studies used in the HHS/DEA analysis involved "intraperitoneal injections," wherein the drugs are injected directly into the rodents. Tr. 185.

[57] Dr. Carbonaro testified that DOI "did not substitute for" stimulants given to the rodents. Tr. 102-03.

significant indicator of abuse potential "[f]or hallucinogens." Tr. 184. Although drug discrimination studies may provide "an indicator for other drugs," Dr. Carbonaro indicated that such studies have "a significant bearing" for hallucinogens. Tr. 184. Dr. Carbonaro testified that these studies provide insight into abuse potential because they are used in comparing new drugs with "drugs . . . that have known abuse potential."[58] Tr. 186. Dr. Carbonaro testified that drug discrimination studies are an "accepted paradigm to assess abuse liability." Tr. 188.

Dr. Carbonaro additionally testified regarding self-administration studies, in which case an animal may "respond[] on a lever" to receive "additional infusions of a drug." Tr. 191. An animal that presses a lever a significant amount of times in order to receive another administration shows that "a drug is being self-administered based on the effects that [are] being produced." Tr. 191. However, Dr. Carbonaro testified that self-administration data "can be misinterpreted." Tr. 191. Additionally, she testified that it is "well known that drugs that work for the serotonin 2A receptor don't produce self-administration." Tr. 192, 194. Regarding other hallucinogens such as LSD, Dr. Carbonaro testified that although self-administration studies are ineffective to study LSD, it is still "know[n] [that] LSD is used and abused."[59] Tr. 195. Dr. Carbonaro indicated that other hallucinogens including psilocybin and DMT were not subject to self-administration, and MDMA "was marginal self-administration" in some studies. Tr. 195-96. Regarding DOM, Dr. Carbonaro testified that "there was one study, and it did not produce self-administration that was significant." Tr. 196.

On redirect, Dr. Carbonaro testified that through drug discrimination studies it is possible to compare the effects of DOI and DOC with a controlled substance such as DOM. Tr. 392-93. She additionally reiterated that self-administration studies "are generally believed not to be reliable" for hallucinogens as "[t]hey are known not to produce or produce very minimal evidence of self-administration in non-human primates or in rodent studies." Tr. 393.

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[58] Dr. Carbonaro explained that when there is an animal trained to press a certain lever whenever a substance like DOM is administered, and then the animal receives DOI and subsequently "produces all lever presses on the DOM lever," DOI would be "said to have substituted" for DOM. Tr. 186. Accordingly, "[b]ased on DOM's known abuse potential . . . it can be inferred that DOI would also have abuse potential." Tr. 186.

[59] Dr. Carbonaro testified that "[a] drug does not have to cause addiction for it to . . . have abuse potential." Tr. 195.

Abuse Potential: Anecdotal Reports

Dr. Carbonaro testified that the abuse potential determination was also based on anecdotal reports[60] regarding DOI and DOC. Tr. 103. Dr. Carbonaro testified that the anecdotal reports indicated that DOI and DOC "produce hallucinogenic effects, both seemingly auditory and visual," and there were additional reports "of psychological harm to some degree." Tr. 103. Amongst these reported effects were classic hallucinogenic effects, visual and auditory hallucinations, fatigue, headaches, gastrointestinal distress, insomnia, and anxiety. Tr. 103-04; Gov't Ex. 7A at 5. Dr. Carbonaro testified that these anecdotal reports are used by HHS "as a note to look at post-market surveillance information based on their industry guidance for abuse potential." Tr. 105. Such reports provide "evidence that people are using [DOI and DOC], the effects that they're observing, [and] how long a drug may effect in a body." Tr. 105. Dr. Carbonaro also testified that she included references to her Eight Factor Analysis in part because of HHS's inclusion of such reports in their scheduling determination. Tr. 105.

Dr. Carbonaro acknowledged that the HHS recommendation noted that use of DOC in combination with other drugs was associated with emergency room admissions and one death. Tr. 105; Gov't Ex. 7A at 5. Dr. Carbonaro further testified that "[b]ased on the information . . . provided to [her] by HHS and [DOI and DOC's] similarity to other substances that are in Schedule I, such as DOM, DOB, . . . LSD and DMT . . . of having the similar mechanism of action, [DOI and DOC are] likely to be abused and have evidence to create hazard to the health of the user or safety to the community." Tr. 106.

On cross-examination, Dr. Carbonaro testified that she personally reviewed Erowid to look up reports relating to DOI and DOC.[61] Tr. 343. In addition to Erowid, Dr. Carbonaro also reviewed Reddit, but acknowledged that information obtained via Reddit was for her own analysis of the anecdotal reports and "was not considered in [the] Eight Factor Analysis." Tr. 345. Dr. Carbonaro acknowledged that posts on Reddit are largely anonymous, with little to no

[60] Amongst the anecdotal reports utilized by HHS and Dr. Carbonaro were reports generated by Alexander Shulgin in two books which provide reports "of the effects of . . . hallucinogens by a small party." Tr. 104. Dr. Carbonaro testified that Shulgin is "a medicinal chemist" who has "synthesized a number of drugs" using precursor chemicals, including DOI and DOC. Tr. 115. Additionally, Dr. Carbonaro testified that anecdotal reports were obtained from Erowid, which is a "public post that anyone can write about any of the effects that drugs produce." Tr. 104.

[61] Dr. Carbonaro testified that there were "not necessarily a large number" of reports relating to DOI and DOC on Erowid. Tr. 343.

verification or fact-checking related to the content of the posts. Tr. 348. Dr. Carbonaro testified that she reviewed these posts "at face value" to identify if "there was an online . . . post that mentioned DOI or DOC."[62] Tr. 357. Dr. Carbonaro testified that "[e]vidence of online forum post[s] is one factor that is considered" when considering the scheduling of a drug or substance. Tr. 358.

21 U.S.C. § 811(c)(2); Scientific Evidence of Pharmacological Effect

HHS states that "the neurochemical effects of DOI and DOC occur primarily through the serotonergic system in the brain." Gov't Ex. 7A at 5. Serotonin stimulation at the 5-HT_{2A} receptors in the brain is believed to be the primary means through which hallucinogens "produce their characteristics." *Id.*

Through data obtained from *in vitro* studies, HHS found that "DOI and DOC have high binding affinity for the 5-HT_2 receptor."[63] *Id.* HHS found that "DOI, like many schedule I hallucinogens, act as agonists at the 5-HT_{2A} receptor"[64] and concluded that "DOI and DOC are agonists at the 5-HT_{2A} receptor, which is likely responsible for their hallucinogenic effects." *Id.* at 5-6.

When evaluating the central nervous system effects of DOI and DOC "using data from animal studies and reported effects in humans," HHS concluded "that pharmacological effects of DOI and DOC are similar to those of the schedule I hallucinogen, DOM." *Id.* at 6.

HHS further identified "psychopharmacological assays" in which DOI and DOC were assessed in overt behavior observations and drug discrimination. *Id.* HHS identified publications discussing overt behavioral responses for DOI, in which "DOI administration induced an increase in wet dog shakes and back muscle contraction" which was "attributed to 5-HT_{2A} receptor activation since pretreatment with MDL100907, a 5-HT_{2A} receptor antagonist, reduced these behavioral effects of DOI." *Id.* HHS determined that "since these data show that the overt behavioral effects produced by DOI are mediated by the 5-HT_{2A} receptor and that

[62] Dr. Carbonaro testified that "online mentions is what [she is] looking for" in reviewing sites like Reddit and Erowid. Tr. 357.
[63] The Eight Factor Analysis indicates that this affinity was evaluated using "DOI as the radioligand to measure binding." Gov't Ex. 7A at 5.
[64] This determination was made using "arachidonic acid release to measure cellular function." Gov't Ex. 7A at 5.

agonism of the 5-HT_{2A} receptor is the primary mechanism of action of typical hallucinogenic responses together suggest that DOI has hallucinogenic effects." *Id.*

HHS found that "[i]n drug discrimination studies[65] with rats[66] trained to discriminate the stimulus effect of schedule I hallucinogens DOM, LSD, or DMT, DOI . . . and DOC . . . fully substituted for each training drug." Gov't Ex. 7A at 7. DOI and DOC failed to substitute for methamphetamine, although DOC "partially substituted for the schedule I substance [MDMA], which elicits both hallucinogenic and stimulatory effects."[67] *Id.* In a study involving rodents "trained to discriminate stimulus effects of DOI from saline, the schedule I hallucinogens DOM, DOB, LSD, and DMT produced full substitution for DOI." *Id.* Based on these drug discrimination studies, HHS concluded "that these data indicate that DOI and DOC have stimulus properties that substantially overlap with those of the schedule I hallucinogens, DOM, DOB, LSD, and DMT." *Id.*

HHS noted that "clinical studies with DOI and DOC have not been conducted in healthy human volunteers . . . [and] there is no data available from standard studies that evaluate the psychoactive and physiological responses produced by these drugs in humans." Gov't Ex. 7A at 7-8. Accordingly, HHS and DEA relied on "anecdotal reports of hallucinogenic experiences with DOI and DOC." *Id.* at 8. HHS found that "[i]n these reports, DOI and DOC are reported to

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[65] The Eight Factor Analysis described drug discrimination studies as "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." Gov't Ex. 7A at 7. According to DEA, "drugs that have discriminative stimulus effects in common with a known drug of abuse are also likely to be abused," and generally "there is strong correspondence between the discriminative effects of drugs of abuse in animals in their effects in humans." *Id.* Therefore, DEA concluded that "drug discrimination is widely used to determine whether or not a drug or substance is pharmacologically similar to a known drug of abuse." *Id.*

[66] Preclinical drug discrimination models involve "a laboratory animal, often a rodent . . . trained to press two separate levers based on different stimulus effects of drug versus its vehicle such as saline (or the absence of a drug stimulus cue)." Gov't Ex. 7A at 7. Once "the animals reliably learn the discriminative stimulus effect of the trained drug . . . a test drug with unknown effect is administered." *Id.* Determining similarities between stimulus effects is based on the animals' lever selections, which "indicates whether the novel or test drug is or is not similar to the learned training drug-associated effect." *Id.* A novel drug producing greater than or equal to "80% drug-appropriate responding . . . is said to have full substitution for the trained drug." *Id.*

[67] Dr. Carbonaro testified that "[a] partial substitution is not a no effect, and that is still considered to have some abuse potential of partial substitution." Tr. 113.

induce hallucinogenic effects, including prominent visual effects." *Id.* DEA additionally noted that the World Health Organization ("WHO")[68] "critical review of DOC mentions its hallucinogenic effects reported by those that self-experimented with DOC and notes the duration of action may last 12 to 24 hours."[69] *Id.* Based on these various findings, DEA concluded that "DOI and DOC produce psychopharmacological effects . . . similar to those produced by other schedule I hallucinogens." *Id.*

Dr. Carbonaro testified that the factor related to the scientific evidence of a substance's pharmacological effects requires her to "evaluate the pharmacological effects of the substance" being reviewed. Tr. 106. In conducting this evaluation, Dr. Carbonaro testified that she "start[s] with some basic binding . . . to see where DOI and DOC bind to and have activity." Tr. 106-07. Dr. Carbonaro again "note[d] the Serotonin 2A receptor because it is . . . necessary but not sufficient to cause hallucinogenic effects." Tr. 107. Accordingly, Dr. Carbonaro "focused on the Serotonin 2A receptor activity" and determined that both DOI and DOC "bind in cell studies and does have agonist effects in cell studies." Tr. 107.

Dr. Carbonaro testified that the pharmacological effects of DOI and DOC are known "[t]o some degree." Tr. 106. Regarding DOI, Dr. Carbonaro testified that she is focused on K_i values, wherein "the smaller the number means . . . [the drug] has greater affinity for a receptor and again a lower concentration." Tr. 107-08. Dr. Carbonaro testified that "information about the affinities" allows researchers to "compare [a drug] back to the affinities of other

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[68] Dr. Carbonaro testified that she relied on information gathered by the World Health Organization in her report, as WHO "did a critical review specific to DOC." Tr. 117. Dr. Carbonaro testified that WHO "did not evaluate DOI." Tr. 117. However, Dr. Carbonaro acknowledged that WHO compared the effects of DOC with DOI, DOB, and DOM, which also "had long duration of action." Tr. 117.

[69] WHO noted that "the long duration of effects is shared by other structurally related hallucinogens including DOI, DOB, and DOM." Gov't Ex. 7A at 8. Dr. Carbonaro agreed that the effects of DOI "can be greater than 24 hours depending on the dose and route of administration." Tr. 115. Dr. Carbonaro further testified that there is "not an antagonist" for such effects, and "if someone was overdosing, you couldn't stop the effect with a Serotonin 2A antagonist because there's not one approved for that part." Tr. 115-16. Dr. Carbonaro explained that antagonists "essentially block a response" by binding to a receptor. Tr. 108. An antagonist taken alone "would have no activity," but "would block the activity of the agonist" if one is administered in competition with the antagonist. Tr. 108-09. "[T]alk down therapy" or benzodiazepine administration may "subdue somebody" during a bad experience with hallucinogens, but those are the only "common ways . . . to . . . stop a challenging experience." Tr. 116.

hallucinogens that have the same activity." Tr. 108. Dr. Carbonaro further testified that DOI may act as an "agonist," which is how researchers describe "that a drug has activity at a certain receptor" and "initiates a response." Tr. 108. Regarding DOC, Dr. Carbonaro testified that it also has "a high affinity for the Serotonin 2A receptors in different cell types" similar to other Schedule I hallucinogens. Tr. 109.

Dr. Carbonaro testified that "the central nervous system essentially is the brain and spinal cord," and for researchers to evaluate a drug for abuse potential, "it must have activity in the central nervous system." Tr. 109. Dr. Carbonaro acknowledged that evaluation of the central nervous system effects of DOI and DOC led to the conclusion that DOI and DOC are similar to the Schedule I controlled substance DOM. Tr. 109-10; Gov't Ex. 7A at 6.

In animal studies, Dr. Carbonaro testified that HHS noted that DOI generated overt responses, including "wet dog shakes[70] and back muscle contractions that seem to be induced by activating the Serotonin 2A receptor."[71] Tr. 110. Dr. Carbonaro indicated that observing rodents demonstrate wet dog shakes after receiving both DOM and DOI, researchers can determine that the two substances have "a similar mechanism of action." Tr. 111. Dr. Carbonaro testified that in drug discrimination studies involving DOM, LSD, and DMT as the training stimulus, "DOI fully substituted for those substances," while in another study in which DOI was the training stimulus, DOM, DOB, LSD, and DMT "produced full substitution for DOI showing there's cross substitution for these substances." Tr. 112-13.

Dr. Carbonaro concluded based on drug discrimination data and HHS's conclusions, "that DOI and DOC have stimulus properties that are substantially similar to DOM, DOB, LSD, and DMT." Tr. 114. In terms of the reliability of these drug discrimination studies, Dr. Carbonaro testified that it is "essentially the gold standard for assessing abuse liability in hallucinogenic substances," and thus DEA "put a lot of weight into drug discrimination for these hallucinogens." Tr. 114.

Dr. Carbonaro concluded that DOI and DOC are "potent Serotonin 2A receptor agonist[s]

[70] Dr. Carbonaro testified that "wet dog shakes" are "a behavior that can be seen in rodents when given a drug that binds at the 2A receptor" which appears similar to a dog shaking to remove water from a bath. Tr. 111.

[71] Dr. Carbonaro testified that HHS deduced the overt effects through an antagonist using MDL 100907, which was "administered in combination with DOI" to block the effect of DOI, suggesting that DOI is "specific to agonist activity at the 2A receptor." Tr. 111.

. . . known to produce very strong psychedelic effects that can vary from person to person and [have], based on . . . mechanism of action and similarity to other drugs that are hallucinogens in Schedule I . . . a similar pharmacological effect to those [Schedule I] drugs." Tr. 117-18.

Dr. Carbonaro testified that in her opinion, there was "adequate scientific evidence" of the pharmacological effects of DOI and DOC. Tr. 143. She further testified that based on the evidence of DOI and DOC's pharmacological effects, they can cause hallucinations and are similar to DOM, LSD, and DMT. Tr. 143-44.

21 U.S.C. § 811(c)(3); State of Current Scientific Knowledge Regarding the Substance

DEA's Eight Factor Analysis states that DOI and DOC "are centrally-acting hallucinogens and part of the phenethylamine hallucinogen family and share structural similarities with schedule I phenethylamine hallucinogens such as DOM." Gov't Ex. 7A at 8. DOI "has a molecular formula of $C_{11}H_{16}INO_2$ and a molecular weight of 321.16 g/mol" while DOC "has a molecular formula of $C_{11}H_{16}C1NO_2$ and a molecular weight of 229.70 g/mol." *Id.* The WHO additionally reports that DOC "is a white, odorless, and crystalline solid." *Id.* HHS determined that DOI and DOC "are not available in approved human drug products in the U.S. or in any other country and no data are available on their medical use in the treatment of any condition." *Id.* at 9.

Dr. Carbonaro testified that Factor 3 of the Eight Factor Analysis includes "other scientific information that is available at the time of drafting" the Analysis. Tr. 118. It is used "to discuss the chemistry of the drug and any medical use relating to that drug." Tr. 118. Dr. Carbonaro testified that the chemistry of DOI and DOC is known, as these substances "have a molecular formula that's been cited that people have synthesized." Tr. 118.

Dr. Carbonaro testified that in her expert opinion, DOI and DOC are similar to other Schedule I controlled substances based on the state of current scientific knowledge. Tr. 144. Dr. Carbonaro illustrated this comparison by drawing the molecular structure for DOM next to the molecular structures of DOI and DOC.[72] Tr. 119; *see* Gov't Ex. 7A at 9. Regarding the medical

[72] When asked to explain the differences in the molecular structure of DOI and DOM, Dr. Carbonaro testified that DOI has "an iodine" whereas DOM has "just another carbon with three hydrogens instead." Tr. 121-22. Dr. Carbonaro testified that "in theory, [DOI and DOM] can have different pharmacology based on a small substitution or modification to a structure." Tr. 123, 238-39. Dr. Carbonaro acknowledged that just because the molecular structure of two

use of DOI and DOC, Dr. Carbonaro concluded that based on HHS's scientific and medical evaluation, "there were no available approved medical drug products that included either DOI or DOC in the United States or in any country." Tr. 123. There is thus "no information on [DOI and DOC's] medical uses for treatment for any condition based on the lack of that data."[73] Tr. 123. As DOI and DOC are not "approved human drug products," Dr. Carbonaro testified that there is "nothing to suggest" that there is a medical use for DOI and DOC "for any condition." Tr. 144.

On cross-examination, Dr. Carbonaro testified that the form of a compound does not determine its pharmacological properties, but the route of administration could impact the pharmacological properties. Tr. 231. She further testified that the salt form of a compound could alter the solubility of the compound, and whether a substance is in salt or free base form is important in determining pharmacological properties.[74] Tr. 231-32. Dr. Carbonaro testified that "current" scientific knowledge "could be any information that's available about the substance." Tr. 235. In ensuring that she is up-to-date with current scientific knowledge, Dr. Carbonaro testified that she "routinely read papers that are published in scientific journals related to drugs of abuse." Tr. 236. Dr. Carbonaro testified that it was unlikely that any of the published studies related to the scheduling of DOI and DOC were based on research done in the last five years, and stated that she "relied on [HHS] for scientific and medical evaluation, [and] if they didn't feel inclined to put [the studies] in their[] [evaluation], [she] didn't take a step further to add" the study to DEA's evaluation. Tr. 236-37. Dr. Carbonaro testified that she is nevertheless aware of

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substances appear similar, the substances could have vastly different effects. Tr. 239.

[73] Dr. Carbonaro described "[i]nvestigational new drugs" ("IND") as "a process for someone to study a drug for clinical implications." Tr. 123-24. Dr. Carbonaro testified that researchers "need to have FDA submission" and approval based on "regulations in place for ethical and safety evaluations of a drug that's going through clinical trials." Tr. 124. Dr. Carbonaro testified that there are currently INDs for hallucinogens such as psilocybin, LSD, MDMA, and DMT, but there are no current hallucinogens "going for the approval process." Tr. 124. Dr. Carbonaro testified that to her knowledge, there are no INDs or new drug applications ("NDA") for DOI or DOC. Tr. 124-25.

[74] Dr. Carbonaro acknowledged a potential discrepancy in the background and analysis wherein the molecular weight of DOI was given based on its free base form and not on its salt-based form, which was provided in the CAS number for DOI. Tr. 234-35; *see* Gov't Ex. 7A at 8. Dr. Carbonaro testified that she deferred "to the chemists" on this portion of the background and analysis, but stated that this potential error was just related to "the chemical information" for DOI and had "nothing to do about the pharmacological activity of it." Tr. 234-35.

studies related to DOI and DOC conducted within the past five years, although these studies may not have been included in the background and analysis. Tr. 237. Dr. Carbonaro testified that she did not believe there was any conflict between the studies and research conducted within the past five years and HHS's ultimate findings related to DOI and DOC. Tr. 237.

21 U.S.C. § 811(c)(4); History and Current Pattern of Abuse

The Eight Factor Analysis provides that the history and current pattern of abuse of DOI and DOC are based on "law enforcement reports and anecdotal reports of DOI and DOC use by drug abusers." Gov't Ex. 7A at 9. The Analysis provides that "law enforcement entities initially encountered DOI and DOC in 2005" based on NFLIS-Drug data. *Id.* DOI and DOC were encountered in "various forms," including powder, tablets, capsules, liquid, and blotter paper. *Id.*

HHS and DEA further noted anecdotal reports "indicat[ing] that individuals are using substances they identified as DOI and DOC for their hallucinogenic effects" on sites such as Erowid. *Id.* The Analysis acknowledges that "it is impossible to know if the street drugs sold to an individual as DOI or DOC are actually the substances they are marketed as" due to the "absence of chemical analysis or evaluation of biological fluids following ingestion." *Id.* In addition to the anecdotal accounts, the Analysis additionally notes that "in animal drug discrimination studies . . . DOI and DOC produced effects that are similar to the effects elicited by schedule I hallucinogens such as DOM, LSD, and DMT." *Id.* at 9-10.

DEA's Analysis additionally notes that "based on available abuse data, public health risk, and drug trafficking data, the WHO recommended to the UN that DOC be controlled internationally" and "[i]n March 2020, the UN Commission on Narcotic Drugs voted to place DOC into schedule I of the 1971 Convention of Psychotropic Substances."[75] *Id.* at 10.

[75] The WHO "reports that DOC has been available in Europe since 2001," and the United Nations Office on Drugs and Crime ("UNODC") provided that "16 non-fatal intoxications had been reported internationally, between 2008 and 2017." Gov't Ex. 7A at 10. In addition to the UNODC data, the European Monitoring Centre for Drugs and Drug Addictions ("EMCDDA") "reported non-fatal intoxications and three deaths associated with DOC . . .." *Id.* DEA also noted reports of DOC drug seizures and collected specimens in Sweden, United Kingdom, France, Norway, Italy, Belgium, Ireland, Slovenia, Spain, Croatia, Denmark, Czech Republic, Luxembourg, and Latvia between 2006 and 2016 in the forms of blotters, powder, and liquid." *Id.*

Dr. Carbonaro testified that there is evidence of a history and pattern of abuse regarding DOI and DOC. Tr. 144-45. She further testified DOI and DOC produce effects similar to drugs such as DOM, LSD, and DMT, and that there is substantial evidence that DOM, LSD, and DMT have a history and pattern of abuse. Tr. 145.

On cross-examination, Dr. Carbonaro testified that the WHO report is based on combined data collected from the UN which "is available in their countries." Tr. 240. Dr. Carbonaro further testified that the report was "largely focused on DOC," although there may have been some discussion of DOI within the report. Tr. 240-41. Dr. Carbonaro acknowledged that the report considered data provided in the UN toxicology portal, and further acknowledged that there were 16 non-fatal intoxications[76] involving DOC between 2008 and 2017. Tr. 241; Gov't Ex. 7A at 10.

Dr. Carbonaro stated that the UN's input related to the scheduling of DOI and DOC is important to ensure that the U.S. meets "treaty obligations." Tr. 242. Although Dr. Carbonaro testified that the UN's scheduling does not "necessarily mirror [U.S.] schedules," DOC would still need to be placed in Schedule I because "it has no medical use." Tr. 243-44.

21 U.S.C. § 811(c)(5); Scope, Duration, and Significance of Abuse

Based on NFLIS-Drug data, DEA concluded that "there has been significant availability, trafficking, and abuse of a number of phenethylamine hallucinogens including DOI and DOC. Gov't Ex. 7A at 10. The summary of the NFLIS-Drug data indicates 40 encounters with DOI[77] and 790 encounters with DOC since 2005 in approximately 39 states.[78] *Id.* These encounters involved samples of DOI and DOC in tablet, capsule, powder, liquid, and blotter paper form. *Id.* DEA further reports "five submissions of DOI and two submissions of DOC reported in the

[76] Dr. Carbonaro testified that a non-fatal intoxication occurs when an individual receives emergency care related to an intoxication, but the intoxication "did not result in a death." Tr. 242. Dr. Carbonaro further testified that the reports could also involve an individual who tested positive for a substance outside of the emergency room setting. Tr. 242.

[77] Dr. Carbonaro acknowledged a discrepancy between Government Exhibits 7 and 7A, in which the reported encounters for DOI remained the same but an additional state was added to the total number of states where DOI was encountered. Tr. 213; *compare* Gov't Ex. 7 at 10 *with* Gov't Ex. 7A at 10. Dr. Carbonaro testified that it was "possible that . . . [she] left off Nevada" when she first generated the background and analysis in August of 2021. Tr. 213.

[78] *See* Gov't Ex. 8.

Microgram Bulletins[79] since 2006."[80] *Id.* at 10. DEA reported law enforcement encounters with DOI in various forms, including as fine white powder, liquid, and on blotter paper. *Id.* at 11. DOC was additionally found on two occasions on blotter paper. *Id.*

Dr. Carbonaro testified that determination of the scope, duration, and significance of abuse relies on "any law enforcement data" collected, as well as any "clinical trial information." Tr. 125. If clinical trial information is lacking, Dr. Carbonaro testified that DEA and HHS will "look at anecdotal evidence of [a substance's] use." Tr. 125. Part of the law enforcement data included NFLIS-Drug information, which Dr. Carbonaro reviewed in reaching her determination that "there is evidence that [DOI and DOC] were seized and encountered and put into the NFLIS-Drug database." Tr. 126. Dr. Carbonaro testified that this factor is different than "history and current pattern of abuse" because DEA "looked more for trends with" NFLIS-Drug. Tr. 129. Dr. Carbonaro explained that drug encounters "very from lab to lab," but typically involve "a law enforcement seizure that's been confirmed in analysis."[81] Tr. 130. Dr. Carbonaro confirmed that there are 40 reported encounters of DOI and 790 reports of DOC in various forms since 2005. Tr. 130.

Dr. Carbonaro testified that the form a drug is encountered in "gives a note of how [the drug] might be used or abused." Tr. 126. She noted that DOI and DOC have been encountered in forms such as powder, tablets, capsules, liquid, and blotter paper. Tr. 126-27. Dr. Carbonaro testified "most drugs that are approved by FDA don't come in a powder," and thus "powder can suggest that [the drugs] are intended for other use." Tr. 134. Dr. Carbonaro testified that "the FDA, to [her] knowledge, doesn't have a compound that's been approved to be administered as a powder form." Tr. 216. Accordingly, Dr. Carbonaro testified that "finding [a substance] in a

[79] *See* Gov't Exs. 11, 12, 13, 14, 15, 16.

[80] The Microgram Bulletin "is a monthly newsletter published by the DEA Office of Forensic Sciences on the detection and analyses of suspected controlled substances." Gov't Ex. 7A at 11. Dr. Carbonaro testified that the Microgram Bulletin "was something that the DEA Office of Forensic Sciences used to publish on a routine basis" which included information "related to drug seizures," although DEA no longer publishes the Bulletin. Tr. 132, 215. Dr. Carbonaro testified that these publications were subject to "an internal peer review process." Tr. 215. Dr. Carbonaro further testified that the Microgram Bulletins referencing DOI and DOC were provided to her prior to her conducting her analysis. Tr. 443-44.

[81] Dr. Carbonaro testified that the drug is found by law enforcement and subsequently tested by a local lab to confirm the identity of the substance. Tr. 130.

powder form shows evidence that it's likely to be an illicit substance."[82] Tr. 216-17. Dr. Carbonaro acknowledged that there are FDA-approved compounds that are presented in encapsulated powder-form, but testified that finding a powdery substance outside of a capsule "usually suggests that it was intended for illicit use."[83] Tr. 217-18.

Dr. Carbonaro testified that she found "one post on Reddit" indicating that an individual used DOI for medicinal purposes, but that was "the only case [she was] aware of where someone gave [DOI] for a clinical use." Tr. 127-28. Dr. Carbonaro affirmed that she saw other reports of individuals using DOI for its hallucinogenic effects. Tr. 128. Dr. Carbonaro further testified that where drug discrimination studies show that a drug has "similar drug discrimination" to other controlled substances, DEA can use such studies in determining the history and current pattern of abuse to "suggest that . . . those drugs are used for their hallucinogenic effects." Tr. 128. Dr. Carbonaro concluded from her review of the available data that DOI and DOC have "evidence of significance of abuse." Tr. 145.

Regarding HHS and DEA's conclusion that NFLIS-Drug demonstrates "significant availability, trafficking, and abuse of a number of phenethylamine hallucinogens including DOI and DOC,"[84] Dr. Carbonaro testified on cross-examination that the definition of significant "varies from drug-to-drug."[85] Tr. 203. Dr. Carbonaro indicated that the approximately 800 reported encounters with DOI and DOC is "pretty significant compared to some of the other drugs in NFLIS-Drug," and reiterated that these numbers may be underreported as the substances are not scheduled and may not be tested for.[86] Tr. 204.

Dr. Carbonaro acknowledged that there have been "no reports since 2019 for DOI," and

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[82] Dr. Carbonaro acknowledged that research drugs and chemicals delivered to labs are often provided in powder form, but testified that the drugs and chemicals are "in adequately labeled bottles and packaging with information about their chemical nature." Tr. 219.

[83] Dr. Carbonaro testified that she believed there were reported law enforcement encounters with DOI in capsule form. Tr. 218.

[84] Gov't Ex. 7A at 10.

[85] Dr. Carbonaro testified that "trafficking" is "[t]he moving of generally illicit substances cross country or over borders," and it is usually identified based on "law enforcement encounters." Tr. 361. While Dr. Carbonaro acknowledged that the term "trafficking" is typically reserved for illicit or controlled substances, she testified that such language is "often in [DEA's] Eight Factor Analysis for new drugs that are not controlled." Tr. 361-62.

[86] On redirect examination, Dr. Carbonaro reiterated that not all drug labs test for DOI and/or DOC or have the ability to test for these substances. Tr. 392.

further acknowledged that when limited to this timeframe, this would not appear to show significant abuse.[87] Tr. 205-06. However, Dr. Carbonaro testified that determining the scope, duration, and significance of abuse considers the "totality from when [a substance] was first encountered." Tr. 206. Dr. Carbonaro testified that she considers "any evidence" of abuse as "significant" evidence. Tr. 206.

Dr. Carbonaro testified that she did not believe it was possible for NFLIS-Drug to contain false positives for DOI and DOC as NFLIS-Drug reflects "confirmed positive[s] for each lab" which are "submitted for external review." Tr. 209-10. Dr. Carbonaro explained that there are different techniques used by each lab for testing, but the NFLIS-Drug reports "are law enforcement encounters [that] have to be confirmed positive for that drug." Tr. 210-11. Dr. Carbonaro testified that the context in which substances are encountered and seized by law enforcement is not always available through NFLIS-Drug, although NFLIS may sometimes provide details about a particular encounter or what other drugs were discovered during the encounter. Tr. 219-21. Dr. Carbonaro testified that the context of the encounter with the drugs and the reason the drugs were ultimately seized depend "on the seizure and the case." Tr. 223.

Regarding the form in which controlled substances are found, Dr. Carbonaro testified that reports of DOI and/or DOC found on blotter paper tabs or in "little baggies" as powders creates an inference that the substance "would be intended for human consumption" and "would be abused." Tr. 339-40. Dr. Carbonaro further acknowledged that if drugs are encountered in an amount greater than the amount needed for one-time personal use, one could make the inference that the drug is intended for distribution. Tr. 402.

21 U.S.C. § 811(c)(6); Risk to the Public Health

According to HHS, "the public health risks resulting from the abuse of DOI and DOC . . . relate primarily to their ability to induce hallucinogenic effects and other sensory distortions, impaired judgment, and strange or dangerous behavior."[88] Gov't Ex. 7A at 11. There have been

[87] Dr. Carbonaro testified that she knows that "during COVID there was a significant reduction in NFLIS reports." Tr. 213. However, she acknowledged that there were no reports of encounters with DOI in 2016 or 2019, and only one reported encounter with DOI in both 2017 and 2018. Tr. 214.

[88] Dr. Carbonaro testified that these conditions would be considered adverse health effects. Tr. 134-35.

"three published reports in . . . 2008, 2014, and 2015 of adverse events associated with DOC" and "no reports of distressing responses or death associated with DOI in medical literature." *Id.* Two of the three adverse event reports involved apparent use of DOC with other drugs, including MDMA, cannabinoids, and opioids. *Id.* The third reported adverse event involved death of an individual whose toxicological analysis was positive for DOC and caffeine. *Id.* HHS concluded that these reports "demonstrate that adverse events and death can occur from the use of DOC," and determined that "since DOI is structurally similar to DOC and produces similar effects to DOC, it is likely that it may produce serious adverse effects similar to DOC." *Id.* at 11-12.

Dr. Carbonaro testified that DEA determined the risk to public health of DOI and DOC by comparing them "to effects that are published in case reports if they exist." Tr. 134. Where case reports are lacking, Dr. Carbonaro testified that DEA considered the "pharmacological similarity [of DOI and DOC] to other Schedule I substances." Tr. 134. Dr. Carbonaro indicated that the pharmacological similarity may indicate whether the risk to public health "would be similar in fashion to those drugs" in Schedule I. Tr. 134.

Dr. Carbonaro testified that there were "three published cases of adverse effects" associated with DOC. Tr. 135. One of these occurrences involved "a 20-year-old man who attended a rave party who was taken to the emergency department" and was unresponsive.[89] Tr. 135. After approximately 22 hours, Dr. Carbonaro testified that the man was released, and his toxicology report tested positive for MDMA and DOC. Tr. 135. A second occurrence involved a 37-year-old man "found dead in his home," who tested positive for DOC and caffeine. Tr. 136. The final occurrence involved an 18-year-old man experiencing hallucinations, agitations, seizures, shaking, dilated pupils, tachycardia, hypertension, and rhabdomyolysis. Tr. 137. Dr. Carbonaro testified that this individual tested positive for DOC in addition to cannabinoids and opioids. Tr. 137.

Dr. Carbonaro testified that "because DOC had reports and [DOI] is similar in structure to DOC[90] and other hallucinogens . . . [DOI] would also likely produce serious adverse

[89] Dr. Carbonaro testified that the individual was experiencing sinus tachycardia, hypertension, dilated pupils, non-responsiveness to light, and rhabdomyolysis, which is "muscles being broken down and then entering the blood stream" that can cause "kidney failure or kidney toxicity." Tr. 135-36.

[90] Regarding DOC, Dr. Carbonaro testified that "there is risk to public health based on the reports." Tr. 146.

effects."[91] Tr. 146.

On cross-examination, Dr. Carbonaro reiterated that the reported death associated with DOC involved "DOC plus caffeine." Tr. 175. Dr. Carbonaro acknowledged that caffeine has "stimulant effects," and further acknowledged that the deceased individual's body was "partially decomposed" prior to testing for substances. Tr. 175-76. Dr. Carbonaro testified that based on the decomposition, it was possible that the deceased individual consumed other controlled substances, but stated that she knew that the toxicologists "tested for a whole number of drugs." Tr. 176. Regarding the other two reported cases, Dr. Carbonaro acknowledged that in each of these encounters the individuals tested positive for other substances in addition to DOI and/or DOC. Tr. 177. Dr. Carbonaro indicated that the adverse health effects suffered by those individuals could thus "[n]ot necessarily" be attributed strictly to DOI and/or DOC. Tr. 177. Dr. Carbonaro testified that symptoms such as a fast-beating heart and breathing issues could be attributed to MDMA, but may also be attributed to DOC and "other hallucinogens that work in the 2A receptor." Tr. 177.

21 U.S.C. § 811(c)(7); Psychic or Physiological Dependence Liability

DEA and HHS found that "the physiological dependence liability of DOI and DOC in animals and humans is not reported in scientific and medical literature." Gov't Ex. 7A at 12. Accordingly, the Eight Factor Analysis concluded that "it is not possible to determine whether DOI and DOC produce physiological dependence following acute or chronic administration." *Id.* However, HHS determined that "DOI and DOC and other related phenethylamine hallucinogens . . . are highly abusable substances," and drug discrimination studies revealed "that DOI and DOC fully substitute to the discriminative stimulus effects of schedule I hallucinogens DOM, LSD, and DMT." *Id.* While HHS noted that hallucinogens "are not usually associated with physical dependence" due to the "rapid development of tolerance," hallucinogen abusers "may develop psychological dependence as evidenced by the continued use of these substances despite knowledge of their potential toxic and adverse effects." *Id.*

Dr. Carbonaro testified that dependence liability is the "willingness for someone to repeatedly take a drug even though they have or they know there are harms." Tr. 139.

[91] Dr. Carbonaro acknowledged that she was unaware of any cases involving DOI that resulted in seizures, loss of consciousness, rhabdomyolysis, or death. Tr. 326-27.

Physiological dependence relates to "withdrawal associated if someone becomes dependent" upon a drug. Tr. 139, 266. Dr. Carbonaro testified that there are "markers of withdrawal that may happen with physiological dependence," as "the body needs [the drug] to continue functioning." Tr. 139. Dr. Carbonaro differentiated physiological dependence from "psychic dependence or . . . psychological dependence" which occurs when an individual "repeatedly" uses a substance while "knowing that there are harms." Tr. 139-40, 269. Dr. Carbonaro testified that "for most hallucinogens that work through the Serotonin 2A receptor, physiological dependence is not really a thing that happens" although "there is evidence of psychic dependence." Tr. 140, 268.

Dr. Carbonaro clarified that "because most people only take [hallucinogens that work through the Serotonin 2A receptor] once . . . there is generally no withdrawal."[92] Tr. 140. However, Dr. Carbonaro testified that there "is evidence based on people willingly taking" DOI and DOC despite "knowing that there are dangers that could happen to themselves or others." Tr. 140-41. Dr. Carbonaro further testified that because DOI and DOC "are similar in pharmacological activity to DOM, LSD, and DMT which have very well-known psychic dependence," DOI and DOC "would also have psychic dependence related to those substances." Tr. 141. Dr. Carbonaro testified that there is "evidence of psychic dependence liability" for DOI and DOC, and these substances have a high potential for abuse. Tr. 146.

On cross-examination, Dr. Carbonaro testified that effects such as euphoria "meet the criteria for psychic dependence."[93] Tr. 269. Dr. Carbonaro acknowledged that certain anecdotal

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[92] Dr. Carbonaro testified that hallucinogens "are not usually associated with physical dependence . . . likely due to their rapid development of tolerance." Tr. 141-42.

[93] Dr. Carbonaro testified that any use of DOI or DOC may constitute abuse if it appears that individuals are "using it intentionally for hallucinogenic effects" without guidance from a medical practitioner. Tr. 273-74. Dr. Carbonaro testified that hallucinogenic effects are considered "an adverse effect" by HHS. Tr. 274. Dr. Carbonaro acknowledged that "[t]here are some people that believe that a hallucinogenic effect is important in . . . therapeutic contexts," but that this is "still under investigation" and stated that "there are harms that also occur in these clinical trials" involving psilocybin. Tr. 275. Dr. Carbonaro testified that guardrails must be in place for clinical research for hallucinogenic substances, including "set and setting," "known dose formulation," and "route of administration" criteria. Tr. 275-76, 400. Dr. Carbonaro testified that there are accounts of individuals "still having a challenging experience in . . . controlled settings." Tr. 321. Dr. Carbonaro stated that she believes that "in laboratory studies, with these specific, carefully screened individuals where their cardiovascular system has been assessed, their mental health has been assessed, [and] there are a lot of parameters that go into

reports indicate that users do not seek to take DOI or DOC again after their first use, but also testified that other reports involve individuals who state that they "will seek out a long-acting phenethylamine hallucinogen." Tr. 269-70. Dr. Carbonaro further testified that "because there are reports of people seeking out long-acting phenethylamines such as DOM and other drugs that have long-acting effects," DOI and DOC may still be found to have psychic dependence even with evidence that most people did not wish to take the drugs again. Tr. 271. Dr. Carbonaro testified that the determination for psychic dependence is based on the "data in its totality," in addition to "drug discrimination data showing that" DOI and DOC are "similar to other drugs, and they have known psychic dependence." Tr. 271-72.

21 U.S.C. § 811(c)(8); Immediate Precursors

The Eight Factor Analysis states that "DOI and DOC are not immediate precursors of a substance already controlled under the CSA as defined by 21 U.S.C. § 802(23)." Gov't Ex. 7A at 12.

Dr. Carbonaro testified that an immediate precursor exists where a "drug could be used to make a substance" through a single chemical reaction. Tr. 142. Dr. Carbonaro reiterated that this final factor does not apply to DOI and DOC as neither fit into the profile of an immediate precursor. Tr. 142.

21 U.S.C. § 812(b)(1)(A); High Potential for Abuse

In DEA's findings for schedule placement, DEA concluded that DOI and DOC have a high potential for abuse, as "HHS mentions that DOI and DOC are phenethylamine hallucinogens with high potential of abuse that produces pharmacological effects qualitatively similar to those of DOM, a schedule I hallucinogen." Gov't Ex. 7A at 12. HHS further determined that DOI and DOC "fully generalize to the discriminative effects produced by DOM," and found that "[i]n humans, DOI and DOC produce classic hallucinogenic effects such as hallucinations, similar to the effects in humans elicited by DOM." *Id.* at 12-13. DEA additionally noted law enforcement encounters with DOI and DOC since 2005 as evidence of

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it," risks of danger pertaining to hallucinogenic substances may be lower. Tr. 319-22. Dr. Carbonaro additionally testified that clinical trials with DOI and DOC may have an added risk due to the "longer duration of action," which may require additional guardrails. Tr. 399, 401.

abuse potential. *Id.* at 13.

Dr. Carbonaro agreed that both DOI and DOC have a high potential for abuse based on her "evaluation and also HHS's mention that [DOI and DOC] have high potential for abuse because they're similar to those of DOM, a Schedule I hallucinogen." Tr. 147. On redirect, Dr. Carbonaro testified that the determination for whether a drug has potential for abuse does not require the drug to cause seizures, loss of consciousness, rhabdomyolysis, or death. Tr. 401-02.

21 U.S.C. § 812(b)(1)(B); Currently Accepted Medical Use in Treatment in the United States

The FDA "has not approved a marketing application for a drug product containing DOI or DOC for any therapeutic indication." Gov't Ex. 7A at 13. Furthermore, DEA and HHS identified "no clinical studies or petitioners . . . that claim an accepted medical use in the U.S." *Id.*

Dr. Carbonaro testified that there are two ways to evaluate currently accepted medical use: (1) "find out if FDA has an approved marketing application for a drug containing DOI or DOC," and (2) if FDA has not approved a marketing application, DEA "does a five part test to analyze a . . . currently accepted medical use." Tr. 147.

Dr. Carbonaro testified that part one of the DEA's five-part test concerns whether a drug's chemistry is known and reproducible. Tr. 147. She testified that this "means that there has to be significant information related to the chemistry that is available and can be reproduced in a certain way." Tr. 147-48. Dr. Carbonaro confirmed that the chemistry of DOI and DOC is known and reproducible. Tr. 148.

The second part of DEA's currently accepted medical use test concerns whether any adequate safety studies have been conducted. Tr. 148. Dr. Carbonaro testified that no adequate safety studies have been done for DOI and DOC, as "[t]here have been no clinical trials related to DOI or DOC that have been published." Tr. 148.

The third part of DEA's test asks whether there is any evidence that adequate and well-controlled studies proved efficacy regarding DOI or DOC. Tr. 148. Dr. Carbonaro testified that there is no evidence of efficacy regarding DOI or DOC, as "there have been no clinical trials." Tr. 148.

The fourth part of the test considers whether the substances have been accepted by any qualified experts. Tr. 149. Again, Dr. Carbonaro testified that "[w]ithout any clinical trials," she

was unsure how any experts could accept DOI or DOC. Tr. 149.

The final part of DEA's test to determine a currently accepted medical use relates to scientific evidence that the efficacy of the substance is widely available. Tr. 149. Dr. Carbonaro testified that this factor focuses on whether "there are publications available through . . . research studies, through databases that . . . can be searchable online." Tr. 149. She testified that the scientific evidence is "generally related to clinical trials." Tr. 149. As Dr. Carbonaro is "not aware of any clinical trial[s]" related to DOI and DOC, she did not see how it was possible for scientific evidence of its efficacy to be widely available. Tr. 149.

21 U.S.C. § 812(b)(1)(C); Lack of Accepted Safety for Use of the Drug or Other Substance Under Medical Supervision

HHS concluded that "use of DOC is associated with serious adverse consequences including deaths," and "[s]ince DOI is structurally similar to DOC and produces effects similar to DOC, it is likely that DOI may produce serious adverse events similar to DOC." Gov't Ex. 7A at 13. Given the lack of currently accepted medical use and thorough investigation, HHS was unable to determine the safety use under medical supervision for DOI and DOC. *Id.* Accordingly, HHS and DEA concluded that "there is a lack of accepted safety use of [DOI and DOC] under medical supervision." *Id.*

Dr. Carbonaro agreed with HHS that "the use of DOC is associated with serious adverse consequences including deaths," and "since DOI is structured similar to DOC, it produces effects similar to DOC." Tr. 150. Accordingly, Dr. Carbonaro agreed that "[i]t is likely that DOI may produce serious adverse effects as well." Tr. 150. "[B]ecause . . . there is no currently accepted medical use and [DOI and DOC have] not been thoroughly investigated as new drugs," Dr. Carbonaro testified that "their safety for use under medical supervision is not determined." Tr. 150.

Dr. Carbonaro further testified that she was unaware of any evidence that healthcare providers in the U.S. have widespread experience with the medical use of DOI and DOC, and did not find any evidence that the use of DOI or DOC is recognized by medical regulators. Tr. 150.

Research Harm

Dr. Carbonaro acknowledged that DOI and DOC "are investigated in research, usually basic research," and that DOI is typically utilized in research more than DOC. Tr. 151. Dr.

Carbonaro testified that data obtained through this research "is important to DEA" but that "generally for these eight factors, [DEA] . . . [relies] on the abuse potential data that is available." Tr. 151. Dr. Carbonaro also acknowledged that certain Schedule I controlled substances, including LSD and MDMA, are currently being researched, and thus concluded that she did not believe placing DOI and DOC into Schedule I would eliminate research. Tr. 151-52. She explained that she is "familiar with the Schedule I researcher process, how those applications come in through DEA, how [DEA] review[s] them, [and] how [DEA] work[s] with HHS."[94] Tr. 152. Dr. Carbonaro testified that she has worked "with Schedule I substances in essentially every step of [her] career before joining government," and thus understands from "a researcher standpoint . . . that research can still be done under the Schedule I researcher program."[95] Tr. 152-53.

On cross-examination, Dr. Carbonaro explained the registration process for researchers, stating that researchers must "submit[] to DEA . . . a bona fide research study," which would include "things like name, address, a protocol, the amount of drug, where the drug is coming from, institutional approval, a CV and papers" in addition to abiding by "state and other regulations." Tr. 245-46. Dr. Carbonaro testified that there is a registration fee of "less than $300" to obtain a Schedule I researcher registration, but the "actual registration fee is often waived." Tr. 246. Dr. Carbonaro further testified that "[t]here are safe requirements" for storage of Schedule I controlled substances that are not applicable for unscheduled substances. Tr. 246-47. Dr. Carbonaro testified that the time to obtain a Schedule I research registration "varies from protocol to protocol," but DEA on average is "under three months . . . to approve a Schedule I researcher registration." Tr. 247. Dr. Carbonaro acknowledged that the timeline can be extended if the submitted protocol in incomplete and requires "back and forth with the investigator to get a complete protocol package."[96] Tr. 247-48.

In addition to the DEA requirements, Dr. Carbonaro acknowledged that researchers will usually require institutional and state level approval and licensure. Tr. 248. Dr. Carbonaro

[94] Dr. Carbonaro testified that she is experienced with handling "the Schedule I researcher program" during her employment with DEA. Tr. 152.
[95] Dr. Carbonaro testified that "many of the studies that were included as evidence [in DEA's analysis] are done in labs that have Schedule I researcher registrations." Tr. 153.
[96] Dr. Carbonaro testified that "most [applications] come in incomplete" to DEA, which extends the approval timeline. Tr. 250-51.

testified that these institutional and state processes would be in excess of the three-month DEA process, but stated that "any protocol" would need to go through the state and institutional procedures to receive approval.[97] Tr. 248-49. Although Dr. Carbonaro previously worked at labs with Schedule I research registrations, she acknowledged that she has never personally needed to apply for one. Tr. 250.

For researchers actively conducting research on a substance that then becomes controlled, Dr. Carbonaro testified that "there will be an effective date that's published . . . so research could continue until that effective date, and if it has not been added to their Schedule I researcher registration or if they don't have one specific to that substance, then it may need to be halted while they're undergoing that process." Tr. 253. Dr. Carbonaro further testified that she believes there "is some discretion" if a researcher is actively researching a newly-scheduled substance while seeking a Schedule I researcher registration, although "[t]hat would be up to the field's discretion." Tr. 254.

Once a controlled substance is scheduled, Dr. Carbonaro testified that the substance "must be purchased from someone that has a DEA registration . . . [o]r they can be synthesized in-house under a Schedule I researcher registration, or can be transferred from one registrant to another." Tr. 254-55. Dr. Carbonaro further acknowledged that DEA may impose quotas for how much of a controlled substance can be produced for research purposes. Tr. 255. Dr. Carbonaro testified that the price for a newly-scheduled controlled substance will not necessarily increase after scheduling, and indicated that certain currently-scheduled substances may actually be cheaper than DOI. Tr. 256.

Dr. Carbonaro acknowledged that there are currently "a lot of studies . . . using DOI as a reference drug compared to other psychedelics, looking at molecular or mechanisms of action . . . comparing them to DOI or just other drugs in general, using that since [DOI] is a known 2A agonist with psychedelic properties." Tr. 257-58. Dr. Carbonaro testified that all of these studies are in preclinical phases.[98] Tr. 258. Dr. Carbonaro testified that she was aware that these

[97] Dr. Carbonaro testified that state and institutional approval would be needed for "any kind of animal or clinical study." Tr. 249.

[98] Dr. Carbonaro testified that prior to clinical research conducted with humans, the drug development process involves "cellular *in vitro*" studies, followed by studies into "different live body systems" and other animals to establish "some level of understanding relating [to] its potential safety." Tr. 259. Dr. Carbonaro testified that "a lot of drugs fail during the preclinical

studies focused on multiple areas of research, including substance abuse disorder treatment, anxiety treatment, anti-inflammatory treatment, and the properties of pain. Tr. 262-63. Dr. Carbonaro testified that she believed that "[m]ost" of the laboratories conducting these studies possessed Schedule I researcher registrations, but could not state definitively that all labs were registered. Tr. 263-64.

Dr. Carbonaro's testimony was primarily focused on the introduction of the Government's documentary evidence and her involvement with the potential scheduling of DOI and DOC, including her review and analysis of the materials entered into evidence through her testimony. Her testimony was internally consistent and logically persuasive. Overall, she presented an objective analysis.[99] There was no indication she harbors any animosity towards the Petitioners or that she has any personal stake in these scheduling proceedings. I therefore find her testimony to be credible and reliable and I will give it significant weight.

SCIENCE POLICY COUNCIL, STUDENTS FOR SENSIBLE DRUG POLICY AND DR. RAUL A RAMOS' CASE

SSDP/Ramos presented their case-in-chief through the testimony of nine witnesses: (1) Dr. Alaina M. Jaster; (2) Dr. Raul A. Ramos; (3) Dr. Harrison Elder; (4) Dr. Lindsay P. Cameron; (5) Mr. Joseph Hennessey; (6) Dr. Jason Younkin; (7) Dr. David Nichols; (8) Dr. Joseph Palamar; and (9) Dr. Mario de la Fuente Revenga.

Dr. Alaina M. Jaster[100]

Background

SSDP/Ramos called Dr. Alaina M. Jaster as an expert witness in neuroscience and substance use disorders, and, in the absence of any objection by the Government, the tribunal accepted Dr. Jaster as an expert in the stated subject matter.[101] Tr. 471-72, 474. Dr. Jaster has a

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phase and never make it to humans." Tr. 260. Dr. Carbonaro acknowledged that preclinical studies could ultimately have value to human clinical research. Tr. 260-61.

[99] I will however, discount Dr. Carbonaro's testimony regarding the Reddit posts she viewed. *See* Gov't Ex. 10. I find these anonymous posts on social media to be unreliable hearsay.

[100] SSDP/Ramos Exhibits 17, 18, 37, 77, and Government Exhibit 17 were offered and admitted through Dr. Jaster.

[101] Dr. Jaster previously served as an expert witness for "a Virginia Subcommittee House

B.S. in Neuroscience and a doctoral degree in Pharmacology and Toxicology from Virginia Commonwealth University ("VCU"). Tr. 465; SSDP/Ramos Ex. 77 at 1. She has published approximately 13 peer-reviewed journal articles, of which seven publications are related to her research on DOI.[102] Tr. 468-69; SSDP/Ramos Ex. 77 at 3. Dr. Jaster testified that she engaged in undergraduate courses related to substance use, and also worked on a variety of projects during her doctorate program where she "received training in a variety of models, substance use not related to [her] [Ph.D.]," including "self-administration and drug discrimination" models. Tr. 469-70. Dr. Jaster has also "worked on various projects looking at minor alterations in chemistry and how that affects behavioral pharmacology outcomes with psychedelic compounds." Tr. 470.

Dr. Jaster currently works as "a post-doctoral research fellow at Wayne State University." Tr. 470; SSDP/Ramos Ex. 77 at 6. Dr. Jaster's research at Wayne State relates to "looking at pharmacology related to endocannabinoids and adolescents, and also identifying patterns of use in risk perceptions of psychedelics among adolescents."[103] Tr. 470-71.

Dr. Jaster's Research of DOI

Dr. Jaster's dissertation[104] research[105] for her doctorate program was focused on an assessment of "DOI and psilocybin in rodent models of substance use disorders, specifically opioid use." Tr. 466-67. Dr. Jaster testified that this research found that "DOI and psilocybin were able to effectively reduce oxycodone place preference in a model called conditioned place preference."[106] Tr. 467. Dr. Jaster testified that her dissertation work "shows [a] change in

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hearing," where she was invited to discuss "the potential therapeutic effects of psychedelics . . . [s]pecifically . . . psilocybin." Tr. 471; SSDP/Ramos Ex. 77 at 6.

[102] Dr. Jaster testified that she also has two other papers "currently in preparation." Tr. 469. She testified that "in preparation" means that the manuscript is being prepared prior to submission to a peer review process. Tr. 469.

[103] Dr. Jaster testified that these projects concern brain health and substance use among youth in Detroit, Michigan. Tr. 471. Dr. Jaster acknowledged that her current research does not involve DOI, although she plans to include DOI in the future. Tr. 473.

[104] *See* SSDP/Ramos Ex. 17. Dr. Jaster testified that only a figure from her dissertation is included in SSDP/Ramos' Exhibit 17, not the entirety of the dissertation. Tr. 472-73. Dr. Jaster testified that her dissertation is "currently in preparation to be published" and thus the full document is "under embargo," but she is able to show certain figures from her research. Tr. 499.

[105] Dr. Jaster has performed neuroscience research across many areas, including cells and tissues, live animal systems, and clinical trials involving humans. Tr. 467-68.

[106] Dr. Jaster testified that this reduction in oxycodone place preference was "attributed to

preference of oxycodone before and after administration of DOI in both male and female rodents."[107] Tr. 497. She testified specifically that her study showed "a statistically significant reduction in [rodent] preference score 24 hours after DOI was given." Tr. 501. Dr. Jaster further testified that the study "suggest[s] that animals who do not receive the DOI intervention did not have a reduction in their drug-seeking behavior." Tr. 504.

Dr. Jaster concluded that these results allow researchers to infer "that both DOI and psilocybin could be potentially useful for developing novel therapeutics for opioid use disorder." Tr. 467. She also explained that "increased drug craving is typically a hallmark of substance abuse disorders," and thus her research is "relevant, because DOI could be used to reduce drug craving and thus reduce returning to an environment where [one] previously used the drug." Tr. 509.

Dr. Jaster testified that activation of the serotonin 2A and 2C receptors, which are the main targets of DOI, "actually produce signaling that is adaptive for behavior instead of maladaptive" depending on the dose and specific area of administration. Tr. 496. Dr. Jaster testified that "instead of producing . . . drug craving effects," activation of these receptors actually produces the opposite effect. Tr. 496-97. Dr. Jaster stated that this finding is "a great first step to developing a potential target and mechanism for developing novel medications for drug craving and substance use disorders." Tr. 497.

21 U.S.C. § 811(c)(1); Actual or Relative Potential for Abuse

Abuse Potential: Drug Discrimination Studies

Dr. Jaster testified that although she was trained to conduct drug discrimination assays, she did not use that particular assay in her dissertation research. Tr. 474-75. Dr. Jaster

involvement of the serotonin 2A receptor." Tr. 467. She stated that her research found that "DOI activation of . . . serotonin 2A receptors in the cortex are influencing behavior that causes the animals to have this decrease in their preference." Tr. 505.

[107] Dr. Jaster testified that her dissertation utilized conditioned place preference, which is "another measure of abuse liability . . . to look at context involvement in drug use." Tr. 500. Dr. Jaster testified that this study involves administration of oxycodone to a rodent on "one side of a chamber," and after a period of time the animal is "trained to go to the side [of the chamber] where they received oxycodone." Tr. 500. On test day, the rodents "are in a drug-free state and placed back in a neutral part of the chamber and allowed to explore," and they "choose to go to the side [of the chamber] where they received oxycodone pretty reliably." Tr. 501.

distinguished the "subjective effects" of drugs with the "physiological effects," and testified that in drug discrimination studies, "even though [a] rodent may be having some physiological effect, it cannot be deemed as a subject effect, similar to what humans may experience following drugs."[108] Tr. 480-82.

Dr. Jaster testified that self-administration studies are "a useful screen for abuse liability," but they are "on a steady decline and . . . other methods are now more widely used, or used in conjunction with drug discrimination measures to determine abuse liability." Tr. 482-83. Dr. Jaster reiterated that one of these other methods to be potentially used in conjunction with drug discrimination is self-administration studies, which allows research subjects to "choose to administer a drug at different rates, at different concentrations." Tr. 484. Dr. Jaster also discussed "intracranial self-stimulation" ("ICSS")[109] studies which involve "an animal . . . hooked up to a probe in their brain that essentially stimulates the reward center of the brain," allowing self-selection "for stimulation of that brain center."[110] Tr. 484.

Dr. Jaster testified that, based on her training in pharmacology and toxicology, "the drug discrimination model alone is not sufficient to determine abuse liability and . . . it needs to be used in conjunction with something more robust such as food versus drug choice, or intracranial self-stimulation, but cannot be relied upon by itself." Tr. 510. In response to a question regarding what she would describe as the "gold standard" for assessing abuse liability, Dr. Jaster stated that "a combination of drug discrimination to understand pharmacological effects, but also potentially self-administration with a drug versus food choice or a drug versus any other reward choice . . . to determine whether or not the animal would self-select if given another option like we do see in humans." Tr. 510-11. Dr. Jaster testified that, in her opinion, drug discrimination studies are not "solely enough on [their] own to determine abuse liability and should be used in

[108] *See* SSDP/Ramos Ex. 37 at 3.

[109] Dr. Jaster explained that ICSS studies are "essentially a way to look at the reward circuitry in the brain, so basically what brain regions are involved in producing the drug craving or the self-selection." Tr. 495. She testified that this is "measured in rodents by inserting a cannula into the brain that provides stimulation to that specific brain region and those neurons which is . . . a natural way without a drug to . . . stimulate that part of the brain." Tr. 495. When the rodents are given drugs, researchers can determine whether the drugs potentially "stimulate that part of the brain." Tr. 495.

[110] Dr. Jaster also identified food versus drug choice studies as another method to assess abuse liability. Tr. 509.

conjunction with other assays to assess abuse liability." Tr. 493.

On cross-examination, Dr. Jaster agreed that drug discrimination studies provide an excellent alternative for classifying hallucinogens on the basis of hallucinogenic activity mediated by the 5-HT2A receptors, and agreed that drug discrimination is a valuable resource for assessing the *in vivo* pharmacology of drugs with unique physiochemical properties. Tr. 513-14. Dr. Jaster further acknowledged that on its own, conditioned place preference may not be favorable in assessing abuse liability.[111] Tr. 516. Dr. Jaster acknowledged that the intracranial stimulation self-stimulation effects of DOI are similar to other psychedelics, including LSD. Tr. 521. However, Dr. Jaster testified that she did not believe LSD, psilocybin, and DOM have high abuse liability, and rather have "very minimal" abuse liability. Tr. 521-22. Dr. Jaster did acknowledge that there are behavioral disruptive effects from psychedelic drugs, and that these effects may limit their future success in clinical trials.[112] Tr. 523.

On redirect examination, Dr. Jaster testified that while drug discrimination studies are useful for determining mechanisms of action, "mechanism of action just refers to the way that the drug targets in the brain and how it produces its effects in the brain." Tr. 526. Dr. Jaster explained that testing for mechanism of action is not the same as testing for abuse liability potential, as abuse liability potential focuses "specifically at behaviors related to substance use . . . as well as looking at the specific . . . rewarding effects in the brain and the circuitry that's specific to reward, which includes . . . dopamine-related function." Tr. 527. Dr. Jaster reiterated that only using drug discrimination provides an incomplete picture of abuse liability, because it only assesses "the specific pharmacological effect of a single class of drugs or comparing it to a class of drugs that is known to not be similar, so just characterizing the mechanism of action of those drugs to substitute for a drug with a similar mechanism of action." Tr. 527-28. Dr. Jaster testified that in the broader scientific community, the direction of study is focusing on "not just one study of mechanism of action, but looking at the broader neurobiology of substance use in a variety of models." Tr. 531.

On re-cross, Dr. Jaster explained that "[t]here are mechanisms of action . . . that have to

[111] Dr. Jaster also did not dispute a statement that condition place preference studies are not considered to be as sensitive or reliable as self-administration studies. Tr. 517.
[112] Dr. Jaster testified that behavioral disruptive effects cannot be inferred as good or bad, as additional context is needed. Tr. 535. Dr. Jaster acknowledged that the four hours of head twitches recorded in rodents receiving DOI amounted to behavioral disruption. Tr. 548.

do with abuse liability, but [she] wouldn't say that" mechanism of action and abuse liability are "the same." Tr. 552-53. She testified that measuring mechanism of action may also measure abuse liability, but it would "depend[] on the mechanism." Tr. 553.

21 U.S.C. § 811(c)(2); Scientific Evidence of Pharmacological Effect

Dr. Jaster testified that head-twitch response is "something that occurs when you give a rodent a psychedelic." Tr. 487. She testified that it has "been formally tested across many labs, and is considered a very good standard of a read out of psychedelic effects."[113] Tr. 487. Upon administration of a 2A receptor agonist, Dr. Jaster testified that "the animals will have an increase in this head-twitch that can be quantified," and varying dosage responses "can be measured and compared across different psychedelics, [and] different doses."[114] Tr. 487-88. Dr. Jaster testified regarding a specific study[115] in which "administration with DOI increases . . . acute head-twitch, which is most notably associated with hallucination effects, or . . . hallucination-like effects in rodents." Tr. 488. However, Dr. Jaster further testified that this study indicated that "when DOI is administered[,] the self-stimulation that happens without any drug . . . actually decreases," which suggests that "DOI does not produce the same reward-based effects in the brain." Tr. 488-89. While certain substances like cocaine, amphetamines, and opioids may "increase self-stimulation very reliably and robustly," Dr. Jaster explained that "DOI actually does the opposite." Tr. 489. Accordingly, Dr. Jaster concluded that this research indicates that DOI "does not produce the same type of abuse liability measured by this assay."[116]

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[113] Dr. Jaster testified that DOI typically results in head-twitches for approximately four hours, while "psilocybin only lasts . . . an hour," which is "consistent with how psilocybin's shorter acting in humans, but DOI is longer." Tr. 503.

[114] Dr. Jaster testified that head twitch response is also used to determine how long the effects of a psychedelic last. Tr. 502.

[115] SSDP/Ramos Ex. 18 at 18.

[116] Dr. Jaster testified that compared to cocaine, amphetamines, and certain opioids, DOI "produces no abuse liability" in the measure used in that study. Tr. 489. Dr. Jaster testified that this "same pattern . . . occur[red] with LSD," in that "animals did not self-stimulate, but they did have a head-twitch response" when receiving LSD. Tr. 490. However, Dr. Jaster stated that "this effect in LSD was not fully blocked by the 2A antagonist, whereas . . . DOI . . . was fully blocked with a 2A antagonist." Tr. 490. Dr. Jaster concluded that this research indicates that specifically for the dose given, the dose of DOI "is enough to produce potential psychedelic effects" but "does not produce reliable or similar self-stimulation as other drugs would do." Tr. 490.

Tr. 489.

Dr. Jaster testified that there have been "one or two" self-administration studies involving psychedelics in non-human primates, and an additional one or two studies with rodents. Tr. 491. Dr. Jaster stated that these studies "showed that psychedelics do not produce self-administration," meaning that "animals will not self-select to take psychedelics." Tr. 491. Dr. Jaster testified that the drug discrimination studies involving DOI and other psychedelics "suggest that similar to other . . . psychedelics [DOI] would not produce self-administration."[117] Tr. 491. Although DOI is thus similar to other psychedelics in terms of the lack of self-administration, Dr. Jaster testified that while psychedelics "may all produce head-twitch . . . it's at different potencies that they produce their maximal effects." Tr. 492. Dr. Jaster testified that "just because [psychedelics are] alike in one assay doesn't mean they're going to be alike in another," although she acknowledged that it is "possible" that they may still be similar.[118] Tr. 492-93.

Dr. Jaster stated that "just because something produces some psychedelic-like effects doesn't mean that it produces negative, or what is deemed, a negative behavior." Tr. 494. Although she acknowledged that drug discrimination is useful as a "measure of the pharmacology," the other studies can target the "whole reward system." Tr. 494. Dr. Jaster testified that behaviorally, just because a substance is a psychedelic does not mean it produces "self-administration or self-stimulation." Tr. 494.

While Dr. Jaster acknowledged that individuals may have a "bad trip" on psychedelics, she testified that to some individuals this may be considered an adverse effect, but "to some it is considered . . . helpful." Tr. 524-25. She testified that the term "bad trip" is a non-scientific term, and is "very subjective" and dependent upon an "individual's experience with the psychedelic compound." Tr. 536. Dr. Jaster described a bad trip as a "potential challenging experience with psychedelics . . . that people just presume less than favorable." Tr. 537. However, she testified that "there is also some historical reports or writings in . . . PiHKAL, where something was potentially challenging or a bad trip, but . . . that challenging experience[]

[117] Dr. Jaster testified that psychedelics may actually "reduce . . . self-stimulation" based on the ICSS studies. Tr. 496.
[118] Dr. Jaster further testified that psychedelics may represent differently in ICSS studies. Tr. 492.

or bad trip[] . . . can produce positive effects in the individual experiencing them."[119] Tr. 537, 540. Dr. Jaster agreed that labelling these challenging experiences as "bad trips" was a means to stigmatize psychedelics in popular culture.[120] Tr. 538.

On re-cross, Dr. Jaster acknowledged that "bad trips" or challenging experiences can produce lingering effects that could last from weeks to years, but testified that this did not amount to suffering for the individual. Tr. 549. Dr. Jaster acknowledged that she had previously posted on social media that "[t]he 'no such thing as a bad trip' rhetoric is so irritating and harmful . . . [b]ad trips exist . . . [s]uffering does not equal growth . . . [and] [i]f you had . . . what you consider a bad trip don't let someone discount your experience." Tr. 550-51; Gov't Ex. 17. Dr. Jaster further acknowledged that hallucinogens may cause harm, but testified that the safety or harm of hallucinogens depends on how those terms are qualified and "the individual's experience on what they deem a harmful or a safe experience." Tr. 553.

Research Harm

Dr. Jaster acknowledged that she had previously conducted research on Schedule I drugs, and that one of her colleagues had a Schedule I registration in order to facilitate this research. Tr. 522-23. Dr. Jaster testified that this research would have been "slightly altered" if DOI was also included in Schedule I, as "experiments with DOI would have to have been halted while [her lab] re-submit[ted] [its] applications to the . . . IACUC, which is a rodent review board."[121] Tr. 533. Dr. Jaster testified that her lab "would have to submit new protocols with the updated DEA application to add DOI to the drug scheduling and then would also have to resubmit that for just the state, and update all of [the] . . . inline protocols, and make sure personnel that would be using DOI would also become trained under the institution in state and federal requirements for the CSA." Tr. 533. Dr. Jaster indicated that although the storage and safety protocols between the Schedule I substances and DOI "are pretty similar," there would be "some added

[119] Dr. Jaster testified that a challenging experience could cause an individual to think about a traumatic experience that could cause emotional discomfort, but that experience triggered by the psychedelic could allow that individual to have "worked through some of that traumatic memory experience." Tr. 541.

[120] Dr. Jaster testified that this stigmatization could discourage people from seeking out treatment and cause them to "potentially self-isolate, furthering their substance use." Tr. 539.

[121] Dr. Jaster acknowledged that IACUC would need to approve the use of DOI in her research even if it was not added to Schedule I of the CSA. Tr. 549.

safety blocks as per the CSA Schedule I requirements for schedule of drugs." Tr. 533-34.

Stigmatization Associated with Scheduling

Dr. Jaster testified that she did not believe any drugs should be scheduled under the CSA. Tr. 524. She testified that the scheduling and criminalization of drugs can lead to imprisonment which results in the division of families and creates increased stigmas for individuals with a criminal record.[122] Tr. 542. Dr. Jaster further testified that criminalization leads people to the black market and may result in substances being "cut . . . with potentially dangerous things" that may lead to overdoses as individuals are unaware of what they are taking. Tr. 542-43. Dr. Jaster testified that, to her knowledge, criminalization has not stopped people from taking drugs, but has instead increased drug overdose[123] and resulted in imprisonment which impacts families. Tr. 543-44.

Dr. Jaster's testimony focused on her research with DOI, drug discrimination studies and the abuse liability of DOI. Her testimony was generally internally consistent although on cross-examination the Government probed some inconsistencies in her testimony about "bad trips" with previous posting she has made on social media. On cross-examination, Dr. Jaster also stated her sincerely held belief that no drugs should be scheduled under the CSA. Thus, her testimony opposing scheduling of DOI and DOC is a foregone conclusion. While acknowledging the candor of Dr. Jaster's testimony that no drugs should be scheduled, the tribunal must also recognize the purpose of the CSA to schedule drugs, as appropriate. Due to the aforementioned inconsistencies in her testimony and her belief that no drugs should be scheduled, I will consider Dr. Jaster's testimony with reduced weight, especially to the extent that her testimony differs from the testimony of other testifying witnesses on the same subject matter.

[122] Dr. Jaster testified that she had personal experience with the effects of drug criminalization on families. Tr. 544-45.

[123] Dr. Jaster discussed the emergence of fentanyl, and testified that "despite efforts from law enforcement . . . to increase penalties for fentanyl trafficking . . . this has not stopped." Tr. 545. Dr. Jaster testified that "this is just an example of how increased laws and increased criminalization actually can lead to more overdoses, because these supplies that were once used safely are now taken away and replaced with something that's adulterated." Tr. 545-46.

Dr. Raul A. Ramos[124]

Background

SSDP/Ramos called Dr. Raul A. Ramos as a witness.[125] Dr. Ramos holds a B.A. in psychology and a Ph.D. in neuroscience from Brandeis University in Waltham, Massachusetts. Tr. 557; SSDP/Ramos Ex. 81 at 1. Dr. Ramos testified that his Ph.D. curriculum consisted of courses on both the general and molecular concepts of neuroscience. Tr. 557. Dr. Ramos did four laboratory rotations during his Ph.D., which were unrelated to psychedelics. Tr. 558. For his dissertation, Dr. Ramos studied "the synaptic plasticity mechanisms that are important for learning and memory," and "how our brain changes and the cells in our brains change at the molecular level to empower animals to learn and alter and change their behavior as a consequence of having learned." Tr. 558-59. Dr. Ramos testified that he conducted several behavioral experiments during this research, and has "a wide expertise in animal behavior experiments." Tr. 559. Dr. Ramos stated this his experiments have covered a range of biology, from the molecular level to "experiments in the entire animal while it's awake and behaving."[126] Tr. 559-60. Dr. Ramos testified that his research has been published in multiple publications that "are highly esteemed peer-reviewed journals that are well respected in the neuroscience

[124] SSDP/Ramos Exhibits 50, 65, and 81 were offered and admitted through Dr. Ramos.

[125] Dr. Ramos testified that he taught an advanced course in the neurobiology of somatosensation at Brandeis University. Tr. 564; SSDP/Ramos Ex. 81 at 1. Dr. Ramos testified that specifically, somatosensation refers to the senses that we experience through the body, such as touch, itch, pain, thermal sensation, proprioception, pressure, and vibration. Tr. 564-66. Dr. Ramos estimated that he has spent thousands of hours during the course of his practice researching somatosensory perception. Tr. 617. Dr. Ramos further testified that he is "up to date on the latest understandings and everything that has to do with somatosensation." Tr. 618. Dr. Ramos testified that there are currently "research groups trying to understand how MDMA alters our perception of touch in humans . . . trying to understand how MDMA alters our perception of pain in rodent models . . . [and] studying psilocybin, ayahuasca, DOI, in the context of touch and pain." Tr. 619. SSDP/Ramos offered Dr. Ramos as an expert witness in "the study of the effects of psychedelics on somatosensory (touch, itch, and pain) perception." Tr. 626; *see* ALJ Ex. 56 at 4. However, as the Government objected to this designation and Dr. Ramos' proposed testimony related to his own research and Schedule I registration experiences rather than opinion testimony on psychedelics and somatosensory perception, he was not recognized as an expert witness. Tr. 625-26.

[126] Dr. Ramos testified that performing experiments across these mediums provides "the opportunity to ask questions more deeply and determine more deeply a mechanistic insight into how the biology is working." Tr. 560.

community." Tr. 561; SSDP/Ramos Ex. 81 at 2-3.

In addition to his Ph.D. curriculum, Dr. Ramos testified that he "trained in the neurobiology course at the Marine Biological Laboratory,"[127] which is "a premier, world-renowned course for training advanced experimental neuroscience techniques."[128] Tr. 561; SSDP/Ramos Ex. 81 at 1. Dr. Ramos testified that after participating in the course as a student, he was invited to teach a course in advanced physiology techniques. Tr. 561. Dr. Ramos is currently a post-doctorate ("postdoc") fellow[129] with the Miller Institute for Basic Research in Science at U.C. Berkeley, and is also a Hanna Gray Fellow[130] with the Howard Hughes Medical Institute ("HHMI"). Tr. 566; SSDP/Ramos Ex. 81 at 1.

Current Handling of DOI in Research

Dr. Ramos testified regarding the steps his lab currently takes to prevent diversion of DOI. He testified that "[f]irst and foremost, every order of DOI that [his] lab has ever placed is recorded and we know exactly how many times we've ordered DOI and how much DOI we have ordered." Tr. 674. Upon receipt of a DOI order, Dr. Ramos testified that "the staff in our lab hand it directly to [him] and [he] place[s] that DOI in a lockbox and only [he has] the key to that lockbox." Tr. 674. Dr. Ramos testified that there is a "strict chain of custody" for the DOI, and he "keep[s] all the DOI that [he has] ever worked with in a lockbox that only [he] can access." Tr. 674-75. Whenever any DOI is taken from the lockbox, Dr. Ramos testified that this amount is recorded for the purposes of the experiments and thus "all of the DOI that's ever used is recorded." Tr. 675. On cross-examination, Dr. Ramos testified that he keeps DOI in a lockbox

[127] Dr. Ramos testified that the Marine Biological Laboratory studies many disciplines of science, including the field of neuroscience. Tr. 563.
[128] Dr. Ramos testified that selection for the course is highly competitive, involving researchers all over the world. Tr. 561-62.
[129] Dr. Ramos explained that a postdoc fellow "is usually the stage that you are at before you become the principal investigator of your own lab," and is "the last stepping stone to becoming an independent investigator at a university." Tr. 566.
[130] Dr. Ramos testified that the Hanna Gray fellowship is one of the most competitive post-doctoral fellowships in the United States, as it provides funding to researchers for eight years. Tr. 567. Dr. Ramos testified that he received $1,500,000 in connection with the Hanna Gray fellowship, which is designed to last him throughout the entire eight years to facilitate his research. Tr. 568-69; SSDP/Ramos Ex. 81 at 2. Dr. Ramos testified that the research proposal he submitted for this grant is related to "studying how DOI alters our perception of . . . touch and pain." Tr. 569.

because he does not want anyone to tamper with it and does not want anyone to take it. Tr. 686. Dr. Ramos testified that "if someone doesn't know that DOI is a hallucinogenic and they aren't instructed in the proper reagent handling techniques, they could accidently expose themselves to DOI without knowing the effects of DOI." Tr. 687.

Dr. Ramos further testified that currently, "[o]rdering DOI is amazingly simple," and he can "log onto [his] lab's ordering system and order DOI as [he] would any other research chemical." Tr. 675. Dr. Ramos testified that his lab utilizes an ordering system wherein researchers can "upload . . . scientific credentials to scientific vendors so that you don't have to do that process for every single order." Tr. 676. Dr. Ramos testified that vendors confirm and verify researcher qualifications, allowing the process to be streamlined. Tr. 676. Dr. Ramos acknowledged that the ordering of chemicals and other lab equipment is typically handled by "lab support staff," and he himself has not "gone through the process of establishing that relationship with a scientific vendor." Tr. 678. However, Dr. Ramos testified that to his knowledge, an individual would not be able to order chemicals outside of formal laboratory channels because "[m]any scientific vendors do not even let you see the price or add a chemical to your cart unless you're registered and affiliated with the university."[131] Tr. 678. Dr. Ramos further testified that "without scientific credentials, individuals should not be able to order DOI for recreational use and even with scientific credentials, scientists would not order DOI for recreational use because that would cause them to lose all of their credibility and their career in science." Tr. 679.

Research Harm

Ramifications on Current Research and Use of DOI

Dr. Ramos testified that his current research is focused on "how DOI changes our perception of touch and pain."[132] Tr. 570. Dr. Ramos is conducting this research in animal

[131] Dr. Ramos testified that he had never ordered chemicals outside of the formal laboratory setting, although he knows that "if you log onto the websites without your scientific credentials, [the websites] don't let you really see much." Tr. 679.

[132] Dr. Ramos testified that his research "has the potential to inform future therapies in humans." Tr. 608. Dr. Ramos acknowledged that he does not yet know the full effects of DOI on somatosensory perception. Tr. 612. Dr. Ramos testified that his current research has found that DOI "can relieve two different types of pain in rodent models," mechanical and thermal pain. Tr. 648.

models by isolating "pain neurons from an animal and wash on DOI onto these neurons and ask[ing] how DOI changes the functional properties of these neurons," but he can also "inject DOI into these animals and measure behaviors that are related to pain." Tr. 570. Dr. Ramos testified that he chose to use DOI in his experiment "[b]ecause it's not a scheduled substance." Tr. 570-71. Dr. Ramos explained that his current lab "does not have a Schedule I license," so he altered his experiment to ensure he could continue his research without taking the additional time needed to obtain a Schedule I license.[133] Tr. 571-72. Dr. Ramos has not published any research related to DOI because his research remains ongoing. Tr. 572, 612.

Dr. Ramos testified that his current research will take approximately two more years to complete, and explained that biology studies are a slow process where projects may take "three to six years" to complete. Tr. 650. Dr. Ramos testified that he hopes to eventually move to an "R1" or "Research 1" university, where he could "collaborate with scientists . . . to advance the findings of [his] experiments in humans and begin to pursue that research." Tr. 651, 654-55. Dr. Ramos testified that the discontinuation of his research as a result of scheduling could mean "that humanity as a whole will not benefit from all of the work that [he has] invested in." Tr. 656. Dr. Ramos explained that science is already a slow process, and further delays will only serve to extend any groundbreaking findings. Tr. 656.

Dr. Ramos testified that "until recently, psychedelic research was considered incredibly taboo," but it is now "experiencing a revitalized effort by the scientific community" and thus there is a lot of progressing research in the field of psychedelics and somatosensation.[134] Tr. 619-20. Dr. Ramos explained that his current research regarding nociception[135] may potentially translate to human subjects in that "many of the molecules that are in [human bodies] and the functions that they undertake, those molecules and those functions are preserved in other mammals such as rodents." Tr. 627-28. Accordingly, Dr. Ramos testified that, by understanding "what molecules DOI is binding to, how those molecules are changing cellular function in the

[133] Dr. Ramos testified that he had been informed by scientists at Berkeley that obtaining a Schedule I license could take approximately one year. Tr. 571. Dr. Ramos testified that he has never worked with a Schedule I controlled substance in the course of his research. Tr. 608.
[134] Dr. Ramos testified that many researchers "are currently in the middle of doing a lot of important work in the context of psychedelics and somatosensation." Tr. 620.
[135] Dr. Ramos testified that nociception is "the physical processing of pain" through receiving physical, chemical, or thermal stimulus and "being able to recognize a stimulus and process that is painful." Tr. 627.

context of pain, we can leverage that understanding in humans as well."[136] Tr. 628. Dr. Ramos explained that "DOI is a highly specific agonist of the 2A receptor . . . [which] makes it a very special research tool."[137] Tr. 628.

On cross-examination, Dr. Ramos agreed that currently, DOI has no accepted medical use, but reiterated that the further study of DOI "could reveal novel, cellular molecular insights into our understanding of pain . . . [a]nd that insight could result in the creation of novel therapies." Tr. 686.

On redirect, Dr. Ramos discussed the various findings related to DOI and how it may either increase or decrease pain. Dr. Ramos testified that "the biology of serotonin is complicated and messy," and acknowledged that "[t]here have been experimental results demonstrating that serotonin in our nervous system can both signal pain and signal against pain." Tr. 695. Dr. Ramos testified that "it continues to be a mystery amongst the scientific community of how and when [serotonin] does one or the [other] and that's why this research is so important." Tr. 695. Dr. Ramos testified that further research will generate a deeper

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[136] Dr. Ramos testified regarding another study focusing on allodynia, which is the phenomenon "when a stimulus that would normally be benign, such as a gentle touch, becomes painful." Tr. 637. In this study, Dr. Ramos testified that researchers determined that "DOI provides . . . animals relief to their allodynia" through the serotonin 2A receptor. Tr. 640, 646; *see* SSDP/Ramos Ex. 50 at 3-4. Dr. Ramos explained that rodents with allodynia, after receiving DOI treatment, were more resistant to pain than prior to receiving the treatment. Tr. 642-43. He additionally testified that "[t]he anti-pain effects of DOI seem to persist for over two hours . . . [which is] very noteworthy in biology." Tr. 643. Dr. Ramos testified that the next step in the research requires understanding why DOI appears to have the ability to relieve pain in rodents and how DOI effects and changes the function of pain neurons. Tr. 646. Dr. Ramos further testified that additional research into DOI "could reveal novel molecules and novel pathways important for our understanding of pain and could potentially inform future therapies for the treatment of pain in humans." Tr. 647.

[137] Dr. Ramos testified that, in an article published in the Journal of Neuroscience in 2009, researchers determined that the serotonin 2A receptor "is expressed in neurons . . . that transmit pain." Tr. 630-31. Dr. Ramos testified that the research revealed that "there are several somatosensory neurons within the dorsal root ganglia [(an organ within which all the neurons that transmit information for touch, itch, and pain are located)] that are very clearly expressing the serotonin 2A receptor, which is the target of DOI." Tr. 634. Dr. Ramos stated that this "means that DOI can directly act on these pain neurons and alter their function." Tr. 635. Accordingly, Dr. Ramos testified that DOI "can be used to tell us more about pain, and it might even be able to have anti-pain properties." Tr. 635. Dr. Ramos acknowledged that the 2009 study indicates that 2A agonists, which include substances like DOI, increase pain, while 2A antagonists reduce pain. Tr. 682-84.

understanding of pain and would be a benefit to the public health, while acknowledging that a disruption to research could harm the public health. Tr. 695-96.

Schedule I Research Approval Process

Dr. Ramos testified that the placement of DOI into Schedule I of the controlled substances act "would totally disrupt [his] ability to perform experiments." Tr. 655. Dr. Ramos testified that "if DOI were scheduled and it became a Schedule I substance, the laboratory that [he is] currently affiliated with does not have a Schedule I license,"[138] and "[f]rom information that [he has] gathered from speaking to [his] colleagues, it seems like" the process to obtain a Schedule I research license "can take about a year."[139] Tr. 655-56, 666. Dr. Ramos further testified that "given [his] two year timeline and two years of funding and all the momentum that [he] would lose, it's quite possible that this scheduling would derail [his] entire research career at Berkeley and cause [him] to not be able to accomplish what [he] need[s] to accomplish in a timely manner and before [his] funding at Berkeley expires."[140] Tr. 656.

In terms of the university approval process at Berkeley, Dr. Ramos testified that "the first step . . . to work with the Schedule I substance is to be added to the laboratory's research protocol, their IACUC[141] protocol just in general." Tr. 669. Dr. Ramos testified that the process

[138] Dr. Ramos testified that other labs at Berkeley have Schedule I licenses, although his current lab does not. Tr. 660.

[139] Dr. Ramos testified that he "consulted with other scientists at UC Berkeley that had acquired their license already and had all the relevant documents necessary to acquire the license." Tr. 667. Dr. Ramos further testified that these individuals were working specifically with psilocybin, and had stated to him that there are several levels of administrative hurdles which cause the registration process to take significant time. Tr. 667-68. Dr. Ramos acknowledged that he has not specifically applied for a Schedule I license, but he is familiar with the approval process for university laboratories. Tr. 668. Dr. Ramos identified two Berkeley researchers that "contributed to [his] understanding of the process," and indicated that both of these individuals possess DEA Schedule I research registrations. Tr. 688-89. Dr. Ramos testified that he has spoken with these individuals about doing research under their Schedule I registrations, and acknowledged that this arrangement is "a possibility," but "they did not feel like they had the breathing room to add [Dr. Ramos] onto their protocols." Tr. 689. Dr. Ramos acknowledged that he has not spoken to anyone at DEA regarding the procedures to obtain a DEA registration. Tr. 692.

[140] Dr. Ramos testified that he would not need to communicate the scheduling of DOI with the institutions funding his research, but stated that he would need to "communicate . . . any alternative experiments" that he would start based on the scheduling. Tr. 702.

[141] Dr. Ramos testified that the IACUC is the "Institute for Animal Use and Care," and consists

to be added to the protocol may take three months. Tr. 669. Upon being added to the protocol, Dr. Ramos testified that a researcher may need to "surrender . . . fingerprints to the state of California and present . . . for a background check." Tr. 669. Dr. Ramos testified that the background check takes an additional three months, bringing the total time to receive university approval up to approximately six months. Tr. 669. In the event the lab does not have a Schedule I research registration with the DEA, Dr. Ramos testified that researchers "need to begin to write a detailed experimental protocol that needs to be added to [the] lab's current research protocol."[142] Tr. 669. Dr. Ramos further testified that the protocols must be submitted to the IACUC, which initiates a lengthy review process. Tr. 671. Once the protocol passes the IACUC process, Dr. Ramos testified that it must be submitted "to the Research Advisory Panel of California and to the DEA." Tr. 671. After receiving approval by the State of California and DEA, Dr. Ramos testified that final university approval would be required to commence the research with the Schedule I substances. Tr. 671-72. Even with university approval, Dr. Ramos stated that additional physical modifications to the lab may be necessary to comply with Schedule I storage requirements.[143] Tr. 672. Dr. Ramos testified that this entire process may take a total of 12 months.[144] Tr. 672.

Dr. Ramos testified that if DOI is placed in Schedule I, he "would start pursuing Schedule I registration and . . . would have to figure out something else at work." Tr. 674. On cross-examination, Dr. Ramos stated that he would not discontinue his research if DOI is scheduled. Tr. 688. He further acknowledged that he is also currently using other substances in his research that do not produce hallucinations, including a "serotonin 2A agonist called AL-34662." Tr. 685.

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of "committee[s] at universities that evaluate whether or not . . . protocols are ethical and up to standards." Tr. 691.

[142] Dr. Ramos testified that this protocol must be "very detailed," and "include the exact experiments that you're proposing to do, the exact amount of the Schedule I substances that you will use." Tr. 670-71. Dr. Ramos testified that it may take weeks to write the protocol, and it must then be submitted to the IACUC for approval. Tr. 671.

[143] Dr. Ramos acknowledged that he has never had to make physical modifications to a lab. Tr. 673.

[144] Dr. Ramos described Dr. Carbonaro's explanation of the approval process as a "gross mischaracterization" because the process is far more complicated and time-consuming than how she explained it. Tr. 673.

Dr. Ramos' testimony centered on his current handling of DOI in his research, the role DOI plays in his research, and the potential disruption to his research in the event that DOI is scheduled and he must obtain a Schedule I registration from DEA. Dr. Ramos presented clear and detailed testimony on these topics that was internally consistent and generally logically persuasive. In particular, the disruption and potential harm to his current research endeavors in the event that DOI is scheduled was supported with numerous details and was compelling. I therefore find Dr. Ramos' testimony to be credible and reliable and I will give it significant weight.

Dr. Harrison Elder[145]

SSDP/Ramos called Dr. Harrison Elder as an expert witness in the study of respiratory depression[146] and substance use disorders,[147] specifically the use of monoamines,[148] including psychedelics, as modulators of respiratory depression. Tr. 747; *see* ALJ Ex. 56 at 2. In the absence of any objection by the Government, the tribunal accepted Dr. Elder as an expert in the stated subject matter. Tr. 747. Dr. Elder received a B.A. in biology from the University of Virginia in 2016 and earned his Ph.D. in pharmacology and toxicology at VCU. Tr. 707; SSDP/Ramos Ex. 74 at 1. Dr. Elder testified that he "learned the basics of cellular and *in vivo* biology during [his] Ph.D. work," and took courses on biochemistry, chemistry, neuropharmacology, pharmacokinetics, and pharmacodynamics. Tr. 708. Dr. Elder has published approximately 12 to 16 academic papers, with several other papers currently in the review process. Tr. 734; SSDP/Ramos Ex. 74 at 3-4.

Dr. Elder completed a post-doctorate fellowship program at Johns Hopkins University in

[145] SSDP/Ramos Exhibit 74 was offered and admitted through Dr. Elder.
[146] Dr. Elder testified that respiratory depression "refers to the slowing of breathing induced by disease or drug." Tr. 742. Dr. Elder further testified that his dissertation work focused on fentanyl and its depression of respiration. Tr. 742-43. Dr. Elder studied agonists of monoamine receptors, including DOI, to determine "their influence . . . on respiration and behavior and if they could reverse fentanyl induced depression." Tr. 743.
[147] Dr. Elder testified that his "entire research career has essentially revolved around substance use disorder and substance abuse." Tr. 745.
[148] Dr. Elder testified that monoamines are "dopamine, serotonin, norepinephrine, adrenaline," and others, although "the three primary monoamines in the central nervous system that mediate behavior, addiction . . . are dopamine, norepinephrine, and serotonin." Tr. 750.

the Behavioral Pharmacology Human Behavioral Pharmacology Unit,[149] and is currently employed as a Senior Manager of Clinical Development in private industry. Tr. 709-10; SSDP/Ramos Ex. 74 at 1. Dr. Elder testified that in his current role, he helps develop drugs by bringing them "through the clinical development process Phase I through III trials and all the regulatory documentation that's needed to successfully get a drug approved." Tr. 710. Dr. Elder explained that this position allows him to be "quite familiar with the regulations surrounding controlled substances and drug development." Tr. 710.

Dr. Elder also worked as a writer at the Psychedelic Science Review, which is an online publication focusing on current psychedelic science.[150] Tr. 718-19; SSDP/Ramos Ex. 74 at 2. Dr. Elder was also a Project Manager and Clinical Liaison for the Misuse, Abuse, and Diversion Drug Event Reporting System ("MADDERS") at Analgesic Solutions, LLC, where he captured, evaluated, and reported instances of misuse, abuse, and diversion of investigational drugs.[151] Tr. 722; SSDP/Ramos Ex. 74 at 2.

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[149] Dr. Elder testified that the JMU Behavioral Pharmacology Research Unit is "considered to be one of the top human behavior pharmacology labs in the country, if not the world." Tr. 711. The majority of Dr. Elder's post-doctorate work related to "human laboratory studies of drugs with abuse potential," and dealt primarily with "cannabinoids and other phytochemicals from the cannabis plant." Tr. 712. Dr. Elder testified that he also worked "with the psychedelic group . . . conducting outside of the human laboratory trials that [he] helped to develop and conduct and publish." Tr. 712. Dr. Elder also testified that he conducted "drug surveillance work," which involved "determining the availability of various cannabinoids and their analogs to the public through retail and other means." Tr. 712. Dr. Elder testified that this surveillance also included psychedelic compounds, both unscheduled and scheduled. Tr. 712-13.

[150] Dr. Elder testified that one particular article he wrote for the Psychedelic Science Review concerned the Eight Factor Analysis, and "how it might be applied to a drug like MDMA." Tr. 719. Dr. Elder testified that the term "psychedelic" has many different definitions, but the most common definition that he subscribes to is that "psychedelics must activate the 5-HT2A receptor or 5-HT2 subtypes in order to produce the psychedelic action." Tr. 748. Dr. Elder stated that MDMA acts as an amphetamine, but also effects the 5-HT2 receptor and thus is "somewhere in between." Tr. 748. Dr. Elder testified that the term psychedelics could encompass unscheduled drugs, and provided, as an example, dextromethorphan, which is a substance that "if taken at the right dose . . . can produce dissociative and some might call hallucinogenic psychedelic effects." Tr. 749-50.

[151] Dr. Elder testified that he would provide "an abridged threat analysis on these investigational drugs to determine if they posed a threat to public health if they were to be approved . . . as a pain medication." Tr. 723. Dr. Elder testified that the data obtained through the MADDERS system was presented to various institutions for consideration in the approval process. Tr. 727.

21 U.S.C. § 811(c)(1); Actual or Relative Potential for Abuse

Dr. Elder acknowledged that he has experience assessing the diversion of controlled substances. Tr. 751. Dr. Elder testified that he has previously acquired DOI for his research, and testified that "[w]hen used in a legitimate purpose, as it usually is in the laboratory, [researchers] simply reach to a chemical supplier . . . that [they] have a prior registration with." Tr. 751-52. Dr. Elder testified that in his dissertation and surveillance work, he has "done research on the availability of various compounds to the general public, research compounds or research chemicals through vendors that may or may not be legitimate." Tr. 752. Dr. Elder stated he has "never come across DOI from any of these vendors that would sell to the general public," and it is "just not something that seems to be widely available." Tr. 752. Dr. Elder acknowledged that he could not say for certain if DOI is "available in other black market sources," but he does not believe it is widely available to the public and has not "seen it diverted from the lab or heard of anyone ever asking to buy it or take it out of the lab." Tr. 752-53. Dr. Elder testified that "[t]here's not a lot of interest in [DOI] . . . when it comes to diversion." Tr. 753.

Dr. Elder testified that he does not "believe that there are any case reports of human use of DOI published in peer review journals." Tr. 753. Dr. Elder acknowledged that there are "forums and online drug discussions where people claim to have taken [DOI], but [he has] never seen a case report or a hospitalization report or anything of that nature published in a medical journal to support humans taking DOI of their own initiative." Tr. 753. Dr. Elder testified that these online reports would be considered "anecdotal and potentially spurious," and although he has seen them published for a narrative "with caveats and limitations . . . you would never be able to publish [the anecdotal reports] because they're uncorroborated reports." Tr. 754. Dr. Elder acknowledged that anecdotal reports could be collected and published as part of a larger study, but it should be subject to limitations and stipulations.[152] Tr. 754-55.

Dr. Elder testified that he has conducted "extensive and exhaustive"[153] searches of grey

[152] Dr. Elder testified that these reports could provide color or background, but should not be considered evidence since the posts are unverifiable. Tr. 755. Dr. Elder identified reports from emergency departments or drug testing centers and scientific studies or surveys as examples of verifiable evidence. Tr. 756. Dr. Elder indicated that "there's many different types of evidence that could corroborate human use of DOI [but] there really is not any." Tr. 756.

[153] Dr. Elder testified that his research required him to evaluate illicit and analog chemicals, which involved review of a vendor's entire catalogue. Tr. 758-59.

market vendors, and has "a pretty in depth knowledge of which drugs were available, which drugs were currently being used on the grey market by those that use novel chemicals," and thus has "a fairly clear picture of what is available to buy to the general public." Tr. 758. Dr. Elder testified that he "never once came across a vendor offering DOI" while he was reviewing the grey market vendors between 2019 and 2023.[154] Tr. 759. Dr. Elder indicated that the DOx class of psychedelics "just don't seem to be very popular with the vendors so not many of them carry any of the DOx series." Tr. 761.

Dr. Elder testified that drugs with a high potential for abuse "tend to share some common core features," including a rapid onset of action, effects on the dopamine system to produce reinforcing, rewarding, and euphoric effects, and a quick offset of action. Tr. 761-62. Dr. Elder stated that the "more condensed pharmacokinetics are more typically seen in drugs with a high potential for abuse." Tr. 762. Dr. Elder testified that the DOx series of drugs "lacks those characteristics," and indicated that these drugs have "no effect on the mesolimbic dopamine system in the way that addictive drugs do, [and have] an extremely protracted onset and duration of action that . . . reports tend to say is extremely unpleasant."[155] Tr. 762.

Dr. Elder indicated that "psychedelic[] drugs were among the least prevalent drugs in ER admissions and not present in almost any overdoses,"[156] and overall make up "a very small proportion of drug abuse related to mortality and injury." Tr. 763. Dr. Elder further testified that the effects of psychiatric drugs "tend to resolve when treated correctly," but acknowledged that there are a "few reports of lasting injury and disability from psychedelic use or over dosage." Tr. 764. Dr. Elder testified that the "long term effects of psychedelics are being studied and have

[154] Dr. Elder testified that "most vendors carried a smaller number of psychedelic drugs or psychedelic adjacent drugs that seemed to be less popular and less discussed on forums and things of that nature." Tr. 759. Dr. Elder testified that the DOx class of psychedelic drugs as a whole are "exceedingly rare," and although some would be available from vendors, "they're not popular recreationally due to the duration of their onset, their duration of effects, [and] their general unpleasantness." Tr. 761.

[155] Dr. Elder testified that DOI and DOC are "quite similar in their pharmacology and their pharmacokinetics and pharmacodynamics." Tr. 763.

[156] Dr. Elder stated that "an overdose on a psychedelic such as psilocybin, a Schedule I psychedelic, might result in some psychiatric symptoms and general disorientation, loss of coordination, but very rarely, if ever, life-threatening symptoms." Tr. 763-64. Dr. Elder reiterated that it is "exceedingly rare for someone to die primarily because of the use of a psychedelic drug." Tr. 767.

been studied for the treatment of various psychiatric morbidities" and "can have positive effects long term." Tr. 765. Dr. Elder explained that there are reports of individuals that initially had challenging experiences with psychedelics but later found the experience to be rewarding and helpful in "moving past certain psychiatric difficulties." Tr. 765. Dr. Elder indicated that the benefits of DOI are still being discovered and researched, but he believed that "[t]he toxicity of psychedelics and DOI, DOC, is minimal compared to other commonly abused or commonly used therapeutics." Tr. 766-67.

Regarding overdoses and drug abuse in general, Dr. Elder testified that "polysubstance use . . . is the rule rather than the exception when it comes to drug abuse." Tr. 767. Dr. Elder indicated that psychostimulant and opioid co-use "is quite common."[157] Tr. 767.

On cross-examination, Dr. Elder testified that drug discrimination studies are a "component of abuse liability assessment, but they're not the end all, be all." Tr. 817. Dr. Elder further testified that drug discrimination studies provide "a piece of evidence that should be taken into account, but . . . not absolutely indicative of abuse liability, just similarities between drugs and their interoceptive effects." Tr. 817-18. Dr. Elder additionally acknowledged that he has relied on internet user forums in writing articles, and reiterated that "reports on internet forums can be useful for background information and when surveyed to provide a rationale for further studies, which is how [he] used them" in his articles. Tr. 819.

On redirect, Dr. Elder testified that an assessment of abuse liability should be a holistic approach that does "not rely on a single measure." Tr. 822. Dr. Elder testified that drug discrimination may indicate that an "animal recognizes certain interoceptive effects . . . [b]ut that doesn't necessarily mean that those effects are abuse-related, reinforcing of the same exact character." Tr. 822-23. Dr. Elder reiterated that drug discrimination studies are a component of the drug's abuse potential. Tr. 822-23.

21 U.S.C. § 811(c)(2); Scientific Evidence of Pharmacological Effect

Dr. Elder testified that "DOI shares core features with certain Schedule I drugs such as the classical psychedelics LSD or psilocybin, but it also is different from those Schedule I

[157] Dr. Elder testified that "you could find a psychedelic amongst several drugs that someone had consumed who had fatally overdosed, but they typically are not determined to be the primary cause of death." Tr. 768.

psychedelic compounds in the sense that it's very selective for receptor subtype." Tr. 769. Dr. Elder stated that DOI "has no affinity for 5-HT1A as LSD and psilocybin and MDMA do and has very little affinity for dopamine." Tr. 772. He further testified that it is likely that the effects of DOI would differ from the other classic psychedelics in Schedule I because the Schedule I psychedelics are "more promiscuous serotonergic agonists in their subjective character and pharmacological effects." Tr. 773-74. Dr. Elder testified that "just having the same mechanism of action doesn't necessarily mean that the effects or the level of the effects are the same." Tr. 775.

Dr. Elder indicated that "[t]here are other 5-HT2A agonists that are not scheduled, not considered abusable," and yet "can cause hallucinogenic effects at a certain dose." Tr. 769. Dr. Elder further stated that "there are many drugs that activate the 5-HT2 receptors that are approved and scheduled in schedules other than Schedule I." Tr. 770.

Research Harm

Dr. Elder testified that DOI "has been important in research for roughly four decades because of its incredible selectivity for these 5-HT2 receptor subtypes, 5-HT2A, 5-HT2C, and to a lesser extent 5-HT2B." Tr. 771. Dr. Elder indicated that this selectivity makes DOI "a very accurate tool for assessing the effects of those receptors, and specifically how they're activated" to produce psychedelic effects.[158] Tr. 771. Dr. Elder explained that other psychedelics such as psilocybin, LSD, mescaline, and dimethyltryptamine "hit numerous receptor subtypes," unlike DOI. Tr. 771.

Dr. Elder testified that the scheduling of a substance "absolutely has bearing on which drugs you choose and have access to for your research, just due to the onerous regulatory, financial, [and] availability issues."[159] Tr. 779. Dr. Elder testified that "there are many hurdles

[158] Dr. Elder testified that DOI "has been instrumental for teasing apart the differential contributions of the different receptors to psychedelic effects." Tr. 771-72.

[159] Dr. Elder testified that he witnessed these issues personally when working with fentanyl analogs that were placed in Schedule I while research was ongoing. Tr. 779-80. Dr. Elder testified that his lab was required to reverse distribute the fentanyl analogs back to DEA "once [they] were done using them or could no longer use them," and that this same reverse distribution occurred when an advisor with a Schedule I license retired and all the drugs registered to him needed to be "sent back to the DEA." Tr. 784. Dr. Elder testified that this reverse distribution process took many months to complete. Tr. 784. He further testified that

to go through when you work with Schedule I drugs," and these hurdles "definitely tend to make you shy away from using Schedule I drugs in your research unless you are a dedicated lab to using Schedule I drugs." Tr. 779. Dr. Elder indicated that scientists will frequently opt to use a non-scheduled substance over a scheduled substance, and stated that this is "one of the reasons that people have opted to use DOI." Tr. 780. Dr. Elder testified that he believes research of DOI would "fall off considerably" if DOI were to be placed in Schedule I, "until some other unscheduled psychedelic was validated for many of those assays." Tr. 780-81.

Dr. Elder testified that one of the benefits of DOI remaining unscheduled is the diversity of research, as scientists do not "go looking around for other interesting effects with precious Schedule I research materials."[160] Tr. 781. Dr. Elder explained that, because of the need to submit specific proposals to the DEA which may be denied if the proposal is too speculative, "research with Schedule I drugs is very directed and targeted, it's less exploratory." Tr. 782.

On cross-examination, Dr. Elder indicated that neither DOI or DOC are currently studied in clinical trials. Tr. 819. Dr. Elder acknowledged that the scheduling of DOI and DOC would not materially impact his current position, but testified that it could potentially impact the design of experiments and background medical knowledge.[161] Tr. 820. Dr. Elder further acknowledged that the reverse distribution he experienced was connected with research to aid DEA in determining whether certain fentanyl analogs should be scheduled, and stated that he was not surprised when these analogs were ultimately scheduled. Tr. 821.

Dr. Elder's testimony focused on substance use disorders and the use of DOI in research. Although Dr. Elder is not currently using DOI in his research, his testimony was genuine and internally consistent. I therefore find his testimony to be credible and reliable and where relevant I will give his testimony the weight that it deserves in light of the other evidence and testimony presented at the hearing.

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although the reverse distribution did not affect the work already done, it "had a cooling effect" on use of the fentanyl analogs in future research due to the administrative difficulties. Tr. 785.

[160] Dr. Elder testified that specifically the anti-inflammatory effects of DOI would "never have been discovered if it was a Schedule I drug." Tr. 781.

[161] Dr. Elder acknowledged that he is not currently working with DOI or DOC in his research. Tr. 820.

Dr. Lindsay P. Cameron[162]

Background

SSDP/Ramos called Dr. Lindsay P. Cameron as an expert witness in the field of neuropsychiatric disorders, and, in the absence of any objection by the Government, the tribunal accepted Dr. Cameron as an expert in the stated subject matter. Tr. 840-41. Dr. Cameron holds a bachelor's degree in pharmacology and therapeutics, and a Ph.D. in neuroscience from the University of California-Davis. Tr. 828-29; SSDP/Ramos Ex. 71 at 1. Dr. Cameron's Ph.D. coursework included courses in molecular and cellular biology, statistics and coding, and neuroscience. Tr. 829. Dr. Cameron's dissertation project involved the synthetization of novel compounds and subsequent testing of these compounds in both *in vitro* and *in vivo* models.[163] Tr. 830. Dr. Cameron currently works at the Department of Psychiatry at Stanford University, where she focuses on addiction. Tr. 832-33; SSDP/Ramos Ex. 71 at 1. Dr. Cameron has published approximately 15 articles, all related to the field of neuropsychiatric disorders.[164] Tr. 838; SSDP/Ramos Ex. 71 at 3-4.

Dr. Cameron testified that she has researched "everything from . . . chemical synthesis up to testing molecular pathways and signaling pathways, both in cell culture as well as in rodent models." Tr. 832. Dr. Cameron also testified that a lot of her research concerns animal behavior, and indicated that there are "a whole bunch of different tests . . . to study anti-depressant like effects, test things [like] anxiety or post-traumatic stress disorder, addiction, [and] things like rewarding feelings." Tr. 833. Dr. Cameron testified that "it's very obvious to see when an animal is motivated to escape or get a reward . . . [s]o those are very common things to test, when testing for something like depression or . . . addictive, drug seeking" and other behaviors. Tr. 834-35.

Dr. Cameron testified that her current work at Stanford involves the neural circuits relating to "fentanyl seeking and fentanyl addiction," and she is "trying to find different therapeutics that may be able to counteract opioid seeking." Tr. 836. Dr. Cameron testified that she has worked substantially with phenethylamines including DOI. Tr. 844. She acknowledged

[162] SSDP/Ramos Exhibit 71 was offered and admitted through Dr. Cameron.
[163] Dr. Cameron testified that her dissertation included the study of many drugs, including "fast-acting anti-depressants . . . like ketamine, LSD, DOI, MDMA, [and] amphetamines." Tr. 835.
[164] Dr. Cameron testified that she specifically wrote on anxiety, depression, PTSD, and addiction neuropsychiatric disorders. Tr. 838.

that she has "not worked with DOC," but stated that "due to its . . . chemical structure, [she] would assume it has very similar effects" as they are "all kind of in the same class." Tr. 844.

21 U.S.C. § 811(c)(1); Actual or Relative Potential for Abuse

Dr. Cameron testified that evaluating a drug's safety profile[165] involves administering different dosages to animals to determine when the animal "starts not behaving well." Tr. 844-45. Dr. Cameron testified that the safety profile also considered whether the benefits of the drug outweigh its costs. Tr. 846. Dr. Cameron explained that a drug should have "minimal toxicity, minimal abuse or dependence potential," and be overall "heavily skewed in the benefits side of things." Tr. 846.

Dr. Cameron testified that DOI's safety profile is "[q]uite safe." Tr. 847-48. Dr. Cameron stated that DOI has "beneficial effects," and causes "growth of . . . cortical neurons . . . increased dendritogenesis, spinogenesis, synaptogenesis, as compared to other fast acting anti-depressants." Tr. 848. Dr. Cameron testified that DOI tends to "show therapeutic properties more so than anything else." Tr. 848. Dr. Cameron further testified that studies revealed that DOI "calms animals down," may be "useful for treating addiction," and can "reverse or block a preference for drug seeking of hedonic drugs, like alcohol or opioids."[166] Tr. 848.

Dr. Cameron testified that it is important for a drug to have low dependence to make it safe, as "part of the safety profile would not be causing . . . physical and/or mental dependence." Tr. 849. Dr. Cameron stated that "[i]n the case of DOI . . . primates who are given access to DOI, do not self-administer." Tr. 849. Dr. Cameron testified that "self-administration is probably the absolute best study . . . with regards to studying addiction," and thus stated that "the fact that primates don't self-administer DOI would suggest that there's not really an abuse liability there." Tr. 849.

In terms of evidence of DOI's abuse potential,[167] Dr. Cameron testified that she has "not

[165] Dr. Cameron testified that a safety profile concerns the toxicity, long-lasting effects, or addictive nature of a substance. Tr. 845.

[166] Dr. Cameron testified that there are "several studies that show that you can reverse the rewarding effects or the rewarding memory of things like alcohol or opioids." Tr. 864. Dr. Cameron further testified that her own research has found that DOI can cause parts of the brain region to strengthen which can "override drug seeking." Tr. 864.

[167] Dr. Cameron testified that abuse potential is "how rewarding a drug is and does it cause physical and mental dependence." Tr. 852. She summarized this as asking whether "an animal

seen basically anything." Tr. 850. When comparing the abuse potential of DOI with other substances, including alcohol, Dr. Cameron testified that DOI "would be at the bottom, absolutely."[168] Tr. 858. Dr. Cameron further testified that drug discrimination studies are not used to study abuse potential, because it is used to "compare how similar two drugs are." Tr. 858. Dr. Cameron indicated that drug discrimination studies can only test "how similar the experience of the drug is," and therefore "in the case of trying to see if something is addictive or not, it would make more sense to compare it against something that is highly addictive." Tr. 862. Dr. Cameron testified that "if someone were to show [her] that DOI was used in drug discrimination with fentanyl and they fully substitute," this could show abuse liability based on the properties of fentanyl, but these studies "have not been done at all." Tr. 862. Dr. Cameron stated that drug discrimination is "not a good measure at all," and is "incredibly old and no one in the field of addiction uses drug discrimination anymore." Tr. 862.

On cross-examination, Dr. Cameron testified that DOI likely has a lower abuse potential than alcohol or opioids, although she acknowledged that this has not been directly tested. Tr. 874. Dr. Cameron testified that she did not believe there were any significant harms related to DOI, although she indicated that further investigation was needed. Tr. 874-75. Dr. Cameron similarly testified that psilocybin does not have many harms, and is "generally quite safe as a drug." Tr. 875. Dr. Cameron indicated that although psilocybin was generally safe, it "should be administered with the right care and under the right conditions." Tr. 875-76. Dr. Cameron also found that LSD was a "pretty safe drug." Tr. 876.

On redirect, Dr. Cameron testified that self-administration studies of LSD, psilocybin, and DOM have been conducted, but animals were found not to self-administer these substances. Tr. 878. Dr. Cameron testified that "animals do not seek them out, they do not self-administer, [and] there's no motivation or any sign of hedonic drug use or compulsive drug seeking," at least with LSD and psilocybin. Tr. 878-79. Dr. Cameron testified that the general scientific consensus regarding DOI is that "there is low abuse potential" and it is a "very useful tool in [the] field to study the serotonin 2A receptor and could have beneficial effects." Tr. 885.

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or a human go and seek [the drug] willingly." Tr. 852. Dr. Cameron further classified abuse potential as whether an individual is "willing to undergo . . . negative things because [they] need that drug so much." Tr. 852.

[168] Dr. Cameron testified that "opioids would be way at the top, with meth and probably alcohol somewhere in there." Tr. 858.

21 U.S.C. § 811(c)(2); Scientific Evidence of Pharmacological Effect

Dr. Cameron testified that there are chemical similarities between DOI and DOC, as they have a "similar safety profile, similar receptor pharmacology in terms of . . . which receptors they target," and are otherwise "quite similar." Tr. 879-80. Regarding the similarities between DOI and DOC and other substances like LSD, Dr. Cameron testified that "they all hit the serotonin 2A receptor." Tr. 880. Dr. Cameron testified that "usually . . . if the molecular structures [of two drugs] have the same core structure, they're going to have similar core action." Tr. 882. Dr. Cameron thus testified that as "we know things about DOI, a lot of what we know can be extrapolated to DOM." Tr. 882. Dr. Cameron further testified that "in the case of DOI, DOM, DOB, DOC . . . they all have kind of a similar core structure, which is targeting [the] serotonin 2A receptor . . . and they do similar things and have similar safety profiles." Tr. 882-83.

Research Harm

Dr. Cameron explained that "every single cell in the brain has serotonin receptors." Tr. 846. She testified that there are "14 different receptors, and the serotonin 2A receptor is the most heavily expressed receptor," and thus is "more common than every other serotonin receptor in the brain." Tr. 846-47. Dr. Cameron testified that the serotonin 2A receptor is "heavily expressed in the prefrontal cortex . . . which is heavily affected in neuropsychiatric disorders." Tr. 847. Dr. Cameron explained that activating the prefrontal cortex is "often seen as a good way to help patients with these disorders," and stated that due to the heavy expression of the serotonin 2A receptor in the brain, it is "key . . . in the involvement of developing anti-depressant compounds." Tr. 847.

Dr. Cameron testified that "there's other 2A agonists that are being investigated for anti-addictive effects for alcohol and for opioids in multiple different countries," as the serotonin 2A receptor appears to "play a role in most anti-addictive pursuits . . .." Tr. 866-67. Dr. Cameron stated that DOI is "very useful because it's one of the most specific 2A agonists, more so than the ones that are being studied right now." Tr. 867. Dr. Cameron stated that she believes DOI has therapeutic effects "more so than any type of addictive or liability effects," but indicated that "a lot of research still needs to be done." Tr. 868. Dr. Cameron testified that the scheduling of

DOI would "affect researchers . . . if . . . it takes years to get a DEA license and start up a lab." Tr. 868. Dr. Cameron further testified that scheduling would affect individual research groups and "impair the field from moving forward." Tr. 869. She concluded that scheduling "would significantly restrict any sort of progress with regards to any type of serotonin research, let alone just neuropsychiatric disorders." Tr. 870. Dr. Cameron testified that in light of the fentanyl crisis, restrictions in DOI research could reduce scientists' ability to understand the role of the serotonin 2A receptor in combatting opioid and addictive use, and ultimately harm individuals suffering from addiction. Tr. 870-71.

On cross-examination, Dr. Cameron reiterated that it "takes a very long time" to obtain a DEA registration. Tr. 876. Dr. Cameron acknowledged that she has not applied for a Schedule I researcher registration,[169] but "[t]he professors that [she] work[s] with have a Schedule I license," so she is "aware of all the steps that are taken and how long that takes."[170] Tr. 877. Dr. Cameron testified that from "starting . . . at an institutional level to get a state approval to getting FDA and DEA approval to finally obtaining the drug," she has never seen this process take less than one year. Tr. 877.

On redirect, Dr. Cameron testified that scheduling DOI "would impair research and progress of many molecules," as the study of DOI may be impaired. Tr. 885. While other substances like LSD and psilocybin are being tested in clinical trials, Dr. Cameron testified that DOI remains "essential for studying the role of the serotonin 2A receptor specifically." Tr. 885-86.

Dr. Cameron's testimony centered on the evaluation of a drug's safety profile and abuse potential, including DOI. Dr. Cameron's testimony was genuine and generally internally consistent. However, her testimony differed from the testimony of Dr. Carbonaro and others

[169] Dr. Cameron testified that applying for a DEA registration is "usually done" through a laboratory's administrative staff. Tr. 878. Dr. Cameron testified that her role in the application involved writing the application with her principal investigator and submitting this application to various administrative offices for approval. Tr. 890. Dr. Cameron also testified that there may be later revisions or "back and forth" related to the application. Tr. 890. Dr. Cameron indicated that the administrative staff may submit the documents, and then supply the researchers with revision questions if any are asked. Tr. 891.

[170] Dr. Cameron testified that she "had to apply for a specific drug" under her professor's license to conduct research, and this process "takes over a year." Tr. 887-88.

regarding drug discrimination and abuse liability. Nevertheless, I find her testimony to be credible and reliable, but to the extent her testimony differs from the testimony of multiple other witnesses, I will give her testimony less weight than I give to the other witnesses' testimony.

Joseph Hennessey

Background

SSDP/Ramos called Joseph Hennessey as a witness.[171] Tr. 894. Mr. Hennessey has a B.S. in biomedical sciences and philosophy, and is currently "an M.D. Ph.D. student at the Medical College of Wisconsin." Tr. 895. During his undergraduate studies, Mr. Hennessey "studied behaviors related to drug addiction and animal models as well as tracing circuitry of neuronal pathways in the brain." Tr. 896. In his Ph.D. program at the Medical College of Wisconsin, Mr. Hennessey has "personally tested hundreds of psychedelics and psychedelic-related compounds" in his study of "a wide variety of aminergic G-protein coupled receptors." Tr. 896. DOI was one of the compounds Mr. Hennessey tested in the course of his research. Tr. 896. Mr. Hennessey has also published two peer-reviewed articles.[172] Tr. 896-97.

Mr. Hennessey testified that his research is "primarily interested in psychedelics," and he was "involved in testing psychedelics . . . across all 12 serotonin GPCRs to get a better understanding of how they activate these receptors and to what degree they differentially activate certain receptors over others." Tr. 906.

Research Harm

Mr. Hennessey testified that the scheduling of DOI "would adversely affect the timeliness that [he has] to complete [his] Ph.D." Tr. 907. Mr. Hennessey explained that he has "already joined a lab that has a Schedule II license from the DEA, but does not have a Schedule I license." Tr. 906. Mr. Hennessey indicated that his lab is "interested in studying psychedelics as it relates to cognitive flexibility in depression." Tr. 906-07. Mr. Hennessey testified that the lab

[171] SSDP/Ramos initially offered Mr. Hennessey as an "expert in pharmacology and the therapeutic effects of DOI and DOC specifically as they relate to serotonin G-protein coupled receptors." Tr. 897. The Government objected to this designation, and SSDP/Ramos withdrew their request to admit Mr. Hennessey as an expert witness. Tr. 902-04.

[172] During *voir dire*, Mr. Hennessey estimated that he wrote approximately five to ten percent of each of his published articles. Tr. 901.

has "already started designing and conducting pilot experiments with DOI in order to get this work moving" and is "targeting a date of April 2nd . . . 2025, to submit an F30 fellowship for this work."[173] Tr. 907. Mr. Hennessey testified that based on his "personal experience speaking with [his] Ph.D. mentors, the scheduling of DOI would adversely affect [their] . . . plans for future research, which includes research into potential treatments for depression and addiction."[174] Tr. 908-09.

Mr. Hennessey primarily testified about how a scheduling of DOI would adversely affect his research and the timeline to complete his Ph.D. His testimony was generally genuine and internally consistent, but did include hearsay regarding how the scheduling of DOI would affect the research plans of his mentors. Therefore, I will give significant weight to his testimony, except for the hearsay testimony which I will afford less weight where others have testified to the same matters based on their first-hand experience.

Dr. Jason Younkin[175]

Background

SSDP/Ramos called Dr. Jason Younkin as an expert witness in the study of crosstalk between dopamine and serotonin receptors, and, over the Government's objection, the tribunal accepted Dr. Younkin as an expert in the stated subject matter. Tr. 924-26. Dr. Younkin holds a Ph.D. in neuroscience from VCU. Tr. 917; SSDP/Ramos Ex. 83 at 1. His Ph.D. curriculum involved courses in biochemistry, neuroscience, anatomy, pharmacology, biostatistics, physiology, and biophysics. Tr. 917-18. Dr. Younkin additionally participated in the Naval Nuclear Electronics Technician Schools, the A-School, the Power School, and Prototype during his time in the military. Tr. 921-22; SSDP/Ramos Ex. 83 at 1. He currently works as an assistant professor in the biology department at Virginia State University. Tr. 924; SSDP/Ramos Ex. 83 at 2.

[173] Mr. Hennessey explained that the fellowship is for M.D. Ph.D. students, and is a "training grant . . . for training the next generation of scientists" and is "a very, very impactful award . . . [that] provides money for funding for research." Tr. 907.
[174] Mr. Hennessey acknowledged that he has "not spoken with anyone at DEA" regarding the Schedule I researcher registration process. Tr. 911.
[175] SSDP/Ramos Exhibit 83 was offered and admitted through Dr. Younkin.

Dr. Younkin's dissertation concerned "anti-psychotic drugs and their effects on three different receptors, their GPCRs." Tr. 919. Dr. Younkin testified that the serotonin 2A receptor was the main receptor of the three studied. Tr. 919. Dr. Younkin testified that his dissertation work also involved "pro-psychotics, which are essentially psychedelics." Tr. 920. Dr. Younkin stated that DOI was the specific psychedelic used in his research. Tr. 920.

Research Harm

Dr. Younkin testified that "to study the effect of an agonist . . . of the heteromer between . . . two receptors, DOI is basically the only one we can use because it is a . . . psychedelic." Tr. 929. Dr. Younkin further testified that DOI is "the only unscheduled psychedelic, and the strongest one in many different assays," and therefore it is "the only real comparison." Tr. 930. Dr. Younkin indicated that he needs DOI "to be able to compare any of the new potential therapeutic psychedelic drugs to the DOI and its effects." Tr. 930-31. While Dr. Younkin acknowledged that there are other agonists of the serotonin 2A receptor, he reiterated that "DOI is the only [hallucinogenic] one that is not scheduled." Tr. 931.

Dr. Younkin testified that scheduling of DOI would impact his research because he does not currently have a comparable substance to research with. Tr. 932. Dr. Younkin estimated that it would take him "at least a year to get a DEA license to be able to have DOI again, plus all the other various psychedelics that are scheduled currently."[176] Tr. 932. Dr. Younkin also testified that further delay in his study could "cost [him] time to become" a principal investigator, as he needs to complete this study "[t]o establish [himself] as a PI and get funding." Tr. 932. Dr. Younkin stated that scheduling will "delay [him] and anybody else who wants to do new research involving psychedelics, because they will have to . . . either . . . join a lab that has a DEA license or get their own DEA license." Tr. 932.

Dr. Younkin primarily testified regarding his use of DOI in research and how the scheduling of DOI would adversely affect his research. Dr. Younkin's testimony was internally

[176] Dr. Younkin testified that a former colleague informed him that it took approximately six months to receive a DEA registration. Tr. 933. However, Dr. Younkin testified that his current university has not applied for a Schedule I registration, and it would take additional time for the university to "figure out" the process. Tr. 932-34.

consistent and generally logically persuasive. Similarly to Dr. Ramos' testimony, I find his description of the disruption and potential harm to his current research endeavors in the event that DOI is scheduled to be compelling. I therefore find Dr. Younkin's testimony to be credible and reliable and I will give it significant weight.

Dr. David Nichols[177]

Background

SSDP/Ramos called Dr. David Nichols as an expert witness[178] in the study of the structure-activity relationships of psychedelic agents, and, in the absence of any objection by the Government, the tribunal accepted Dr. Nichols as an expert in the stated subject matter. Tr. 952. Dr. Nichols has a B.S. in chemistry and a Ph.D. in medicinal chemistry from the College of Pharmacy at the University of Iowa in the Department of Division of Medicinal Chemistry. Tr. 940-41; SSDP/Ramos Ex. 79 at 1. Dr. Nichols' Ph.D. coursework involved analytical chemistry, organic chemistry, advanced organic chemistry, mechanistic chemistry, biochemistry, and pharmacology. Tr. 941-42. Dr. Nichols' dissertation related to the synthesis of novel molecules that fit into the category of psychedelics.[179] Tr. 943. Upon completion of his Ph.D. program, Dr. Nichols "spent time as a postdoctoral fellow in pharmacology, learning more about how biological assays were run, how to interpret biological data, that sort of thing." Tr. 942-43. Dr. Nichols taught pharmacology at Purdue, and also worked as an adjunct professor at the Indiana University School of Medicine.[180] Tr. 948: SSDP/Ramos Ex. 79 at 1. Dr. Nichols has published approximately 300 peer-reviewed articles in his career, with more than half being related to the

[177] SSDP/Ramos Exhibit 79 was offered and admitted through Dr. Nichols.
[178] Dr. Nichols testified that he has "testified in a couple of criminal cases," as well as "a number of cases where pharmaceutical companies had a patent, and some other company was trying to invalidate their patent" wherein Dr. Nichols "testified as an expert with respect to the chemistry and pharmacology of those drugs and whether it was a legitimate discovery or not." Tr. 951.
[179] Dr. Nichols testified that he "developed the synthesis for making the optical isomers of DOI, and that was the patent that [he] received while [he] was a graduate student." Tr. 944. Dr. Nichols explained the drug development process as "understanding when you modify one molecule and it changes its biological activity, and does that give you a new drug, or does it give you a new direction? Or you can do a series of modifications and find something that's the most active." Tr. 951.
[180] Dr. Nichols taught courses on chemistry, medicinal chemistry, and pharmacology. Tr. 948.

structure activity relationships of psychedelic agents.[181] Tr. 946-47; SSDP/Ramos Ex. 79 at 2-22.

Dr. Nichols first began working with psychedelic agents in 1969 as part of his graduate practice. Tr. 952-53. Dr. Nichols testified that he remains up-to-date with developments in the field of psychedelics, and explained that "you pretty much have to keep up with what other people are doing."[182] Tr. 955. Dr. Nichols further testified that his initial research "was focused on understanding the kinds of drugs that would have similar properties and what their targets were in the body." Tr. 972. Dr. Nichols testified that upon his retirement in 2012, he has remained involved in the psychedelic research community, and is also the co-founder "of a startup company that's studying psychedelics as anti-inflammatory agents."[183] Tr. 973.

Research Harm

Dr. Nichols acknowledged that the Controlled Substances Act was not passed until 1970, one year after he began his work with psychedelics. Tr. 953. Dr. Nichols testified that passage of the CSA did not largely affect his research as "the compounds that [he] worked with, by and large, were not included as controlled substances in the DEA registration." Tr. 954. Dr. Nichols testified that it was "after [he] got to Purdue and wanted to continue this work in [his] own laboratory that [he] had to get a Schedule I license and started putting the compounds in that license that [he] was working with."[184] Tr. 953-54. Dr. Nichols explained that prior to scheduling, substances were "just kept . . . in bottles that were in drawers," as his lab did not "really have to worry about diversion." Tr. 954. Upon arriving at Purdue, Dr. Nichols was required to have a safe and other security measures for handling controlled substances, including maintaining an inventory of all controlled substances. Tr. 954. In addition to the safety and recordkeeping requirements, Dr. Nichols testified that his lab was subject to "random inspections

[181] Dr. Nichols testified that most of his articles were published in the Journal of Medicinal Chemistry, while others were published in pharmacology journals. Tr. 947-48.
[182] Dr. Nichols testified that "you see if [other scientists] make breakthroughs and that may affect what you do or give you a different perspective." Tr. 955.
[183] Dr. Nichols testified that he continues to publish papers related to psychedelics. Tr. 973.
[184] Dr. Nichols testified that he started working for Purdue in 1974 and applied for a DEA registration at that time. Tr. 970. Dr. Nichols testified that his work at Purdue was funded by NIDA to study the structure activity relationships of psychedelics. Tr. 972. Dr. Nichols explained that there "wasn't much known about psychedelics" at that time. Tr. 972.

of . . . inventory at various times." Tr. 956.

Dr. Nichols testified that "psychedelics are very safe molecules, so it was never a safety issue." Tr. 970. Dr. Nichols testified that "[b]asically, we just had to do things in a way that was acceptable to the [DEA], which meant keeping records." Tr. 970. Dr. Nichols explained that his lab "had to keep . . . track of how much they took out and when they took it out and that sort of thing, so regular inventories, and then the DEA would come in randomly at various times to check and see if . . . inventory was up to snuff." Tr. 970. Dr. Nichols testified that he has never seen evidence of the diversion of DOI, and further testified that he does not believe DOI "ever became popular." Tr. 971-72. Dr. Nichols testified that he also "would read Microgram sometimes," but he could not "recall ever seeing an incidence of DOI."[185] Tr. 971-72. Dr. Nichols indicated that it was his "impression . . . [that DOI] wasn't a very popular drug because it was very long-lasting." Tr. 972.

Dr. Nichols testified that he was at Purdue for 38 years, and during this time "the regulations became more stringent." Tr. 956. Dr. Nichols testified that the process changed, requiring researchers to provide information on the experiments they were conducting, how much of a controlled substance would be used in those experiments, and the amount of test subjects involved. Tr. 956. Additionally, Dr. Nichols testified that researchers were required to obtain review from the FDA, and labs became subject to more frequent inspections. Tr. 956. Dr. Nichols testified that even when working with trivial amounts of controlled substances that would be well-below a human dose, he "still had to keep the same records." Tr. 957.

Dr. Nichols testified that other researchers were often "envious" to find that he was working with psychedelics, because it is considered "too much of a headache to get into that field." Tr. 958, 977. Dr. Nichols explained that many considered psychedelics research to be too difficult to obtain funding for, and thus there was an overall impediment to research for scientists seeking to enter the area of study. Tr. 958. Dr. Nichols explained that researchers may only have a limited amount of time to secure grants for research, and failure to obtain a grant could impact that researcher's ability to obtain tenure or promotion. Tr. 959. Accordingly, he testified that psychedelics is a "risky field," and that he was "one of the very few that was doing

[185] Dr. Nichols reiterated that he did not recall seeing any seizures of DOI in the Microgram Bulletins, but indicated that he could "believe" that law enforcement may have found DOI during seizures. Tr. 990-91.

any research on psychedelics." Tr. 959.

Dr. Nichols discussed the recent discoveries connected with psychedelics research. He testified that "psilocybin . . . can reverse the symptoms of treatment-resistant depression" through a single dose, and can "attenuate alcohol-seeking behavior in humans who have alcohol use disorder." Tr. 974-75. He further testified that substances like LSD and DMT "can reverse anxiety and depression." Tr. 975. Since approximately 2016 when studies first began being published, Dr. Nichols testified that "psychedelics have been shown to have tremendous potential in treating central nervous system disorders, depression, anxiety, and substance use disorders." Tr. 975-76. Dr. Nichols testified that these discoveries "would've happened much sooner had these not been controlled substances." Tr. 976. Dr. Nichols testified that "[t]he government still doesn't fund research with psychedelics" and that "[m]ost of the research has been funded by philanthropists." Tr. 977. Dr. Nichols concluded that "this idea that [psychedelics are] dangerous substances and their regulation by the DEA . . . has been a disinhibiting effect" that has "kept people out of the field for more than 50 years." Tr. 977.

Regarding the current process of obtaining a DEA registration, Dr. Nichols testified that it is "more difficult [to obtain a DEA registration] than it was when [he] started [his] work." Tr. 966. From his time at Purdue, Dr. Nichols testified he saw the registration process "evolve over the period of time . . . as the regulations and oversight became more and more onerous." Tr. 966. Dr. Nichols testified that his son has a Schedule I researcher registration, but that it took his son "about a year to get a license" as DEA had to conduct a second inspection because "they lost the results of the [first] inspection." Tr. 966, 990. Dr. Nichols testified that this was not the only instance he has heard involving difficulty obtaining a Schedule I registration. Tr. 966. Dr. Nichols testified that he has assisted approximately six to ten people in obtaining a DEA registration by providing general counsel into the proper methods to obtain one. Tr. 969. Dr. Nichols disputed "[t]he claim . . . that by regulating [psychedelics], it doesn't keep legitimate researchers out of the field," as "it does, in fact" keep researchers out of the field. Tr. 977-78. Dr. Nichols testified that "[h]aving to get the safe, having your records inspected all the time, the application procedures, it's a disincentive for people to be in this field." Tr. 978.

Dr. Nichols testified that overall, the scheduling of psychedelics was "[t]erribly damaging" to the public health. Tr. 979. Dr. Nichols further testified that placement of DOI into Schedule I "would be a disaster," as it is "the only substance that acts at these types of receptors

that's available for researchers to use that don't have a Schedule I license." Tr. 979. Dr. Nichols testified that the serotonin 2A receptor "is extremely important in controlling things like addiction, depression, end-of-life anxiety" and other areas. Tr. 981. Dr. Nichols explained that if scientists want to study this receptor, "there are very few tools," and all of these tools are "psychedelics, and the only psychedelic that's not controlled is DOI." Tr. 981. Dr. Nichols testified that DOI has been "used as a chemical tool to study [the serotonin 2A receptor]" in over 800 publications. Tr. 981.

On cross-examination, Dr. Nichols agreed that controlled substances "should be locked up" to prevent diversion. Tr. 986-87. Dr. Nichols reiterated that he believes that the current recordkeeping requirements are "onerous" and "disincentivize[] people who want to get into the field." Tr. 987. Dr. Nichols explained that the process of applying for a license to specifically research psychedelics will cause many investigators, "unless they're dedicated to the field," to give up their work. Tr. 989. Dr. Nichols contrasted this with non-scheduled substances, wherein researchers can simply purchase chemicals and run experiments to satisfy their curiosities. Tr. 988. Dr. Nichols did acknowledge that it was "reasonable to keep records." Tr. 989.

On redirect, Dr. Nichols testified that scientists "have to keep records of . . . experiments, so somebody could potentially reproduce them in the future" regardless of whether the substances involved in the experiments are controlled or not. Tr. 993. Dr. Nichols testified that the DEA's recordkeeping requirements became onerous when he needed to keep track of the individuals authorized to handle the controlled substances and needed to ensure the inventories were proper. Tr. 994. Dr. Nichols indicated that the DEA required "a different inventory, different type of records." Tr. 994. Dr. Nichols explained that he was devoted to the study of psychedelics and thus did not mind keeping up with the requirements to study Schedule I substances, but stated that "[i]f [a researcher] wanted to do research or look at the Serotonin 2A Receptor and look at the psychedelics, they would've been disinclined to do it because it would've required record keeping . . . a safe . . . [DEA] investigation, a background check, [and] listing what they were going to do." Tr. 994-95. Dr. Nichols testified that if "you weren't devoted to studying [psychedelics] as a scientific exercise, you wouldn't" undertake all of the regulatory requirements and would not conduct your research in this area. Tr. 995.

Dr. Nichols testified that "[i]n academics, sometimes, you just can't wait," and thus the time it takes to obtain a license may just not be "compatible with what you want to do." Tr. 995-

96.

Dr. Nichols primarily testified regarding his research work with psychedelics over the past 55 years and the changes that have occurred due to increased regulation over this time period and their effect on research. Dr. Nichols recognized the need for security and record keeping requirements to prevent diversion while at the same time noting that the need for a Schedule I researcher registration can be a disincentive for researchers to study psychedelics. His testimony was generally genuine and internally consistent, although some of his testimony included hearsay. Overall, however, I find Dr. Nichols' testimony to be credible and reliable and I will give it significant weight.

Dr. Joseph Palamar[186]

SSDP/Ramos called Dr. Joseph Palamar as an expert witness in drug use epidemiology, and, in the absence of any objection by the Government, the tribunal accepted Dr. Palamar as an expert in the stated subject matter. Tr. 1052-53. Dr. Palamar has an associate's degree in criminal justice and a B.A. in forensic psychology. Tr. 1045; SSDP/Ramos Ex. 84 at 1. Dr. Palamar additionally holds two master's degrees, one in educational psychology and another in public health. Tr. 1045; SSDP/Ramos Ex. 84 at 1. Dr. Palamar also holds a Ph.D. in public health. Tr. 1045; SSDP/Ramos Ex. 84 at 1. His Ph.D. coursework involved standard public health classes in addition to statistics. Tr. 1046. Dr. Palamar testified that he focused his studies on drug use and drug-related data. Tr. 1046. Dr. Palamar's dissertation focused on stigma related to drug use, where he "personally oversaw the survey of over a thousand people, young adults in New York City, focusing on scales that [he] developed." Tr. 1047. Dr. Palamar testified that he "published . . . multiple papers based on" this survey and "won the dissertation of the year award given at NYU Steinhardt based on that work." Tr. 1047. Dr. Palamar explained that his dissertation focused "very much on the prevalence of drug use and correlates of drug use." Tr. 1048. Dr. Palamar indicated that "prevalence and correlates largely relate to the epidemiology[187] of drug use behavior." Tr. 1048. Dr. Palamar has published approximately

[186] SSDP/Ramos Exhibits 84 and 85 were offered and admitted through Dr. Palamar.
[187] Dr. Palamar testified that epidemiology is "essentially . . . the study of the distribution of diseases." Tr. 1049. As a drug use epidemiologist, Dr. Palamar explained that he focuses "more

200 peer-reviewed papers on the topic of drug use epidemiology. Tr. 1049; SSDP/Ramos Ex. 84 at 9-26.

Dr. Palamar currently works as an associate professor of population health at the NYU Grossman School of Medicine. Tr. 1050; SSDP/Ramos Ex. 84 at 1. Dr. Palamar's position at the Grossman School is entirely research-based, although he has also been teaching statistics to undergraduate students for approximately 15 years. Tr. 1050. Dr. Palamar also works as the Deputy Director of the National Drug Early Warning System ("NDEWS"), where he works on monitoring emerging drug trends "with a focus on novel psychoactive substances."[188] Tr. 1053; SSDP/Ramos Ex. 84 at 2. Dr. Palamar testified that NDEWS is funded through NIDA. Tr. 1054. Dr. Palamar has additional grants allowing him to focus on research concerning "the high-risk nightclub scene" based on its propensity for "party drugs and psychedelics." Tr. 1054; SSDP/Ramos Ex. 84 at 8-9.

21 U.S.C. §§ 811(c)(4), (5); History and Current Pattern of Abuse/Scope, Duration, and Significance of Abuse

During his work with NDEWS, Dr. Palamar testified that he focuses on "monitoring . . . emerging trends" in drug use. Tr. 1059. Dr. Palamar prepared a summary of the epidemiology of use and illicit availability of DOI and DOC based on the data obtained through NDEWS, which was offered as evidence in these proceedings. Tr. 1060-61; SSDP/Ramos Ex. 85. Dr. Palamar acknowledged that social media is a particular source he uses to collect emerging drug data, "with a particular focus on Reddit."[189] Tr. 1095-96.

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on the way drug use is distributed throughout society," rather than focusing on diseases. Tr. 1049.

[188] Dr. Palamar testified that NDEWS focuses specifically on "novel drugs that have recently been discovered that become problematic, such as synthetic cannabinoids . . . bath salts, synthetic cathinones," as well as "fentanyl and its analogues and other novel opioids . . . [and] psychedelics as well." Tr. 1053-54.

[189] Dr. Palamar testified that his "colleagues at NDEWS, every week . . . scrape Reddit for drug-related information to try to . . . monitor emerging trends." Tr. 1100. Dr. Palamar explained that the Reddit review process requires researchers to first identify if the drug discussed online is real, "[b]ecause a lot of people have no idea what they are using." Tr. 1100. He acknowledged that Reddit is "an indicator," particularly if a large number of individuals are discussing a drug or substance online. Tr. 1100. Dr. Palamar testified that researchers "don't look at the reliability of the content," but instead "focus primarily on . . . counts of mentions of drugs." Tr. 1101. Dr. Palamar explained that "web scraping" solely focuses on when a drug or substance is mentioned online. Tr. 1101. Dr. Palamar acknowledged that NDEWS has recently begun looking at

Regarding trends of substances submitted to DEA NFLIS labs testing positive for DOI and DOC,[190] Dr. Palamar testified that these statistics were "downloaded from the publicly available DEA NFLIS data query system." Tr. 1062. Dr. Palamar testified that this data covered a period from 2005 to 2020, and is indicative of the availability of the drugs. Tr. 1062. Dr. Palamar testified that the number of submissions testing positive for DOI ranged from 0 to 12 per year, with the peak of 12 detections occurring in 2012 and no detections between 2019 and 2022. Tr. 1062. Dr. Palamar testified that the number of submissions testing positive for DOC ranged from 1 to 152 per year, with the peak of 152 detections in 2012. Tr. 1062. Dr. Palamar further testified that there was a "steep decrease" in detections of DOC through 2020, with six total detections between 2020 and 2022. Tr. 1062. Dr. Palamar concluded from this data that "it appears that neither of these substances are . . . available, or illicitly available to the public." Tr. 1063. While Dr. Palamar acknowledged that this data says little in regards to the use of DOI and DOC, he testified that "it does indicate availability, which . . . is associated with use, but . . . it doesn't mean that one necessarily predicts the other," although "availability is a pretty good indicator" of use.[191] Tr. 1063. Dr. Palamar indicated that in terms of availability, "with these DO compounds . . . availability is almost nonexistent, at least according to DEA NFLIS submissions." Tr. 1063.

Regarding the high intensity drug trafficking area ("HIDTA") seizures[192] testing positive for DOI and DOC,[193] Dr. Palamar testified that "between 2017 and 2022, only three seizures were reported as testing positive for DOC."[194] Tr. 1064-65. Dr. Palamar testified that the "dosage units seized" in these three encounters were "55, 34, and 8."[195] Tr. 1065. Dr. Palamar

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content as well, but web scraping and mention counts are the primary means through which social media is used. Tr. 1101-02.

[190] SSDP/Ramos Ex. 85 at 1.

[191] Dr. Palamar explained that "for example, as fentanyl availability goes up, overdose deaths go up." Tr. 1063.

[192] Dr. Palamar testified that "HIDTA was enacted by Congress decades ago to focus on problematic drug areas throughout the United States," and is based on police department seizures of drugs that are then submitted through a data system and compiled nationally. Tr. 1064.

[193] SSDP/Ramos Ex. 85 at 2.

[194] Dr. Palamar testified that all three of these seizures occurred in Washington state. Tr. 1065.

[195] Dr. Palamar testified that dosing units "typically indicate[] that a seizure was . . . in pill form." Tr. 1065. However, Dr. Palamar testified that he believed that for these seizures, the substances were "probably in tab form because dosing units are an actual unit, like a pre-specified unit, such as a pill." Tr. 1065. Dr. Palamar testified that seizures recorded in weight

further testified that there were "no recorded seizures of DOI within that time frame." Tr. 1065. Dr. Palamar explained that seizures are indicative of "availability or illicit availability." Tr. 1066. Accordingly, Dr. Palamar testified that the data suggests that DOI and DOC "are . . . not really available." Tr. 1066. Although he acknowledged that there are some encounters with DOC, Dr. Palamar indicated that it remains "very rare."[196] Tr. 1066-67.

Regarding the number of instances of reported lifetime use of DOI and DOC in the National Survey on Drug Use and Health ("NSDUH"),[197] Dr. Palamar testified that the NSDUH showed "a total of nine mentions of lifetime DOI use and 32 mentions of DOC use between 2005 and 2022."[198] Tr. 1076. Dr. Palamar explained that since approximately 2020, the NSDUH surveys are conducted "half via the web and roughly half via in-person survey."[199] Tr. 1070. He testified that the NSDUH focuses on "traditional drugs, like cocaine, marijuana, methamphetamine, [and] LSD," but indicated that "there's also an option where . . . people can type in names of drugs they've used that . . . were not specifically asked about because there are thousands of . . . drugs." Tr. 1071. Dr. Palamar testified that the decision not to include certain drugs was likely because "they think a drug is not very prevalent." Tr. 1071. Dr. Palamar further testified that only a "handful" of psychedelics are included in the NSDUH, including

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form is typically indicative of substances found as powder. Tr. 1065. Dr. Palamar explained that "tabs" are similar to blotter paper, in that it is essentially "a tiny piece of paper that somebody puts in their mouth," although tabs are typically larger than blotter paper appearing as "a thicker piece of paper." Tr. 1065-66.

[196] Dr. Palamar compared the reported numbers of DOI and DOC with fentanyl, in which there are "tens of thousands of seizures" reported. Tr. 1067.

[197] SSDP/Ramos Ex. 85 at 3. Dr. Palamar testified that in his opinion, NSDUH is the "leading . . . national drug survey in the United States." Tr. 1068. Dr. Palamar testified that NSDUH is "used to track drug prevalence and correlates throughout the . . . United States." Tr. 1068. Dr. Palamar explained that NSDUH was originally a "household survey," although it now focuses on "non-institutionalized individuals," which includes homeless persons and individuals living in temporary housing. Tr. 1068. Dr. Palamar testified that NSDUH is "funded by SAMHSA," which is a government organization focused on drug epidemiology. Tr. 1069.

[198] Dr. Palamar explained that "lifetime use" just pertains to "if somebody has ever used in their lifetime as per self-report." Tr. 1074-75. Dr. Palamar testified that the NSDUH thus does not allow researchers to determine whether a response pertains to current or past use. Tr. 1075. Dr. Palamar stated that an individual could disclose use of DOI and/or DOC on the NSDUH, but this use may be related to use "half a century ago" if the individual is elderly. Tr. 1075-76.

[199] On cross-examination, Dr. Palamar acknowledged that individuals in the active military, the incarcerated, or individuals in nursing homes, mental institutions, and long-term care facilities are not included in the NSDUH survey. Tr. 1116.

psilocybin, mescaline, and LSD.[200] Tr. 1072-73. Dr. Palamar stated that, to his knowledge, the DOx class of drugs "have never been included" in the NSDUH, and if they were ever included it has been a "few decades" since they were last listed.[201] Tr. 1073. Dr. Palamar explained that reports of use of DOI and DOC are based on individuals listing or typing-in DOI and/or DOC in the survey sections wherein they are asked to disclose drug use outside of the substances already listed.[202] Tr. 1073-74. Dr. Palamar indicated that he would not "personally . . . directly equate prevalence to risk," but stated that "if . . . it seems extremely rare . . . it seems like fewer people are using it, which would probably equate to a lower likelihood of adverse outcomes." Tr. 1077.

Regarding the percentage of New York City nightclub and festival attendees reporting past-year use of DOC and willingness to use if offered,[203] Dr. Palamar testified that between 2016 and 2022, "the unweighted prevalence [of DOC] ranged from 0 percent to 0.4 percent," which indicates that "essentially nobody reported using this compound within that time frame."[204] Tr. 1082. Dr. Palamar further testified that the survey revealed that the willingness to use DOC if offered was "less than one percent."[205] Tr. 1085. Dr. Palamar testified that "most drugs are more highly prevalent across time" when compared to the reported numbers for

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[200] Dr. Palamar testified that there are some questions on "somewhat rare drugs," including three tryptamines which are combined into a single question on the NSDUH. Tr. 1073.

[201] Dr. Palamar reiterated that he has never seen any of the DOx class of drugs, including DOI and DOC, on the NSDUH. Tr. 1073. Dr. Palamar testified that the DOx compounds are "more old school," and "[i]f they were popular at all, they were more popular in . . . the 1960s." Tr. 1075.

[202] Dr. Palamar testified that among the write-in substances, phenethylamines in the "2C category" were the most commonly added, and these were "much more prevalent than" the DOx drugs. Tr. 1078.

[203] SSDP/Ramos Ex. 85 at 4. Dr. Palamar explained that this study was conducted by surveying "people entering nightclubs throughout New York City," who were asked "about use of close to 100 drugs to try and monitor prevalence of use." Tr. 1080. Dr. Palamar testified that he received a training grant to conduct this survey to aid in "monitoring the use of the novel or new psychoactive substances because these drugs . . . [are] very hard to track." Tr. 1080. Dr. Palamar stated that the survey does include a few DOx substances. Tr. 1081. Dr. Palamar testified that the data provided to the tribunal only relates to self-reported use, although he also testified that his survey would involve hair and saliva testing to detect unreported use and he never detected DOI or DOC, or any DOx substance use, in those tests. Tr. 1080-82.

[204] Dr. Palamar testified that DOI was not asked about on the survey between 2016 and 2022. Tr. 1082. Dr. Palamar indicated that DOI may have been included in the survey once, but received "zero responses." Tr. 1084.

[205] Dr. Palamar testified that "drugs like cocaine or MDMA" have a much higher percentage of willingness to use if offered. Tr. 1086.

DOC.[206] Tr. 1086.

Dr. Palamar additionally testified that "New York City nightclub and festival attendees were also asked about DOI in 2016 and 2017, but the question was dropped due to low or no reported use." Tr. 1088. Dr. Palamar indicated that only 0.1 percent of New York City nightclub and festival attendees reported use of any DOx substance in 2024. Tr. 1088. Dr. Palamar testified that in extrapolating the data obtained from New York City nightclub and festival attendees nationwide, he would expect the numbers reflected by the New York City population to be "higher because this population is at much higher risk for use of drugs . . . than the general population."[207] Tr. 1090.

Dr. Palamar testified that the NDEWS Rapid Street Reporting Initiative[208] surveys found that 0.02 percent of approximately 6,000 participants reported past-year DOC use. Tr. 1092. Dr. Palamar testified that NDEWS also issues an email alert to subscribers[209] on a weekly basis "to rapidly alert scientists and the public about . . . things that [NDEWS] think[s] are important . . . or alerts with respect to drug use, with a particular focus on novel drugs." Tr. 1093.

On cross-examination, Dr. Palamar indicated that he has not reviewed any DEA Microgram Bulletins.[210] Tr. 1112. Dr. Palamar further testified that he was not surprised that none of the Microgram Bulletins or reported seizures of DOI occurred in New York State, and was also not surprised that there were only five reported seizures of DOC in New York. Tr. 1112-13. Dr. Palamar stated that he believed "novel" was a proper term to describe the DOx drugs, and that it is a better term to use than "new." Tr. 1113. Dr. Palamar did not dispute a statement that DOx compounds have been available on the illicit market for several decades but

[206] Dr. Palamar testified that "[t]here are a few drugs that are of very low prevalence," including NBOMe, which is "a very dangerous psychedelic phenetylamine . . . that is . . . even more prevalent than the [DOx]" substances. Tr. 1086-87.
[207] Dr. Palamar provided an example using the drug ecstasy, and testified that "if five percent of [the New York City nightclub] population used a drug like ecstasy, [he] would expect that that's exponentially higher than what the general population prevalence is." Tr. 1090.
[208] Dr. Palamar explained that the Rapid Street Reporting Initiative consists of sending "a group of recruiters to a . . . city of concern that might have high rates of drug use" to conduct a survey of "typically a couple hundred people throughout various venues to pick up on possible emerging drug trends." Tr. 1092.
[209] Dr. Palamar testified that NDEWS has approximately 5,000 prescribers on the email alert. Tr. 1094.
[210] Dr. Palamar testified that he has never heard of the Microgram Bulletin, although he remains up-to-date with current reports, including reports issued by DEA. Tr. 1121.

failed to sustain popularity, and that DOx can be quite potent and misrepresented or sold as LSD. Tr. 1114-15.

Dr. Palamar further acknowledged that the NSDUH survey is purely voluntary, and agreed that there is no way to confirm whether an individual actually used the drug that they reported they used in the survey. Tr. 1117. Regarding abuse of controlled substances, Dr. Palamar distinguished abuse from illicit use, and indicated that he believed that MDMA is being used in an illicit manner. Tr. 1118.

Dr. Palamar's testimony focused on the patterns and trends of abuse of drugs, including DOI and DOC. Dr. Palamar's testimony was internally consistent and generally logically persuasive, however his statistical studies mostly involved club drugs used in New York City that were self-reported by individuals without corroboration. There were also groups of people not included in the surveys, such as institutionalized people. Thus, although I find Dr. Palamar's testimony credible, I recognize limits in the applicability, and potentially reliability, of his surveys and I will weight his testimony accordingly.

Dr. Mario de la Fuente Revenga[211]

SSDP/Ramos called Dr. Mario de la Fuente Revenga as an expert witness in the study of medicinal chemistry and the neuropharmacology of psychedelics, and, in the absence of any objection by the Government, the tribunal accepted Dr. de la Fuente Revenga as an expert in the stated subject matter. Tr. 1144-45. Dr. de la Fuente Revenga is a Doctor of Pharmacy and a Doctor of Medicinal Chemistry. Tr. 1128; SSDP/Ramos Ex. 82 at 3. Dr. de la Fuente Revenga received his degrees from the University Complutense of Madrid in Spain. Tr. 1129-30; SSDP/Ramos Ex. 82 at 3. Dr. de la Fuente Revenga's curriculum included courses in pharmaceutical sciences, chemistry, biology, botany, pharmacology, and public health. Tr. 1130. Dr. de la Fuente Revenga testified that his Doctor of Medicinal Chemistry degree was "more focused on drug discovery," and therefore included courses on organic chemistry, organic synthesis, pharmacology, structural biology, and analytical methods.[212] Tr. 1132.

[211] SSDP/Ramos Exhibits 8, 9, 10, 11, 19, and 82 were offered and admitted through Dr. de la Fuente Revenga.

[212] Dr. de la Fuente Revenga testified that "all the groundwork to get [his] dissertation involved a

Upon completing his Ph.D. program, Dr. de la Fuente Revenga began studying ayahuasca at the University Autonoma Barcelona. Tr. 1134; SSDP/Ramos Ex. 82 at 3. Dr. de la Fuente Revenga next came to the United States, where he started a project related to "the study of the neuropharmacology of antipsychotics."[213] Tr. 1135. Dr. de la Fuente Revenga has approximately 35 publications, mostly in the areas of medicinal chemistry and pharmacology. Tr. 1136-37; SSDP/Ramos Ex. 82 at 5-7. Dr. de la Fuente Revenga testified that he began working with DOI in approximately 2017, as his first publication concerning DOI was released in 2019. Tr. 1136. In 2022, Dr. de la Fuente Revenga was hired by Radius Pharmaceuticals as their executive director of discovery, where he initiated discovery efforts "to expand the neuroscience franchise."[214] Tr. 1142; SSDP/Ramos Ex. 82 at 2-3.

Dr. de la Fuente Revenga testified that DOI "is an excellent tool drug" and is "very stable, which is always a perk in terms of using drugs repeatedly." Tr. 1143. Dr. de la Fuente Revenga explained that DOI's extended duration is useful in studying small mammals due to their "high metabolic rate."[215] Tr. 1143. Dr. de la Fuente Revenga testified that DOI is also "an excellent benchmark and positive control for head-twitch experiments."[216] Tr. 1144. Regarding his familiarity with the use and study of DOI, Dr. de la Fuente Revenga stated that he "would be confidently in the top three worldwide by scientific production, volume and impact factor in the

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lot of neuroscience training," and that his work for his dissertation involved a discovery that DMT "is a partial agonist at the melatonin receptor." Tr. 1133. Aside from DMT, Dr. de la Fuente Revenga testified that the majority of his Ph.D. program involved working with a modality that was "akin to a tryptamine." Tr. 1134. Dr. de la Fuente Revenga testified that "while [he was] not exactly working on psychedelics, [he] was working around the exact same kind of chemistry." Tr. 1134.

[213] Dr. de la Fuente Revenga testified that the study of antipsychotics "is a little bit of departure from the psychedelic field except that psychedelics are commonly used in this kind of research as a benchmark for the development of antipsychotics." Tr. 1135.

[214] Dr. de la Fuente Revenga testified that the neuroscience franchise "was very much focused on drugs in the sphere of cannabinoids and psychedelics." Tr. 1142.

[215] Dr. de la Fuente Revenga testified that DOI "produces a stimulation of the same receptors of [psilocybin] stimulate, but its pharmacokinetics allow it to be in the mouse brain for a duration of time comparable to what a human experience would be like." Tr. 1143-44.

[216] Dr. de la Fuente Revenga has published articles pertaining to head-twitch responses in rodents using fully-automated detection methods. Tr. 1154. Dr. de la Fuente Revenga testified that any study "using the semi- or fully-automated head-twitch is of much greater value to . . . understanding and . . . assessment of what a drug does than any visual . . . assessment." Tr. 1155.

use of . . . DOI in the research lab, not clinical." Tr. 1144.

21 U.S.C. § 811(c)(1); Actual or Relative Potential for Abuse

Dr. de la Fuente Revenga testified that he is interested in determining "the boundaries of what define head-twitch-positive psychedelic drugs versus head-twitch-negative non-psychedelic drugs." Tr. 1155. Dr. de la Fuente Revenga indicated that he is "in head-twitch very heavily to try to learn more on what makes [psychedelic] drugs different, even though they stimulate the same receptor." Tr. 1156. Dr. de la Fuente Revenga is also researching head-twitch responses to "try to make sense of how much drug is needed to get what level of response, how do things correlate, how do things happen at the same time, and also to study how these responses can be confounded or mixed up with other receptors because . . . psychedelics are diverse."[217] Tr. 1156.

Dr. de la Fuente Revenga testified that head-twitch responses say "[n]othing" about a drug's abuse potential and are "not a model of abuse." Tr. 1156-57. Dr. de la Fuente Revenga acknowledged that "[h]ead-twitch is a model that has good, correlative power to determine the potency of psychedelics across species more precisely, mice and human," but stated that there are "plenty of drugs that induce head-twitch that are not psychedelics."[218] Tr. 1156-57. Dr. de la Fuente Revenga testified that head-twitch provides a "readout that is clearly dependent on the same receptor that psychedelics target" and may be valid for making conclusions on the stimulation of a receptor, but are invalid for making findings related to abuse potential. Tr. 1157.

Regarding the interpretation of data, Dr. de la Fuente Revenga testified that the DEA "has absolutely nothing at stake" in interpreting research, thus allowing the Agency to "overinterpret as much as they want because . . . no drug is going to come back and appeal to the Supreme Court because they don't have that ability." Tr. 1160. Dr. de la Fuente Revenga further testified that DEA "very largely overinterpreted" the available pre-clinical data "in its effort to establish abuse." Tr. 1161. Dr. de la Fuente Revenga stated that if DEA "can make the statement that the data available in animals established high-abuse potential, by the same token [the Petitioners]

[217] Dr. de la Fuente Revenga testified that psychedelics have "different pharmacological actions." Tr. 1156.

[218] Specifically, Dr. de la Fuente Revenga discussed a substance called "5-hydroxytryptophan," which is a supplement that "produces very reliable heavy head-twitch." Tr. 1200. Dr. de la Fuente Revenga testified that this substance is "not psychoactive by any stretch of imagination," and yet can "generalize for LSD" in drug discrimination studies. Tr. 1200-01.

can conclude that [DOI and DOC are] very promising therapeutic agents." Tr. 1162.

Dr. de la Fuente Revenga further explained that DOI "has incredibly long pharmacokinetics and pharmacodynamics," which means it "takes forever to kick in." Tr. 1162. Dr. de la Fuente Revenga testified that this long-lasting effect is "something that psychonauts are not going to love . . . because it lasts for no less than 12 hours." Tr. 1162-63. Dr. de la Fuente Revenga further testified that "if this is a drug that has been known for decades . . . available from regular chemical suppliers for decades, and . . . didn't quite find its niche in the community, one might wonder why is that, given that it's clearly a psychedelic, it's clearly a Serotonin 2A agonist." Tr. 1163. Dr. de la Fuente Revenga stated that he does not "believe there's true use [of DOI] in the community . . . except maybe some anecdotal cases that [he does not] even know if [he] give[s] true validity to." Tr. 1163. As an expert in pharmacology, Dr. de la Fuente Revenga further stated that the "delayed onset of action" with DOI is "very deterrent for people to abuse DOI."[219] Tr. 1163. Dr. de la Fuente Revenga compared the effects of DOI to salvia, and indicated that DOI may produce dysphoric effects similar to salvia but for an extended period of time. Tr. 1164. Accordingly, Dr. de la Fuente Revenga testified that DOI is "not a drug that can be abused because . . . people have better drugs to abuse, if you want to use the term." Tr. 1164.

Dr. de la Fuente Revenga testified regarding the four-prong test for potential for abuse. Tr. 1169-78. Regarding Abuse Prong A, Dr. de la Fuente Revenga testified that he does not believe "there's any evidence, factual evidence, that there's anyone taking DOI. No one in an emergency room that has had a blood test that tested positive for DOI." Tr. 1170. Dr. de la Fuente Revenga testified that "[t]he only credible report is probably Alexander Shulgin,"[220] but "[n]o one would ever make decisions based on only one." Tr. 1170. Dr. de la Fuente Revenga explained that DEA's analysis of the abuse probability "lacks in quantitative data analysis and a true assessment of the depth." Tr. 1170-71. Dr. de la Fuente Revenga indicated that the number of law enforcement encounters is "miniscule compared to any other drugs in these categories," and thus he does not agree that there is "evidence of individuals taking" DOI.[221] Tr. 1171.

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[219] Dr. de la Fuente Revenga testified that a dealer who attempts to pass off DOI as LSD will "run out of business real fast." Tr. 1164.

[220] Dr. de la Fuente Revenga testified that he does not "know if [he] can take at face value reports on Reddit or Erowid." Tr. 1171.

[221] Dr. de la Fuente Revenga testified that, in terms of quantitative data, "all [he has] had access to is that lousy table of encounters or NFLIS . . . where all [he] see[s] [is] a peak of cases in

Dr. de la Fuente Revenga was not asked specifically about Abuse Prong B, regarding significant diversion of the drugs, but he testified that he believed this prong was important. Tr. 1172. However, Dr. de la Fuente Revenga testified that DEA's finding that there was a lack of significant diversion of DOI and DOC from legitimate channels was key to the ultimate abuse potential analysis. Tr. 1177. Dr. de la Fuente Revenga stated that DOI and DOC "are available, probably more available from legitimate channels than lousy drug dealers in the street," and yet DEA found no significant routes of diversion.[222] Tr. 1177-78. Dr. de la Fuente Revenga concluded that this is because "[t]here's no demand. No one prefers DOI over anything else." Tr. 1177-78.

Dr. de la Fuente Revenga was asked about Abuse Prong C. Tr. 1172. Dr. de la Fuente Revenga stated that he did not "disagree with the analogies that the DEA presented in terms of DOI having . . . similarity to LSD . . . in these animals, in these cells, and in these proteins." Tr. 1175. However, he testified that "the context is important" and the presence of drugs like LSD and MDMA in the community, but the absence of DOI, reveals through the "natural selection process" for recreational drugs that DOI "is not a drug that anyone would like to mess with." Tr. 1175-76.

Regarding Abuse Prong D, Dr. de la Fuente Revenga testified that DOI and DOC are by "no means" new drugs. Tr. 1176. He acknowledged that the "effects on pharmacological actions are similar to DOM and LSD," and further acknowledged that drug discrimination studies, although imperfect, may "establish some similarity." Tr. 1176. However, Dr. de la Fuente Revenga testified that abuse cannot be determined from drug discrimination studies. Tr. 1176. Although HHS and DEA found that it was reasonable to assume that DOI and DOC have substantial capability to be a hazard to health and safety, Dr. de la Fuente Revenga stated that "the facts are that that has not happened." Tr. 1176-77.

On cross-examination, Dr. de la Fuente Revenga agreed that psychedelics, including substances like DOI, psilocybin, and LSD, are psychoactive compounds that profoundly affect

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which [DOI is] identified in 2009 and then a very sharp decline with a complete disappearance since." Tr. 1173-74. Accordingly, Dr. de la Fuente Revenga testified that "for all we know, maybe DOI is not even out there anymore." Tr. 1174.

[222] Dr. de la Fuente Revenga testified that DOI and DOC have been available from chemical distributors for decades, which provides the "perfect channel" for diversion since a DEA license is not required to sell to users, and yet there is still no "evidence of substantial use." Tr. 1177.

various mental domains, particularly sensory perceptions and thought processes. Tr. 1189. However, Dr. de la Fuente Revenga did not agree that the acute psychoactive symptoms and drug abuse potential of DOI and other psychedelics preclude their routine use in daily clinical practice.[223] Tr. 1189-90. Dr. de la Fuente Revenga also did not disagree that "[c]lassical psychedelics such as LSD, psilocybin, mescaline, and DOI have been recognized for their capacity to profoundly dysregulate various mental domains, particularly sensory perception and thought process." Tr. 1192; SSDP/Ramos Ex. 19 at 2. Dr. de la Fuente Revenga did not agree that drug discrimination studies are useful in determining the comparable effects of drugs. Tr. 1194. However, Dr. de la Fuente Revenga did acknowledge that he wrote an article in 2020 which discussed the use of drug discrimination studies and head-twitch response in determining the comparable effects of a substance called "quipazine" to classic psychedelics. Tr. 1194-95.

Regarding law enforcement encounters with DOI, Dr. de la Fuente Revenga reiterated that the number of encounters in NFLIS appeared "really clearly low." Tr. 1198. When discussing an encounter with DOI by law enforcement in the form of blotter paper, Dr. de la Fuente Revenga acknowledged that he has never used blotter paper in his research with DOI but indicated that this "doesn't change anything." Tr. 1199.

On redirect, Dr. de la Fuente Revenga testified that "we know in humans that repeated exposure with certain psychedelics, like LSD, leads to basically no effect, at least not the effects that are more distinctive, elicited by the substances." Tr. 1207-08. Dr. de la Fuente Revenga explained that this means that "[e]ven if psychedelics had a very high effect on reward, the subject will get nothing out of doing more" because the effects of further doses do not create the same response. Tr. 1208. Accordingly, Dr. de la Fuente Revenga stated that "no matter how high the craving is" for a substance, the subject will have "basically . . . the same flat response" upon administration. Tr. 1208.

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[223] Dr. de la Fuente Revenga acknowledged that a statement to this effect was made in an article authored by him and other researchers. Tr. 1190; SSDP/Ramos Ex. 9 at 2. However, Dr. de la Fuente Revenga explained that research articles are collaborative and certain statements made in such articles may contain differing opinions. Tr. 1201-02. Dr. de la Fuente Revenga testified that he would not label the statement made in the article as a disagreement between himself and another researcher, but indicated that his colleague did have a "different outlook into how he traditionally approached psychedelics." Tr. 1202. Dr. de la Fuente Revenga further stated that science evolves and changes, and opinions expressed in articles may similarly change over time. Tr. 1203.

On re-cross, Dr. de la Fuente Revenga testified that "head-twitch can give you insights into how psychedelics don't produce abuse liability, which is a completely different angle and direction" than using head-twitch response to assess abuse liability.[224] Tr. 1210.

Research Harm

Dr. de la Fuente Revenga testified that the study of psychedelics has revealed that "there is certainly something that psychedelics do in very basic domains of behavior from which [scientists] can extract features that might bear some therapeutic potential."[225] Tr. 1158. Dr. de la Fuente Revenga explained that with DOI "people are not really interested" in it recreationally because of its adverse effects, but that it is "an amazing research tool that any researcher, whether they're [in] neuroscience or not, has access to."[226] Tr. 1164. Dr. de la Fuente Revenga testified that the proposed scheduling of DOI "is just wasting taxpayers' money," and contrasted the proposed scheduling to the lifting of the COVID-19 pandemic restrictions. Tr. 1174. Dr. de la Fuente Revenga stated that "COVID still kills people . . . [but] as far as [he is] concerned, DOI has killed no one." Tr. 1174. Dr. de la Fuente Revenga testified that "the measures need to be commensurate to the effort needed to buffer certain risks." Tr. 1174-75.

Dr. de la Fuente Revenga testified that "[a]s it stands right now, DOI has harmed no one, so [DEA's proposed scheduling] effort will be very successful at protecting no one, given that DOI has had its test run out there and has yet to produce any significant problems." Tr. 1178-79. When compared to his finding that DOI has yet to produce any significant problems, Dr. de la Fuente Revenga testified that DOI "is an amazing tool for . . . researchers across any discipline for the ability of having access to one somewhat selective tool to study the effects of psychedelics in whatever system of their choosing." Tr. 1179. Dr. de la Fuente Revenga stated

[224] Dr. de la Fuente Revenga acknowledged that SSDP/Ramos Exhibit 11 used head-twitch response to determine ramification of abuse, but reiterated that head-twitch is insufficient to determine abuse liability. Tr. 1209-10. Dr. de la Fuente Revenga testified that he is "critical of overinterpreting" head-twitch response data. Tr. 1211.

[225] Dr. de la Fuente Revenga provided an example that DOI has been found to "accelerate[] fear extension" and improve adaptive responses in mice, which can be extrapolated to "what we could expect from a pharmacotherapy from someone that's struggling with mental health, [to] improve upon their adaptive responses." Tr. 1159.

[226] Dr. de la Fuente Revenga reiterated that DOI is "an amazing research tool" and that he has not "seen any convincing evidence that it's abused in the community." Tr. 1165.

that DOI is a "gateway drug to do the science" and "the perfect entry spot for [researchers] to maybe later apply their license for LSD, psilocybin, whatever they want." Tr. 1179. Dr. de la Fuente Revenga testified that DEA should "keep DOI out of the schedule since it seems to pose no problems to the community and it's incredibly helpful to the scientific community." Tr. 1179.

Dr. de la Fuente Revenga indicated that placement of DOI into Schedule I would effectively suppress "a good chunk of the research that can come out of it, even research that might argue that DOI should never see the light of day ever again." Tr. 1179-80. Dr. de la Fuente Revenga stated that he is familiar with the DEA registration process for researchers, and indicated that it is "tedious" and that ultimately complying with the record-keeping requirements for Schedule I registrations generates significant time-wasting. Tr. 1180. Dr. de la Fuente Revenga concluded that placement of DOI into Schedule I "will be a botched job" based on "[d]ecades of the drug being available from chemical suppliers, [with] not a single encounter in the emergency room." Tr. 1180.

On cross-examination, Dr. de la Fuente Revenga stated that placement of DOI into Schedule I would effectively strip "the entire realm of science of using this drug . . . because a lot of other areas don't normally deal with DEA licenses for the use of controlled substances." Tr. 1182. Dr. de la Fuente Revenga acknowledged that researchers could still study DOI if it is scheduled, but indicated that "every day you work with a scheduled substance you have to go through the hassle of annotate[ing] amounts, double check[ing], involv[ing] several people because the person that is using it might not be the person that has the license," and may require scientists to postpone experiments if the individual holding the DEA registration is not present in the lab. Tr. 1183.

Dr. de la Fuente Revenga's testimony focused on the use of DOI on research and DOI's potential for abuse. Dr. de la Fuente Revenga's testimony was generally internally consistent, but on cross-examination he admitted a perceived conflict between his testimony regarding drug discrimination studies and an article he wrote in 2020 regarding such studies. Thus, although I find his testimony generally credible, to the extent it differs from the testimony of other witnesses, I will give his testimony less weight.

PANACEA PLANT SCIENCES' CASE

Panacea presented its case-in-chief through the written testimony[227] of one witness: David Heldreth.

David Heldreth

Background

Mr. Heldreth founded Panacea in 2017 "to study natural products such as cannabis, lavender, peyote and psilocybin-containing mushrooms." ALJ Ex. 77 at 4. Mr. Heldreth explained that Panacea must use DOI "at times . . . to conduct research on a phenomenon or to study a delivery system." *Id.* Mr. Heldreth indicated that Panacea is also "investigating the use of DOI and DOC for the treatment of conditions such as PTSD, anxiety, depression, asthma[,] cancer and others."[228] *Id.* at 5.

Mr. Heldreth stated that he has worked with indigenous groups who "have told [Panacea] that they would prefer these synthetic items such as DOI and DOC be utilized for research and medical development." *Id.* Mr. Heldreth also indicated that scheduling of DOI and DOC will create added burdens for companies and researchers to comply with the regulatory requirements and associated costs. *Id.* Mr. Heldreth stated that Panacea is "in possession of DOI and DOC," and "will eventually destroy [its] stock of these compounds, or mail them to another country to conduct research with partners, rather than seek a DEA license and comply with the odious regulations, costs and fees." *Id.*

Due to the written nature of the testimony, Mr. Heldreth was not subject to cross-examination. The submitted written testimony was also not made under oath. Additionally, the written testimony contains hearsay, the reliability of which the tribunal is unable to assess based on the fact that the statements were not made under oath and not subject to cross-examination. For these reasons, I will consider Mr. Heldreth's written testimony with reduced weight.[229]

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[227] *See* supra at 1, n.3.
[228] Mr. Heldreth indicated that Panacea "has filed patent applications for a variety of uses of these substances." ALJ Ex. 77 at 5.
[229] *See* ALJ Ex. 91 (Order Denying Government's Motion to Strike and for Order Finding Waiver) at 2 n.4 (citing *Eric David Thomas, M.D.*, 87 Fed. Reg. 30,266, 30,272 (2022) (affording written evidence limited weight due to the limited ability to assess its credibility)

GOVERNMENT'S REBUTTAL CASE

The Government presented its rebuttal case through the testimony of one witness: Theresa M. Carbonaro, Ph.D.

Theresa M. Carbonaro, Ph.D.[230]

Determination of Abuse Potential

Dr. Carbonaro testified that self-stimulation studies are "similar to self-administration where a rodent is doing an activity to receive the drug" and is "another test to assess if a drug is rewarding or reinforcing."[231] Tr. 1221. Dr. Carbonaro reiterated that self-administration studies are not a reliable indicator of abuse liability with respect to hallucinogens, because "this is not a behavior that's often shown with hallucinogens, specifically that go through the Serotonin 2A

(citing *Michael S. Moore, M.D.*, 76 Fed. Reg. 45,867, 45,873 (2011) (evaluating the weight to be attached to written evidence in light of the fact that the authors were not subjected to the rigors of cross examination)); *see also, e.g., Gary A. Matusow, D.O.*, 87 Fed. Reg. 35,795, 35,797 n.13 (2022); *Stephen E. Owusu, D.P.M.*, 87 Fed. Reg. 3,343, 3,351 n.21 (2022); *William Ralph Kinkaid, M.D.*, 86 Fed. Reg. 40,636, 40,641 (2021).

[230] Government Exhibit 18 was offered and admitted through Dr. Carbonaro during the Government's rebuttal case.

[231] On cross-examination, Dr. Carbonaro acknowledged that she was not familiar with the basics of ICSS studies outside of their focus on reward behavior. Tr. 1240. Dr. Carbonaro stated that she has never conducted experiments using ICSS, but indicated that she has "gone to conferences where . . . ICSS data [is] presented, but not specific to hallucinogens." Tr. 1240. Dr. Carbonaro reiterated that she did not believe ICSS studies were "really effective for this class of drugs," meaning hallucinogens. Tr. 1241.

receptor."[232] Tr. 1222, 1229. Regarding condition place preference studies,[233] Dr. Carbonaro acknowledged that these studies are useful "to some degree in assessing abuse liability" by focusing on reinforcing effects. Tr. 1223. However, Dr. Carbonaro testified that HHS determined that condition place preference is "not considered to be [as] sensitive or reliable as self-administration."[234] Tr. 1223; Gov't Ex. 18 at 22. Dr. Carbonaro testified that "[t]here are a lot of external factors that play into conditioned place preference that make it well known to be less reliable to assess drug abuse liability."[235] Tr. 1223-24.

Regarding drug discrimination studies, Dr. Carbonaro testified that HHS has found that "whatever bodily sensations that an animal has known to be paired with a known drug of abuse, a test drug could be assessed to see if it has similar effects compared to a known drug of abuse and some degree if it substitutes based on some parameter, generally over 80 percent responding

[232] Dr. Carbonaro testified that self-administration studies "would [provide information] for other substances, but not for Serotonin 2A receptor-mediated hallucinogens" like DOI and DOC. Tr. 1229. On cross-examination, Dr. Carbonaro acknowledged that self-administration studies show whether drugs "have rewarding affects and reinforcement properties" that may show abuse liability. Tr. 1245. Dr. Carbonaro reiterated that psychedelics are used "in a different way than other drugs," and thus the lack of self-administration of DOI or DOC by animals did not impact her determination regarding abuse liability. Tr. 1246. Dr. Carbonaro stated that self-administration "doesn't work in this model." Tr. 1246. Dr. Carbonaro further reiterated that it is "well-known and well-discussed" that self-administration is "not something that happens with psychedelics through the 2A receptor," which differs from cannabinoids, stimulants, or depressants which may involve self-administration. Tr. 1246-47. Dr. Carbonaro stated that absent the self-administration studies, "[w]e . . . know that people use these substances," and therefore "they have known abuse potential, known harms." Tr. 1247. In terms of addiction, Dr. Carbonaro acknowledged the "notion of tolerance" found with psychedelics, but indicated that addiction is just "a harm component" of the Eight Factor Analysis, but is not a necessary finding to schedule a drug. Tr. 1258-59. Dr. Carbonaro did not believe that addiction was applicable to the class of psychedelics among which DOI and DOC are included. Tr. 1259.

[233] Dr. Carbonaro described condition place preference studies as a study wherein "animals pair the effects of drugs with one side of a chamber or one . . . condition . . . and then are given a test drug to see if it produces effects that might be considered . . . reinforcing." Tr. 1223.

[234] On cross-examination, Dr. Carbonaro testified that conditional place preference testing is subject to a number of external factors unrelated to the drugs administered that can alter the results of the test. Tr. 1242.

[235] Regarding the figure presented by Dr. Jaster, Dr. Carbonaro testified that she could not interpret that data "without understanding what drug was administered, when it was administered, how it was administered, [or] if there were other drugs also administered." Tr. 1227.

on the drug-paired lever, that it may have abuse potential."[236] Tr. 1225; Gov't Ex. 18 at 22. Dr. Carbonaro explained that after an animal is trained to press a lever for a known drug of abuse "[w]hen given a new drug and given a different dose, if they press the lever that's paired with the known drug over 80 percent of the time, then that's coined 'full substitution.'"[237] Tr. 1225. Dr. Carbonaro testified that DOI and DOC produced full substitution for LSD, DOM, and DOB when tested. Tr. 1226. Dr. Carbonaro testified that drug discrimination "is sensitive to the mechanism of action," and requires the "training drug" to have the same mechanism of action "to see if that drug will have an effect similar to that."[238] Tr. 1226. Dr. Carbonaro stated that "if the new drug has an effect through the Serotonin 2A receptor, then it should substitute." Tr. 1226-27. Dr. Carbonaro acknowledged that before a drug goes through clinical trials, there must be information provided regarding whether the drug "has these similar effects to a known drug of abuse in animal drug discrimination studies." Tr. 1229; Gov't Ex. 18 at 9.

Dr. Carbonaro testified that she agreed with HHS's definition of "abuse potential," and stated that it is "the likelihood that abuse will occur with a particular drug product or substance with [central nervous system] activity." Tr. 1230. Dr. Carbonaro explained that dependence liability is "the predictive measure if a drug could produce dependence, whether it be physiological or psychological . . .." Tr. 1232. Dr. Carbonaro reiterated that "[p]hysiological dependence usually is essentially . . . the body has adapted, so it needs the drug, whereas . . . psychic dependence is . . . using the drug in a way that . . . harms are known but [one is] still willing to use it." Tr. 1231. Dr. Carbonaro further testified that she did not believe that the CSA "make[s] note of needing dependence liability for a drug to be placed in Schedule I." Tr. 1231. Regarding psychic dependence, Dr. Carbonaro testified that she "concurred with FDA or HHS's

[236] Dr. Carbonaro testified that NIDA has a "longstanding contract . . . to assess drug discrimination." Tr. 1230. Dr. Carbonaro further testified that NIDA concurred with the HHS medical and scientific evaluation regarding DOI and DOC. Tr. 1237.

[237] Dr. Carbonaro testified that "[p]artial substitution is generally over 40 percent lever responding of the drug-paired lever versus the saline-paired lever or vehicle-paired level." Tr. 1225-26.

[238] Dr. Carbonaro testified that "to assess a drug in the Eight Factor Analysis, we have to compare it to a drug with a similar mechanism of action and known effects. And so . . . to assess abuse liability, it really is dependent on a drug that has a similar mechanism of action, which is why" drug discrimination studies are used." Tr. 1228.

evaluation that there could be" psychic dependence with respect to DOI and DOC.[239] Tr. 1231-32.

Dr. Carbonaro testified that, pursuant to the Eight Factor Analysis requirements, drugs must be compared to drugs "in a similar class." Tr. 1233. Accordingly, Dr. Carbonaro indicated that it would not be fair to compare DOI and DOC to alcohol. Tr. 1233. Dr. Carbonaro testified that she is not aware of a "specific criteria" that needed to be met regarding the number of users of a drug to constitute abuse potential. Tr. 1233. She further testified that she was not aware of any specific numerical requirement related to adverse events or deaths. Tr. 1233-34. Dr. Carbonaro acknowledged that death statistics are a "component of harm," but there is no specific number required under the Eight Factor Analysis. Tr. 1234.

Dr. Carbonaro testified that clinical data would be needed to assess the safety of a particular drug. Tr. 1234. She stated that she is unaware of any clinical trials that have occurred related to DOI or DOC. Tr. 1234.

Dr. Carbonaro also discussed the comparison of DOI and DOC with the "2C" phenethylamines, and testified that DOI and DOC are "very similar in structure and activity" to these substances that were largely scheduled in the Synthetic Drug Abuse Prevention Act of 2012. Tr. 1236-37.

On cross-examination, Dr. Carbonaro acknowledged that "a large portion of [her] Eight Factor Analysis" concerned DOI's discrimination with other similar drugs of abuse. Tr. 1243. She also acknowledged that there are certain non-psychoactive substances that could discriminate for psychoactive substances in drug discrimination studies. Tr. 1242-43. In supporting her belief that DOI specifically possesses similar psychoactive properties to the known drugs of abuse, Dr. Carbonaro testified that "there's enough drug discrimination evidence . . . [to] make[] [her] believe that this is not . . . a false-positive or false-negative." Tr. 1243. Dr. Carbonaro testified that the difference between DOI and the non-psychoactive substances found to substitute for the known drugs of abuse is the knowledge that DOI "is a serotonin 2A receptor agonist, similar to these drugs in the drug discrimination paradigm." Tr. 1244. Dr. Carbonaro

[239] On cross-examination, Dr. Carbonaro reiterated that physiological dependence is "generally not shown for most classic hallucinogens that work through the 2A receptor," including DOI. Tr. 1248. Dr. Carbonaro explained that "physical dependence relies on a dopamine effect," which is not applicable to the pathways of psychedelics like DOI and DOC. Tr. 1248.

further testified that "there is common knowledge that [DOI and DOC] are psychedelics or hallucinogens, based on the evidence that is there. And there are drug seizures for both DOI and DOC." Tr. 1244. Dr. Carbonaro stated that "it's not just drug discrimination," but there is "other data that also show that it has activity." Tr. 1244.

Dr. Carbonaro testified that she believes there is a willingness in the general public to take DOI, and indicated that this belief is formed by "law enforcement seizures of DOI."[240] Tr. 1249. Dr. Carbonaro testified that there is also a larger reported number of seizures of DOC, but stated that seizures are not "a strong contributor in the Eight Factor Analysis for putting something into Schedule I." Tr. 1249.

Dr. Carbonaro testified that her personal Eight Factor Analysis consisted of reading and reviewing the HHS report and updating it with reported law enforcement encounter data. Tr. 1250. On redirect, Dr. Carbonaro reiterated that she did not believe DOI or DOC have a currently accepted medical use. Tr. 1262-63.

Research Harm

Dr. Carbonaro discussed the IACUC approval process, and indicated that such approval is needed for the studies involving animals with vertebrae.[241] Tr. 1235. Dr. Carbonaro testified that IACUC approval would be needed prior to administration of drugs to animals and regardless of whether the drug involved was controlled or not. Tr. 1235. Dr. Carbonaro testified that upon scheduling, researchers would not be required to subsequently obtain renewed IACUC approval if they had already achieved it for their research. Tr. 1235. Dr. Carbonaro additionally testified that "most of [the preparation needed to submit an application for a DEA Schedule I research registration] would be needed for general research anyway."[242] Tr. 1256. Dr. Carbonaro

[240] Dr. Carbonaro acknowledged that, since DOI and DOC are not scheduled substances, "encounters" would be a preferable term to "seizures." Tr. 1252. Dr. Carbonaro reiterated that she is not aware of a threshold finding of encounters needed to schedule a drug, and stated that there are some substances with "as little as one" encounter or no encounters placed in Schedule I. Tr. 1252. On redirect, Dr. Carbonaro agreed that law enforcement may "seize" substances believing them to be illicit, only for the substance to later be tested and found to be a non-controlled substance like DOI or DOC. Tr. 1262.

[241] Dr. Carbonaro testified that certain studies involving animals such as worms or zebrafish do not require IACUC approval. Tr. 1235.

[242] Dr. Carbonaro acknowledged that the storage requirements would be unique to scheduled substances, but stated that "most of the procedures to getting a DEA registration would follow in

testified that starting from the initial procedures needed to conduct general research to receiving a DEA registration, the "numbers vary, depending on the type of study" being conducted. Tr. 1257. Although Dr. Carbonaro indicated that she only "know[s] the part that DEA is involved in," she testified that, regardless of whether a DEA registration is needed, the time to obtain approval to conduct general research could take a year. Tr. 1257.

Regarding the number of researchers holding Schedule I registrations overall, Dr. Carbonaro testified that the number of Schedule I researchers has increased in the last 15 years. Tr. 1235-36. Dr. Carbonaro further testified that it is common for researchers to work with other researchers already in possession of a DEA registration, and indicated that especially "for students and post-docs, that's . . . mostly how it is done."[243] Tr. 1237.

On cross-examination, Dr. Carbonaro acknowledged that clinical trials would be useful in developing further understanding of DOI, and that potential scheduling could impact the speed at which clinical trials could take place. Tr. 1253. However, Dr. Carbonaro testified that she did not believe that scheduling DOI would have a "significant impact" on research. Tr. 1253. Dr. Carbonaro testified that much of the data that has been published concerning DOI "seemed to be in labs that have Schedule I Researcher registrations." Tr. 1254. Dr. Carbonaro testified that she believes that "all research is good," and thus agreed that it would be important to continue studying DOI for its potential anti-addictive properties. Tr. 1260. However, Dr. Carbonaro testified that she believed science remains "pretty far away from having potential therapeutic uses of DOI." Tr. 1253. Dr. Carbonaro did agree that overall, understating the potential therapeutic uses of DOI would benefit the general public. Tr. 1263-64.

On redirect, Dr. Carbonaro acknowledged that she did not hear any of the Petitioners' witnesses indicate that they would cease their research in the event DOI is scheduled. Tr. 1263.

ANALYSIS

Pursuant to 21 U.S.C. Section 811(a), "the Attorney General may by rule (1) add to such a schedule . . . if he (A) finds that such drug or other substance has a potential for abuse, and (B) makes with respect to such drug or other substance the findings prescribed by subsection (b) of

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line with doing bona fide research." Tr. 1256.

[243] Dr. Carbonaro testified that there are also situations where "investigators work with . . . another . . . registrant." Tr. 1238.

section 812 of this title for the schedule in which such drug is to be placed." The "[r]ules of the Attorney General under [section 811] shall be made on the record after opportunity for a hearing pursuant to the rulemaking procedures prescribed by [the Administrative Procedure Act]." 21 U.S.C. § 811.

Before initiating a proceeding to control a drug or other substance, the Attorney General shall "after gathering the necessary data, request from the Secretary[244] a scientific and medical evaluation, and his recommendations, as to whether such drug or other substance should be so controlled." 21 U.S.C. § 811(b). "The recommendations of the Secretary to the Attorney General shall be binding on the Attorney General as to such scientific and medical matters." *Id.* Upon receipt of the HHS scientific and medical evaluation and recommendation, "[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 . . .." *Id.*

The Attorney General is required to consider the following factors with respect to each drug or other substance proposed to be controlled: (1) "[i]ts actual or relative potential for abuse;" (2) "[s]cientific evidence of its pharmacological effect, if known;" (3) "[t]he state of current scientific knowledge regarding the drug or other substance;" (4) "[i]ts history and current pattern of abuse;" (5) "[t]he scope, duration, and significance of abuse;" (6) "[w]hat, if any, risk there is to the public health;" (7) "[i]ts psychic or physiological dependence liability;" and (8) "[w]hether the substance is an immediate precursor of a substance already controlled under this subchapter." 21 U.S.C. § 811(c).

"Except where control is required by United States obligations under an international treaty . . . and except in the case of an immediate precursor, a drug or other substance may not be placed in any schedule unless the findings required for such schedule are made with respect to such drug or other substance." 21 U.S.C. § 812(b). Placement of a drug or other substance into Schedule I requires finding that: (A) "[t]he drug or other substance has a high potential for abuse;" (B) "[t]he drug or other substance has no currently accepted medical use in treatment in the United States;" and (C) "[t]here is a lack of accepted safety for use of the drug or other substance under medical supervision." 21 U.S.C. § 812(b)(1)(A)-(C). Notably, a drug or other

[244] The Secretary of HHS. *See* 21 U.S.C. § 802(24).

substance may only be placed in one of the other four remaining schedules if "[t]he drug or other substance has a currently accepted medical use in treatment in the United States."[245] 21 U.S.C. § 812(b)(2)(B), (3)(B), (4)(B), (5)(B).

As the proponent for the issuance of the proposed rule, the Government has the burden of proof. 21 C.F.R. § 1316.56. The burden of proof at this administrative hearing is a preponderance-of-the-evidence standard. *Steadman v. SEC*, 450 U.S. 91, 100-01 (1981). The Administrator's factual findings will be sustained on review to the extent they are supported by "substantial evidence." *Hoxie v. DEA*, 419 F.3d 477, 482 (6th Cir. 2005). The Supreme Court has defined "substantial evidence" as such "relevant evidence as a reasonable mind might accept as adequate to support a conclusion." *Consolidated Edison Co. v. NLRB*, 305 U.S. 197, 229 (1938). While "the possibility of drawing two inconsistent conclusions from the evidence" does not limit the Administrator's ability to find facts on either side of the contested issues in the case, *Shatz v. U.S. Dep't of Justice*, 873 F.2d 1089, 1092 (8th Cir. 1989) (citing *Trawick v. DEA*, 861 F.2d 72, 77 (4th Cir. 1988) (quoting *Consolo v. Fed. Mar. Comm'n*, 383 U.S. 607, 620 (1966))), all "important aspect[s] of the problem," such as evidence or explanations that runs counter to the Government's evidence, must be considered. *Wedgewood Vill. Pharmacy v. DEA*, 509 F.3d 541, 549 (D.C. Cir. 2007) (citing *Morall v. DEA*, 412 F.3d 165, 177 (D.C. Cir. 2005)). The ultimate disposition of the case must "be in accordance with the weight of the evidence, not simply supported by enough evidence to justify, if the trial were to a jury, a refusal to direct a verdict when the conclusion sought to be drawn from it is one of fact for the jury." *Steadman*, 450 U.S. at 99 (internal quotation marks omitted).

Regarding the exercise of discretionary authority, the courts have recognized that gross deviations from past agency precedent must be adequately supported, *Morall*, 412 F.3d at 183, but "mere unevenness" in application does not, standing alone, render a particular discretionary action unwarranted. *Chein v. DEA*, 533 F.3d 828, 835 (D.C. Cir. 2008) (citing *Morall*, 412 F.3d at 183 (quoting *Butz v. Glover Livestock Comm'n Co.*, 411 U.S. 182, 188 (1973))). It is well-settled that since the Administrative Law Judge has had the opportunity to observe the demeanor and conduct of hearing witnesses, the factual findings set forth in this Recommended Decision are entitled to significant deference, *Universal Camera Corp. v. NLRB*, 340 U.S. 474, 496

[245] A drug or other substance may also be placed in Schedule II if it has "a currently accepted medical use with severe restrictions." 21 U.S.C. § 812(b)(2)(B).

(1951), and that this Recommended Decision constitutes an important part of the record that must be considered in the Administrator's decision. *Morall*, 412 F.3d at 179. However, any recommendations set forth herein regarding the exercise of discretion are by no means binding on the Administrator and do not limit the exercise of that discretion. 5 U.S.C. § 557(b); *River Forest Pharmacy, Inc. v. DEA*, 501 F.2d 1202, 1206 (7th Cir. 1974); *Attorney General's Manual on the Administrative Procedure Act* § 8 (1947).

SCHEDULING OF DOI AND DOC

Consideration of the Eight Factors under 21 U.S.C. § 811(c)

The CSA requires the consideration of eight factors with respect to each drug or other substance proposed to be controlled or removed from the schedules of controlled substances. 21 U.S.C. § 811(c); *see supra* at 97.

(1) Actual or Relative Potential for Abuse

The substantial evidence standard requires consideration of "whether there is substantial evidence in the administrative record to support the Administrator's determination that [a drug or substance] is 'so related in [its] action to a drug or drugs already listed as having a high potential for abuse' that it is likely [the drug or substance] 'will have the same potentiality for abuse as such drugs.'" *Grinspoon v. DEA*, 828 F.2d 881, 895 (1st Cir. 1987).

As detailed above, the legislative history of the CSA suggests the consideration of four prongs in determining whether a particular drug or substance has a potential for abuse under Factor 1 of 21 U.S.C. § 811(c): a) if individuals are taking the drug or substance in amounts sufficient to create a hazard to their health or to the safety of others or to the community ("Abuse Factor A"); b) if there is significant diversion of the drug or substance from legitimate channels ("Abuse Factor B"); c) if individuals are taking the drug or substance on their own initiative rather than on the basis of medical advice from a properly licensed practitioner ("Abuse Factor C"); and d) if the drug is a new drug so related in its action to a drug or substance already listed as having a potential for abuse such that it is likely the new drug or substance will have the same potential for abuse ("Abuse Factor D"). Tr. 95, 157, 398; Gov't Ex. 7A at 3-4.

Regarding Abuse Factor A, there is substantial record evidence that DOI and DOC have already been encountered by law enforcement in the United States and that there are already individuals using DOI and DOC for their hallucinogenic effects in amounts sufficient to create a health hazard. Tr. 96, 159-62; Gov't Ex. 7A at 3-4.

Petitioners addressed this factor, but ultimately did not present any substantial evidence that contradicts these findings. Specifically, Dr. de la Fuente Revenga argued that the number of law enforcement encounters with DOI was "miniscule compared to any other drugs" in the same category and thus indicative that individuals are not using DOI regularly, but failed to offer any specific comparison in support of his argument. *See supra* at 85. Dr. de la Fuente Revenga also failed to explain why he believed that DEA's analysis of DOI abuse probability "lacks in quantitative data analysis and true assessment of the depth." *Id*. Further, Dr. Elder contested the evidentiary value of anecdotal evidence of DOI usage, but acknowledged that anecdotal reports could be legitimately collected and published as part of a larger study. *See supra* at 58. Dr. Elder also failed to address the above noted law enforcement encounters with DOI as verifiable evidence of usage. *Id*.

Accordingly, this tribunal finds that Abuse Factor A weighs towards a finding that DOI and DOC have a potential for abuse.

Regarding Abuse Factor B, there is substantial record evidence that although DOI and DOC are available for legitimate purchase and use in scientific research, DOI and DOC are not approved as drug products for medical use in the United States, thus there are no *applicable*, legitimate drug channels from which DOI and DOC can be diverted. Tr. 96-97, 752, 1163, 1262-63; Gov't Ex. 7A at 4.

Petitioners addressed this factor, but ultimately did not present any substantial evidence that contradicts these findings. Specifically, Dr. Elder and Dr. de la Fuente Revenga discussed diversion potential in the context of the legitimate purchase and use of DOI and DOC for scientific research, which, as noted, is not applicable to the current matter. *See supra* at 59, 86.

Accordingly, this tribunal finds that Abuse Factor B weighs neither for nor against a finding that DOI and DOC have a potential for abuse.

Regarding Abuse Factor C, there is substantial record evidence that individuals are taking DOI and DOC on their own initiative rather than on the basis of medical advice from a properly licensed practitioner because, as noted above, there are individuals using DOI and DOC even

though DOI and DOC are not approved as drug products for medical use in the United States. Tr. 98, 752, 1163, 1262-63; Gov't Ex. 7A at 4.

Petitioners addressed this factor, but ultimately did not present any substantial evidence that contradicts these findings. When asked about this factor, Dr. de la Fuente Revenga again pointed to an alleged absence of DOI usage without offering any specific evidence to support his claim. *See supra* at 85-86.

Accordingly, this tribunal finds that Abuse Factor C weighs towards a finding that DOI and DOC have a potential for abuse.

Finally, regarding Abuse Factor D, there is substantial record evidence that the effects and action of DOI and DOC are similar to other schedule I hallucinogens, such as DOM and LSD, that are already listed as having a potential for abuse, and thus it is likely that DOI and DOC will have the same potential for abuse. Tr. 100-06, 147, 184, 186, 188, 392-93, 521, 1175-76, 1189, 1192, 1225-26, 1243-44; Gov't Ex. 7A at 4-5.

Petitioners addressed this factor, but ultimately did not present any substantial evidence that contradicts these findings. Specifically, Dr. de la Fuente Revenga contested categorizing DOI and DOC as "new" drugs, but also acknowledged that DOI and DOC are similar in pharmacological effects and action to DOM and LSD. *See supra* at 86.

Accordingly, this tribunal finds that Abuse Factor D weighs towards a finding that DOI and DOC have a potential for abuse.

In sum, upon consideration of the four prongs used to determine whether a particular drug or substance has a potential for abuse, this tribunal finds that three out of the four prongs weigh towards a finding that DOI and DOC have a potential for abuse. As such, this tribunal finds that the record contains substantial evidence of the potential for abuse of DOI and DOC under Factor 1 of 21 U.S.C. § 811(c).

Accordingly, this tribunal finds that Factor 1 of 21 U.S.C. § 811(c) weighs in favor of the scheduling of DOI and DOC.

(2) Scientific Evidence of Pharmacological Effect

As detailed above, and in consideration of the scientific evidence of DOI and DOC's pharmacological effects pursuant to Factor 2 of 21 U.S.C. § 811(c), this tribunal finds that there is substantial record evidence that DOI and DOC produce their respective pharmacological

effects through the same primary biological means that other schedule I hallucinogens, such as DOM and LSD, produce their own through, and with very similar pharmacological effects. Tr. 106-14, 115-18, 143-44; Gov't Ex. 7A at 5-8.

Petitioners addressed this factor, but ultimately did not present any substantial evidence that contradicts these findings. While Dr. Jaster contested the overall abuse liability of DOI in comparison to other substances like cocaine and amphetamines, Dr. Jaster also acknowledged the similarities between DOI and other schedule I hallucinogens in structure, action, and effects. *See supra* at 44-46. Further, while Dr. Elder pointed to some of the differences between DOI and other schedule I psychedelics in action, as well as speculated that the potential effects of DOI might be different or to a different level, he too acknowledged that "DOI shares core features" with the classic schedule I psychedelics such as LSD. *See supra* at 60. Dr. Cameron also testified to the similarities in structure, action, and effects between DOI and DOC and substances like DOM and LSD. *See supra* at 66.

Accordingly, this tribunal finds that Factor 2 of 21 U.S.C. § 811(c) weighs in favor of the scheduling of DOI and DOC.

(3) The State of Current Scientific Knowledge

As detailed above, and in consideration of the state of current scientific knowledge regarding DOI and DOC pursuant to Factor 3 of 21 U.S.C. § 811(c), this tribunal finds that there is substantial record evidence that the chemistry of DOI and DOC is known. Tr. 118; Gov't Ex. 7A at 8. This tribunal also finds that there is substantial record evidence that it is known that DOI and DOC are similar to other schedule I controlled substances. Tr. 119, 144; Gov't Ex. 7A at 8-9. Further, this tribunal finds that there is substantial record evidence that DOI and DOC are not currently available as or included in any approved medical drug products in the United States or any other country. Tr. 123; Gov't Ex. 7A at 9. Finally, this tribunal finds that there is substantial record evidence that there is no official information available regarding any potential medical uses for DOI and DOC. Tr. 123, 144. Petitioners did not directly address this factor in their testimony. However, in their post-hearing brief, SSDP/Ramos state "[p]etitioners do not dispute the fact that DOI and DOC are chemically similar to other psychedelics like DOM in that it has an affinity for the 5-HT2 serotonin receptors." ALJ Ex. 87 at 19 (citing Gov't Ex. 7 at 5).

Accordingly, this tribunal finds that Factor 3 of 21 U.S.C. § 811(c) weighs in favor of the scheduling of DOI and DOC.

(4) History and Current Pattern of Abuse

As detailed above, and in consideration of the history and current pattern of abuse regarding DOI and DOC pursuant to Factor 4 of 21 U.S.C. § 811(c), this tribunal finds that there is substantial record evidence that U.S. law enforcement has encountered DOI and DOC over the last twenty years. Tr. 96, 159-62; Gov't Ex. 7A at 3-4, 9. This tribunal also finds that there is substantial record evidence that U.S. law enforcement has encountered DOI and DOC in various forms including powder, tablets, capsules, liquid, and blotter paper. Tr. 419; Gov't Ex. 7A at 9. Further, this tribunal finds that there is substantial record evidence that individuals are using street substances they identify as DOI and DOC for their hallucinogenic effects. Tr. 96, 159-62; Gov't Ex. 7A at 3-4, 9. This tribunal also finds that there is substantial record evidence that DOI and DOC have been documented producing effects similar to those of schedule I hallucinogens such as DOM, LSD, and DMT. Tr. 144-45; Gov't Ex. 7A at 9-10. This tribunal finds that there is substantial record evidence that based on data collected from the UN including available abuse data, public health risk data, and drug trafficking data, the WHO has recommended to the UN that DOC be controlled internationally. Tr. 240-41; Gov't Ex. 7A at 10. Finally, this tribunal finds that there is substantial record evidence that in March 2020, the UN Commission on Narcotic Drugs voted to place DOC into its own schedule I of the 1971 Convention of Psychotropic Substances. Tr. 242-44; Gov't Ex. 7A at 10.

Petitioners addressed this factor, but ultimately did not present any substantial evidence that contradicts these findings. Although Dr. Palamar argued that what he characterized as the low reporting by individuals of DOI and DOC use in the NSDUH data suggests low use in general, he also indicated that he would not "personally . . . directly equate prevalence to risk" as well as failed to fully explain why this reporting of DOI and DOC use should be considered low enough to dismiss. *See supra* at 80. Specifically, Dr. Palamar did not offer a comparison to the relevant data regarding schedule I hallucinogens such as DOM, LSD, and DMT, other than to note that only a "handful" of psychedelics are included in the NSDUH and that the DOx class of drugs has never been included in the NSDUH. *Id.* Dr. Palamar also pointed to what he characterized as a low prevalence of DOI and DOC in New York City nightclub and festival

attendee self-reporting and NDEWS Rapid Street Reporting Initiative surveys, but again failed to fully explain why this reporting should be considered low enough to dismiss, and again failed to offer a comparison to any similar reporting regarding other schedule I hallucinogens. *See supra* at 80-81.

Accordingly, this tribunal finds that Factor 4 of 21 U.S.C. § 811(c) weighs in favor of the scheduling of DOI and DOC.

(5) Scope, Duration, and Significance of Abuse

As detailed above, and in consideration of the scope, duration, and significance of abuse regarding DOI and DOC pursuant to Factor 5 of 21 U.S.C. § 811(c), this tribunal finds that there is substantial record evidence that there has been significant availability, trafficking, and abuse of DOI and DOC evidenced by NFLIS-Drug data, which found, since 2005, at least 830 encounters by U.S. law enforcement with at least one of these substances, found in a variety of forms, and across at least 39 states. Tr. 125-27, 129-30, 203-04; Gov't Ex. 7A at 10. This tribunal further finds that there is substantial record evidence that there has been significant availability, trafficking, and abuse of DOI and DOC evidenced by five submissions of DOI and two submissions of DOC reported in the Microgram Bulletins since 2006, with the substances again found in multiple forms across multiple states. Gov't Ex. 7A at 10-11.

Dr. Carbonaro testified that although the definition of "significant" varies from drug to drug, approximately 800 reported encounters with DOI and DOC is "pretty significant compared to some of the other drugs in NFLIS-Drug." Tr. 204. Although Dr. Carbonaro did not offer a specific comparison to the relevant data regarding any schedule I hallucinogens such as DOM, LSD, or DMT, Dr. Carbonaro testified that there is not "one definition of significance" and that considerations of significance would account for the totality of encounters with a drug and would be only "one part of the analysis." Tr. 203, 206-07. Dr. Carbonaro ultimately asserted that she would consider "any evidence" of abuse as "significant" evidence. Tr. 206-07.

Petitioners addressed this factor, but ultimately did not present any substantial evidence that contradicts these findings. Although Dr. Palamar concluded from the NFLIS-Drug data that the availability of DOI and DOC was insignificant due to what he characterized as relatively low numbers of official incidents and detections involving DOI and DOC, as above, he failed to fully explain why these numbers should be considered low enough to dismiss. *See supra* at 78.

Specifically, and rather than offering a comparison to the relevant data regarding other schedule I hallucinogens, Dr. Palamar only offered a comparison to the reported numbers of incidents involving fentanyl in support of his argument. *Id*. Further, Dr. Palamar admitted that he was not familiar with and has not reviewed the Microgram Bulletins. Tr. 1112.

Accordingly, this tribunal finds that Factor 5 of 21 U.S.C. § 811(c) weighs in favor of the scheduling of DOI and DOC.

(6) Risk to the Public Health

As detailed above, and in consideration of the risk to the public health regarding DOI and DOC pursuant to Factor 6 of 21 U.S.C. § 811(c), this tribunal finds that there is substantial record evidence that DOC creates a public health risk through DOC's documented ability to induce a variety of adverse health effects alone and/or in combination with other substances, with such adverse health effects including hallucinogenic effects, sensory distortions, impaired judgment, dangerous behavior, seizures, loss of consciousness, organ failure, and death. Tr. 134-37, 146, 175-77; Gov't Ex. 7A at 11-12. Regarding DOI, this tribunal finds that there is substantial record evidence that DOI too creates a public health risk because the structural similarity between DOI and DOC results in a likelihood that DOI could produce similar adverse health effects to those documented from use of DOC. Tr. 134-37, 146, 175-77; Gov't Ex. 7A at 11-12. Petitioners did not directly address this factor in their testimony. To the extent Petitioners' witnesses touched on this factor in conjunction with their discussion of other factors, that has been considered *infra* as part of this Recommended Decision.

Accordingly, this tribunal finds that Factor 6 of 21 U.S.C. § 811(c) weighs in favor of the scheduling of DOI and DOC.

(7) Psychic or Physiological Dependence Liability

As detailed above, and in consideration of the psychic or physiological dependence liability regarding DOI and DOC pursuant to Factor 7 of 21 U.S.C. § 811(c), this tribunal finds that there is substantial record evidence that while the physiological dependence liability of DOI and DOC is not specifically reported in scientific and medical literature – and thus cannot be definitively determined – DOI and DOC can be considered "highly abusable," psychologically, with similar pharmacological effects to schedule I hallucinogens such as DOM, LSD, and DMT,

all substances which, while not usually associated with physical dependence, can involve strong psychological dependence. Tr. 140-41, 271-74, 146, 268; Gov't Ex. 7A at 12. Petitioners did not directly address this factor in their testimony. To the extent Petitioners' witnesses touched on this factor in conjunction with their discussion of other factors, that has been considered *infra* as part of this Recommended Decision.

Accordingly, this tribunal finds that Factor 7 of 21 U.S.C. § 811(c) weighs in favor of the scheduling of DOI and DOC.

(8) Immediate Precursors

The parties stipulated that "DOI and DOC are not immediate precursors of any controlled substance of the CSA as defined by 21 U.S.C. 802(23)." Stipulation 4. Therefore, based on the stipulation, and as further detailed above, and in consideration of any immediate precursors regarding DOI and DOC pursuant to Factor 8 of 21 U.S.C. § 811(c), this tribunal finds that there is substantial record evidence that DOI and DOC are not immediate precursors of any substance already controlled under the CSA as defined by 21 U.S.C. § 802(23), thus Factor 8 does not apply to DOI and DOC. Tr. 142; Gov't Ex. 7A at 12.

Accordingly, this tribunal finds that Factor 8 of 21 U.S.C. § 811(c) does not weigh either for or against the scheduling of DOI and DOC.

In sum, upon consideration of the eight factors under 21 U.S.C. § 811(c), this tribunal finds that there is substantial record evidence that seven out of the eight factors weigh in favor of the scheduling of DOI and DOC. As detailed above, this tribunal finds that there is substantial record evidence that DOI and DOC share similar actions and effects with other schedule I hallucinogens, while not currently available or considered for any medical use and harboring a noteworthy potential for both abuse and public health risk. Further, this tribunal finds that there is substantial record evidence that there have already been a multitude of documented encounters and incidents involving potential abuse of DOI and DOC.

Accordingly, this tribunal finds that consideration of the eight factors of 21 U.S.C. § 811(c) weighs in favor of the scheduling of DOI and DOC.

Consideration of the Three Factors under 21 U.S.C. § 812(b)

The CSA requires the evaluation of a drug or other substance's abuse potential, accepted medical use, and safety for use under medical supervision for placement in the appropriate CSA schedule – I, II, III, IV, or V. 21 U.S.C. § 812(b); *see supra* at 97-98. The tribunal finds that DOI and DOC meet the following criteria for placement in Schedule I of the CSA pursuant to 21 U.S.C. § 812(b)(1).

(A) High Potential for Abuse

As described above in the analysis for Factor 1 of 21 U.S.C. § 811(c), the legislative history of the CSA suggests the consideration of four prongs in determining whether a particular drug or substance has a potential for abuse: a) if individuals are taking the drug or substance in amounts sufficient to create a hazard to their health or to the safety of others or to the community ("Abuse Factor A"); b) if there is significant diversion of the drug or substance from legitimate channels ("Abuse Factor B"); c) if individuals are taking the drug or substance on their own initiative rather than on the basis of medical advice from a properly licensed practitioner ("Abuse Factor C"); and d) if the drug is a new drug so related in its action to a drug or substance already listed as having a potential for abuse such that it is likely the new drug or substance will have the same potential for abuse ("Abuse Factor D"). Tr. 95, 157, 398; Gov't Ex. 7A at 3-4.

Regarding the requirements for schedule placement under the CSA, and in consideration of the high potential for abuse of DOI and DOC pursuant to Factor A of 21 U.S.C. § 812(b)(1), this tribunal finds and reiterates that there is substantial record evidence that three out of the four prongs described above weigh towards a finding that DOI and DOC have a high potential for abuse.

Regarding Abuse Factor A, this tribunal finds and reiterates that there is substantial record evidence that DOI and DOC have been encountered by law enforcement in the United States since 2005 and that there are already individuals using DOI and DOC for their hallucinogenic effects in amounts sufficient to create a health hazard. Tr. 96, 159-62; Gov't Ex. 7A at 3-4, 13. As described above, Petitioners addressed this factor, but ultimately did not present any substantial evidence that contradicts these findings. Accordingly, this tribunal finds that Abuse Factor A weighs towards a finding that DOI and DOC have a high potential for

abuse.

Regarding Abuse Factor B, this tribunal finds and reiterates that there is substantial record evidence that although DOI and DOC are available for legitimate purchase and use in scientific research, DOI and DOC are not approved as drug products for medical use in the United States, thus there are no *applicable,* legitimate drug channels from which DOI and DOC can be diverted. Tr. 96-97, 752, 1163, 1262-63; Gov't Ex. 7A at 4. As described above, Petitioners addressed this factor, but ultimately did not present any substantial evidence that contradicts these findings. Accordingly, this tribunal finds that Abuse Factor B weighs neither for nor against a finding that DOI and DOC have a high potential for abuse.

Regarding Abuse Factor C, this tribunal finds and reiterates that there is substantial record evidence that individuals are taking DOI and DOC on their own initiative rather than on the basis of medical advice from a properly licensed practitioner because, as noted above, there are individuals using DOI and DOC even though DOI and DOC are not approved as drug products for medical use in the United States. Tr. 98, 752, 1163, 1262-63; Gov't Ex. 7A at 4. As described above, Petitioners addressed this factor, but ultimately did not present any substantial evidence that contradicts these findings. Accordingly, this tribunal finds that Abuse Factor C weighs towards a finding that DOI and DOC have a high potential for abuse.

Finally, regarding Abuse Factor D, this tribunal finds and reiterates that there is substantial record evidence that the pharmacological actions and effects of DOI and DOC are similar to other schedule I hallucinogens such that it is likely that DOI and DOC will have the same potential for abuse. Tr. 100-06, 147, 184, 186, 188, 392-93, 521, 1175-76, 1189, 1192, 1225-26, 1243-44; Gov't Ex. 7A at 4-5, 12-13. As described above, Petitioners addressed this factor, but ultimately did not present any substantial evidence that contradicts these findings. Accordingly, this tribunal finds that Abuse Factor D weighs towards a finding that DOI and DOC have a high potential for abuse.

In sum, upon consideration of the four prongs used to determine whether a particular drug or substance has a potential for abuse, this tribunal finds that three out of the four prongs weigh towards a finding that DOI and DOC have a potential for abuse. As such, this tribunal finds that the record contains substantial evidence of a high potential for abuse of DOI and DOC under Factor A of 21 U.S.C. § 812(b)(1).

Accordingly, this tribunal finds that Factor A of 21 U.S.C. § 812(b)(1) supports the

placement of DOI and DOC into Schedule I.

(B) Accepted Medical Use for Treatment in the United States

Regarding the requirements for schedule placement under the CSA, and in consideration of any accepted medical use for treatment with DOI and DOC in the United States pursuant to Factor B of 21 U.S.C. § 812(b)(1), this tribunal finds that there is substantial record evidence that DOI and DOC have no currently accepted medical use for treatment in the United States. Specifically, and as described *supra* at 36-37, DEA uses a five-part test to determine whether there is a currently accepted medical use for a substance, such as with DOI and DOC, where the FDA has not approved a marketing application for a drug product containing the substance for any therapeutic indication. Tr. 147; Gov't Ex. 7A at 13; *United States v. Green*, 222 F. Supp. 3d 267, 271-72 (W.D.N.Y. 2016) (citing *Alliance for Cannabis Therapeutics v. DEA*, 15 F.3d 1131, 1135 (D.C. Cir. 1994)).

Pertaining to part one of the test, this tribunal finds that there is substantial record evidence that the chemistry of DOI and DOC is known and reproducible. Tr. 118-19, 144, 147-48; Gov't Ex. 7A at 5-9.

For part two of the test, this tribunal finds that there is substantial record evidence, from both the Government and Petitioners, that no adequate safety studies have been conducted for DOI and DOC because there have been no clinical trials related to DOI or DOC. Tr. 98, 148, 819, 1234; Gov't Ex. 7A at 7, 13.

Similarly, for part three of the test, this tribunal finds that there is substantial record evidence, from both the Government and Petitioners, that there have not been adequate and well-controlled studies that have proven the efficacy regarding DOI and DOC because there have been no clinical trials related to DOI or DOC. Tr. 98, 148, 819, 1234; Gov't Ex. 7A at 7, 13.

For part four of the test, this tribunal finds that there is substantial record evidence, from both the Government and Petitioners, that DOI and DOC have not been accepted by any qualified experts because, again, there have been no clinical trials related to DOI or DOC. Tr. 98, 149, 819, 1234; Gov't Ex. 7A at 7, 13.

Finally, for part five of the test, this tribunal finds that there is substantial record evidence, from both the Government and Petitioners, that there is no widely available scientific evidence of the efficacy of DOI and DOC because, once more, there have been no clinical trials

related to DOI or DOC. Tr. 98, 149, 819, 1234; Gov't Ex. 7A at 7, 13.

In sum, and in consideration of the above-described five-part test to determine whether there is a currently accepted medical use for DOI and DOC, this tribunal finds substantial record evidence that DOI and DOC have no currently accepted medical use for treatment in the United States. While not addressing the five-part test specifically, Petitioners' witness Dr. Ramos agreed that currently DOI has no accepted medical use. Tr. 686. Furthermore, the parties stipulated that "[t]here is no documentation in medical literature of the human use of DOI." Stipulation 1; *see also* ALJ Exs. 53 at 3, 87 at 13.

Accordingly, this tribunal finds that Factor B of 21 U.S.C. § 812(b)(1) supports the placement of DOI and DOC into Schedule I.

(C) Accepted Safety for Use Under Medical Supervision

Regarding the requirements for schedule placement under the CSA, and in consideration of any accepted safety for use of DOI and DOC under medical supervision pursuant to Factor C of 21 U.S.C. § 812(b)(1), this tribunal finds that there is substantial record evidence that there is no accepted safety for use of DOI and DOC under medical supervision because DOI and DOC do not currently have any accepted medical use. Tr. 150, 686; Gov't Ex. 7A at 13.

Accordingly, this tribunal finds that Factor C of 21 U.S.C. § 812(b)(1) supports the placement of DOI and DOC into Schedule I.

In sum, upon consideration of the three factors under 21 U.S.C. § 812(b)(1), this tribunal finds that there is substantial record evidence that all three factors support the placement of DOI and DOC into Schedule I. As detailed above, this tribunal finds that there is substantial record evidence that DOI and DOC have a high potential for abuse, have no currently accepted medical use for treatment in the United States, and that there is a lack of accepted safety for use of these drugs under medical supervision.

Accordingly, this tribunal finds that consideration of the three factors of 21 U.S.C. § 812(b)(1) supports the placement of DOI and DOC into Schedule I.

International Treaties, Conventions, and Protocols Requiring Control

Under the CSA, "[i]f control is required by United States obligations under international

treaties, conventions, or protocols . . . the Attorney General shall issue an order controlling such drug under the schedule he deems most appropriate to carry out such obligations, without regard to the findings required by [21 U.S.C. Sections 811(a) or 812(b)] and without regard to the procedures prescribed by [21 U.S.C. Section 811(a), (b)]." 21 U.S.C. § 811(d)(1). Additionally, the CSA provides that:

> When the United States receives notification of a scheduling decision pursuant to article 2 of the Convention on Psychotropic Substances that a drug or other substance has been added or transferred to a schedule specified in the notification . . . the Secretary of Health and Human Services[246] after consultation with the Attorney General, shall first determine whether existing legal controls . . . and the controls required by the Federal Food, Drug, and Cosmetic Act, meet the requirements of the schedule specified in the notification or schedule notice and shall take the following action: . . . (B) If such requirements are not met by such existing controls and the Secretary of Health and Humans Services concurs in the scheduling decision or schedule notice transmitted by the notification, the Secretary shall recommend to the Attorney General that he initiate proceedings for scheduling the drug or substance, pursuant to [21 U.S.C. Section 811(a), (b)].

21 U.S.C. § 811(d)(3)(B).

The United States is a party to the 1971 United Nations Convention on Psychotropic Substances ("1971 Convention"). *Notice of Proposed Rulemaking*, 88 Fed. Reg. at 86,280; *Convention on Psychotropic Substances*, Feb. 21, 1971, 32 U.S.T. 543, 1019 U.N.T.S. 175 (as amended). The 1971 Convention grants the Commission on Narcotic Drugs Council ("CND") that authority to add substances into Schedules I-IV. *Convention on Psychotropic Substances* art. 2. On March 4, 2020, CND added DOC to Schedule I of the 1971 Convention. *See* Comm. On Narcotic Drugs, Rep. on Its Sixty-Third Session, U.N. Doc. E/CN.7/2020/15, at 22 (2020). On May 7, 2020, the Secretary-General of the United Nations notified the Secretary of State of the United States of the placement of DOC into Schedule I. Gov't Ex. 9.

Upon the scheduling of new substances by CND, "[a] Party having given such notice with respect to a previously uncontrolled substance added to Schedule I shall take into account,

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[246] *See* Memorandum of Understanding with the National Institute on Drug Abuse, 50 Fed. Reg. 9518, 9519 (1985) (providing that FDA shall act at the lead agency within HHS in carrying out the Secretary's scheduling responsibilities under the CSA, with the concurrence of NIDA); *see also Recommendations for Anabolic Steroids Under Section 1903 of the Anabolic Steroids Act of 1990; Delegation of Authority*, 58 Fed. Reg. 35,460, 35,460 (1993) (delegating the Secretary of HHS's authority to make domestic drug scheduling recommendations to the Assistant Secretary for Health of HHS).

as far as possible, the special control measures enumerated in article 7."[247] *Convention on Psychotropic Substances* art. 2. In addition to the special control measures, parties must "[r]equire licenses for manufacture, trade and distribution as provided in article 8 for substances in Schedule II" and comply with various import and export obligations. *Id.*; *Notice of Proposed Rulemaking*, 88 Fed. Reg. at 86,280.

In their post-hearing brief, SSDP/Ramos "propose that neither the Single Convention[248] nor the CSA requires DEA to place DOC in Schedule I or Schedule II." ALJ Ex. 87 at 41. In supporting this argument, SSDP/Ramos rely on a Memorandum Opinion for the Attorney General issued by the Office of Legal Counsel on April 11, 2024 ("Memorandum Opinion"). *Id.* (citing to 48 Op. O.L.C. __ (April 11, 2024)). SSDP/Ramos assert that "[b]ased upon the Memorandum Opinion . . . DEA is not required to place DOC under Schedule I to comply with international treaty obligations."[249] *Id.*

While the relevance of the Memorandum Opinion to these proceedings appears tenuous,[250] the tribunal nevertheless considers the arguments presented by SSDP/Ramos and finds, even in consideration of the non-binding opinions expressed in the Memorandum Opinion, that SSDP/Ramos' argument is unsuccessful. The Memorandum Opinion finds that "DEA

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[247] The "special control measures" regarding substances in Schedule I direct parties to: (1) "Prohibit all use except for scientific and very limited medical purposes by duly authorized persons . . .;" (2) "Require that manufacture, trade, distribution and possession be under a special license or prior authorization;" (3) "Provide for close supervision of the activities and acts mentioned in [(1)] and [(2)];" (4) Restrict the amount supplied to a duly authorized person to the quantity required for his authorized purpose;" (5) "Require that persons performing medical or scientific functions keep records concerning the acquisition of the substances and the details of their use, such records to be preserved for at least two years after the last use recorded therein;" and (6) "Prohibit export and import except when both the exporter and importer are the competent authorities or agencies of the exporting and importing country or region, respectively, or other persons or enterprises which are specifically authorized by the competent authorities of their country or region for the purpose." *Convention on Psychotropic Substances* art. 7.

[248] SSDP/Ramos' reference to "the Single Convention" is misplaced, as the applicable treaty obligations at issue in these proceedings arise under the 1971 Convention.

[249] SSDP/Ramos propose that DEA may satisfy treaty obligations by "placing DOC in Schedule III through V while imposing additional controls pursuant to the CSA's regulatory authorities," but "believe a more appropriate resolution would be not to schedule DOC and institute additional control measures." ALJ Ex. 87 at 41-42. The lack of a currently accepted medical use for DOC prevents its inclusion in any Schedule outside of Schedule I, pursuant to 21 U.S.C. § 812(b).

[250] The Memorandum Opinion specifically answers questions related to U.S. treaty obligations under the 1961 United Nations Single Convention on Narcotic Drugs with respect to Marijuana.

[may] satisfy the United States' international obligations by *supplementing scheduling decisions* with regulatory action, *at least in circumstances where there is a modest gap* between [treaty obligation] requirements and the specific controls *that follow from a drug's placement on a particular schedule*." 48 Op. O.L.C. at 28 (emphasis added). The Memorandum Opinion concludes this general discussion by stating that the Office of Legal Counsel "believe[s] that the CSA provides DEA with the discretion to decide, at least in some circumstances, that . . . *a scheduling and regulatory approach* is the most appropriate way to strike a balance between the CSA's varied – and potentially conflicting – purposes of curtailing the improper use of drugs with abuse potential, complying with the United States' international obligations, and *ensuring that medically useful drugs* remain available for legitimate purposes." *Id.* at 32 (citing 21 U.S.C. § 801(1), (2), (7)) (emphasis added).

As already discussed, the 1971 Convention requires the United States to undertake minimum requirements with respect to scheduled substances, including requiring appropriate licensure for manufacture, trade, and distribution of such substances. *See Convention on Psychotropic Substances* art. 2. The Memorandum Opinion seemingly only contemplates the use of regulatory action as a supplement to scheduling decisions where a particular schedule presents a "modest" departure from the requirements of a treaty. Pursuant to 21 U.S.C. Section 812(b), a substance that lacks a currently accepted medical use in treatment in the United States is foreclosed from placement in any schedule aside from Schedule I. Accordingly, the only relief available under the theory posited by SSDP/Ramos would involve leaving DOC unscheduled with the addition of "control measures." *See* ALJ Ex. 87 at 42. This is not a situation of a "modest gap" between a drug's placement on a schedule and international obligations, but rather a Marianas Trench between a non-controlled substance and the applicable international treaty obligations. Furthermore, it does not appear that the Memorandum Opinion cited by SSDP/Ramos even contemplates such an arrangement, and rather expresses a (non-binding) opinion that DEA may use regulatory action *in conjunction with* schedule placement to appease treaty requirements.

The relief contemplated by SSDP/Ramos is simply untenable. DOC has been placed in Schedule I of the 1971 Convention. The obligations imposed by such placement necessitate implementation of minimum requirements which cannot be met by DEA without controlling DOC. As the tribunal finds that there is no currently accepted medical use for DOC and that

DEA cannot meet international obligations through regulatory control measures alone, the tribunal ultimately finds that DOC must be controlled under the CSA as a Schedule I substance pursuant to the obligations incurred by the United States under the 1971 Convention.

Potential Research Harm

The Petitioners contend that Scheduling of these two drugs, particularly DOI, would result in harm to researchers who use these drugs in scientific studies. Much of the testimony presented by the Petitioners' witnesses focused on the harm that scheduling of DOI would have on ongoing or future research. In fact, eight of the nine witnesses called by SSDP/Ramos testified regarding research harm.[251] *See supra* at 47-48, 51-55, 61-62, 66-67, 68-69, 70, 72-76, 88-89. Of these witnesses, Dr. Ramos, Dr. Younkin, and Mr. Hennessey are using DOI in their ongoing research projects. Tr. 674, 907, 930.

In describing the research harm that would ensue from the scheduling of DOI as a Schedule I controlled substance, the witnesses referenced the need to obtain a DEA Schedule I researcher registration. According to the testifying witnesses, this harm manifests itself in added time,[252] costs, and administrative burden associated with obtaining a DEA Schedule I registration as well as potential harm that would ensue due to researchers choosing not to use DOI, resulting in scientific discoveries made in less efficient ways or not at all. *See supra* at 47-48, 51-55, 61-62, 66-67, 68-69, 70, 72-76, 88-89; *see also* ALJ Ex. 87 at 24.

In her testimony regarding potential research harm, Dr. Carbonaro largely agreed with the effects on research that would result from needing a Schedule I registration. *See supra* at 37-40, 95-96. However, she initially downplayed the burden to obtain a registration, testifying that applications for such registrations can be processed by DEA in as little as three months.[253] Tr. 247. In her rebuttal testimony, Dr. Carbonaro expanded on her previous testimony by explaining that she only "know[s] the part that DEA is involved in" as to obtaining a Schedule I researcher

[251] Dr. Palamar was the only SSDP/Ramos witness not to testify regarding research harm.
[252] Several of the SSDP/Ramos witnesses testified that the total time to obtain a Schedule I researcher registration would be about a year, based on protocol changes and approvals they would need from their institutions, before they could even submit an application to DEA. Tr. 533, 571, 655-56, 666, 669-72, 876-77, 932, 990.
[253] Dr. Carbonaro acknowledged there may be other requirements that a researcher's institution has that must be met before an application can be submitted to DEA. Tr. 248-49. Institutional requirements were testified to by several of the Petitioners' witnesses. Tr. 47, 54-55, 67.

registration and that the entire timeline to obtain a Schedule I researcher registration "can vary pretty drastically" and that the DEA registration process "could take a year." Tr. 1257.

Based on the testimony of the witnesses, I find that that the Scheduling of DOI would result in research harm.[254] Although the harm to future research is somewhat speculative, I find that there would be harm to current research and that such harm would be particularly acute in the research being conducted by Dr. Ramos and Dr. Younkin. Dr. Ramos detailed that the laboratory that he currently works with does not have a Schedule I registration and that it would take about a year to obtain a Schedule I registration. Tr. 655-56, 666. He further detailed that given that he has two more years of research work and two years of funding remaining, the Scheduling of DOI would cause his research to lose momentum and he may not be able complete his research before funding expires. Tr. 656. Similarly, Dr. Younkin detailed that it would take him at least a year to get a Schedule I registration so that he could use DOI to continue his current research with zebrafish. Tr. 932.

Having established that research harm will occur, the tribunal turns to the question as to whether research harm falls within the criteria to be considered for whether to schedule a drug. The factors to be considered under the 8-factor analysis and the 3-factor analysis have already been discussed and evaluated *supra*. None of these factors specify that the effect on research with the drug is a matter that should be considered. However, in their post-hearing brief, SSDP/Ramos contend that research harm may properly be considered under Factor 6 (risk to public health) of the 8-factor analysis. *See* ALJ Ex. 87 at 22-28. SSDP/Ramos argue that "[h]eretofore, [Factor 6] has been taken to mean the negative impact that a drug may have on public health," but that the "positive impact" of DOI and DOC "to unlock the solutions of some of the largest public health threats" and "to help scientists understand the mechanisms of the body and brain" should also be considered. ALJ Ex. 87 at 23. SSDP/Ramos then argue that a cost-benefit analysis for scheduling of DOI and DOC shows there are "almost no harms" associated with their human use, but that they are "vital" to research. ALJ Ex. 87 at 23-24. However, SSDP/Ramos do not point to any case law in support of their proposition that research

[254] Although passing general references were made about the use of DOC in research, there was no specific testimony about research harm ensuing from the scheduling of DOC. Therefore, the tribunal is unable to make a finding that research harm would result from scheduling DOC.

harm can properly be considered under Factor 6, much less that a cost-benefit analysis should be performed that pits the risks of harm to individuals against the risks of harm to research.

In its post-hearing brief, the Government counters that the courts have addressed the consideration of research harm as part of the statutory factors analyzed for the scheduling of drugs and found that it should have no bearing on the placement of a drug in Schedule I. ALJ Ex. 86 at 31-32 (citing *Grinspoon v. DEA*, 828 F.2d 881 (1st Cir. 1987)). The Government aptly points, in part, to this passage from the First Circuit's ruling in *Grinspoon*:

> [The Petitioner] has identified nothing in the CSA, its legislative history, or its implementing regulations that can be read to require the Administrator to consider the impact of a scheduling determination upon legitimate scientific research. From our review of the CSA, we can only conclude that Congress has already weighed the costs and benefits of legitimate research on dangerous drugs and has determined, in a categorical manner that if the three Schedule I criteria are satisfied, *see* 21 U.S.C. § 812(b)(1), then the substance should be subject to Schedule I controls even if this action will create administrative and other burdens for researchers.

Grinspoon, 827 F.2d at 897.

Based on the absence in the statute of any mention that research harm should be considered under the relevant factors as well as the First Circuit's affirmative finding that research harm is not considered if a drug otherwise satisfies the criteria for placement in Schedule I, the tribunal finds that any evidence of research harm does not factor into the determination of the scheduling of DOI and DOC. In making a finding that the effect of scheduling on research cannot be properly considered under the statutory construct for the scheduling of drugs and the applicable case law, this tribunal does not discount the value of research. On the contrary, the tribunal was impressed by the past and current research conducted by the Petitioners' witnesses and with the dedication and sacrifices they have made to pursue their research with professionalism and academic rigor. However, the tribunal cannot recommend the prioritization of research pursuits over the protection of public health, by recommending that DOI and DOC remain uncontrolled drugs, where DOI and DOC have been shown to meet the criteria under the 8-factor test and the 3-factor test (and in the case of DOC under the 1971 Convention) to be controlled as Schedule I drugs.

RECOMMENDATION

Considering the entire record before me, I find that the record contains substantial evidence regarding the eight factors required for consideration under 21 U.S.C. § 811(c) to support recommending the scheduling of DOI and DOC. Furthermore, I find that the record contains substantial evidence regarding the three factors required for consideration under 21 U.S.C. § 812(b)(1) to support recommending the placement of DOI and DOC in Schedule I. Finally, I find that the international treaty obligations of the United States under the 1971 Convention support recommending the scheduling of DOC as a Schedule I controlled substance.

Dated: June 20, 2025

PAUL SOEFFING
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PAUL E. SOEFFING
U.S. Administrative Law Judge

CERTIFICATE OF SERVICE

This is to certify that the undersigned, on June 20, 2025, caused a copy of the foregoing to be delivered to the following recipients: (1) Frank W. Mann, Esq., Counsel for the Government, via email at Francis.W.Mann@dea.gov and to the DEA Government Mailbox at dea.registration.litigation@dea.gov; (2) Kayla L. Kreinheder, Esq., Counsel for the Government, via email at Kayla.L.Kreinheder@dea.gov and to the DEA Government Mailbox at dea.registration.litigation@dea.gov; (3) Alexis B. Attanasio, Esq., Counsel for the Government, via email at Alexis.B.Attanasio@dea.gov and to the DEA Government Mailbox at dea.registration.litigation@dea.gov; (4) Paul A. Dean, Esq., Counsel for the Government, via email at Paul.A.Dean@dea.gov and to the DEA Government Mailbox at dea.registration.litigation@dea.gov; (5) David Heldreth, CEO of Panacea Plant Sciences, via email at davidh@panaceaplantsciences.net; (6) Brett J. Phelps, Esq., Counsel for Science Policy Council, Students for Sensible Drug Policy, via email at brett@brettphelpslaw.com; and (7) Robert T. Rush, Esq., Counsel for Dr. Raul A. Ramos, via email at rrush@rrushlaw.com.

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Tayonna A. Eubanks
Secretary (CTR)
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