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

Thursday,
November 14, 2024

700 Army Navy Drive
Arlington, Virginia

The above-entitled matter came on for hearing, pursuant to notice, at 9:00 a.m. EST

BEFORE:

THE HONORABLE PAUL E. SOEFFING,
Administrative Law Judge

APPEARANCES:

On Behalf of the Government:

FRANK W. MANN, ESQ.
KAYLA L. KREINHEDER, ESQ.
ALEXIS B. ATTANASIO, ESQ.
Office of Chief Counsel
Drug Enforcement Administration
8701 Morrissette Drive
Springfield, VA 22152
(571) 362-7908

On Behalf of the Science Policy Counsel, Students for Sensible Drug Policy:

BRETT PHELPS, ESQ.
Phelps Law Office
1917 Hot Springs Boulevard
Las Vegas, NM 87701
brett@brettphelpslaw.com
(505) 425-5129

On Behalf of Dr. Raul A. Ramos:

ROBERT T. RUSH, ESQ.
Law Office of Robert T. Rush
600 17th Street
Suite 2800 South
Denver, CO 80202
rrush@rrushlaw.com
(201) 759-1493

ALSO PRESENT:

THERESA M. CARBONARO, Goverment's Expert
T.J. GLEASON, Law Clerk
ALAINA M. JASTER, Petitioner's Expert

CONTENTS

P-R-O-C-E-E-D-I-N-G-S

(9:03 a.m.)

JUDGE SOEFFING: Very good. We're back on the record. Dr. Ramos is on the stand. I remind you, Dr. Ramos, you're still under oath. And Mr. Mann, you may conduct your voir dire of the witness.

VOIR DIRE

BY MR. MANN:

Q Good morning, Dr. Ramos.

A Good morning.

Q Dr. Ramos, have you ever worked with a Schedule I controlled substance?

A I have not. No.

Q Have you ever tested or used a psychedelic in any research?

A Yes, I have been working every day with DOI for the last two and a half years.

Q And the purpose, is that to assess the use of DOI as a therapy?

A My research, at its core, because my research is basic neuroscience where I perform experiments in rodent models, the premise of my research has the potential to inform future therapies in humans.

Q All right. Are you testing any other psychedelics?

A Just DOI.

Q No other scheduled controlled substances?

A No, sir.

Q Are you testing any non-controlled substances other than DOI?

A My research is primarily focused on DOI.

Q What are you planning to testify about today?

A I'm planning to testify about the potential anti-pain properties of DOI.

Q That's all you're testifying about, correct?

A I'm not sure how much -- I can't predict --

Q What are you testifying about today?

JUDGE SOEFFING: Hold on one second. The mic is apparently too close here.

THE WITNESS: Okay. Yeah, yeah.

JUDGE SOEFFING: Sorry.

THE WITNESS: I find the question confusing because I can't predict what the future is, right? I'm here to answer questions for both

my party and the Government's party.

MR. MANN: All right. One moment. Is it fair to say, Dr. Ramos, that you will testify about the study of serotonin and serotonin receptors, that it is fundamental for advancing our understanding of the brain as well as the spinal cord and the peripheral nervous system?

THE WITNESS: Yes, sir.

BY MR. MANN:

Q And that you will primarily testify about your current research, is that correct?

A Yes, sir.

Q And that you are not here to testify about the Eight Factor test, is that correct?

A Yes, sir.

Q Thank you. Now, I want to look at your CV. That would be Exhibit 81. Do you have that in front of you? Now, it would be fair to say that DOI is not mentioned anywhere in your CV. Is that correct?

A Yes, sir.

Q And do any of these publications concern DOI?

A No, I think that we couldn't --

Q Yes or no?

A No.

Q Do any of these research grants concern DOI?

A Yes.

Q Which one?

A The Hannah H. Gray Fellow Award by the Howard Hughes Medical Institute.

Q Okay. And that is a project that is ongoing, correct?

A Yes, sir.

Q All right. Do you have a copy of your research proposal for that?

A Not on me.

Q You didn't bring that. Do you have a copy of the research protocol for that?

A Not on me.

Q You didn't bring that. Is that correct?

A Yes, sir.

Q All right. And you're not testing any other psychedelics to determine the effects on somatosensory perceptions, correct?

A No, sir. Just DOI.

Q And you've been working on this, I'm sorry, I asked you that already. You've been working on this project for two years?

A Yes, sir.

Q And you have at least two years more to go, is that correct?

A Yes, sir.

Q And you don't know the full effects of DOI on somatosensory perception, do you?

A No, sir.

Q And you've authored no papers on this particular specialty, this effect of DOI on somatosensory perception, correct?

A Not yet.

Q And none of your work on DOI has been peer reviewed?

A Not yet.

Q And none of it has been published, is that correct?

A Not yet.

Q Now, I noticed that in your CV you wrote, fellows will receive, and I'm reading from the top of page two, fellows will receive funding through their academic institution for postdoctoral training. Is that correct?

A Yes, sir.

Q So you're still in training, aren't you?

A That is how scientists generally talk

about their work.

Q Yes or no, are you still in training?

A Yes. Yes.

Q And this research grant dealing with the Miller Postdoctoral Research Fellowship Award, that has nothing to do with psychedelics, does it not?

A The award was given to me for the study of MDMA, and I've been using the funding to study DOI because the grant allowed the breathing room.

Q So we're talking about the same grant, 2022 to 2025?

A Yes, sir.

Q But you're not studying MDMA?

A No. The grant gave me the opportunity to refocus my research on DOI.

Q Could you tell me, Doctor, your study is, it's fair to say your study is only half done, correct?

A Yes, sir.

Q Could you tell me how engaging in a half completed study qualifies you to be an expert in the effects of psychedelics on somatosensory perception when you don't even know the full effects of somatosensory perception?

A Yes, sir. I can tell you how that qualifies me as an expert. I've spent the last 10 years training in experimental neuroscience techniques. I've been reading about somatosensation and performing experiments on touch, itch, and pain neurons since 2019. This project, I've been thinking about it intellectually for probably over five years and been working on it every day for the last two and a half years. This is not science. Doesn't happen overnight. Science is slow and it takes a long time. Biology is slow. So saying that I'm not an expert because there are no publications is a mischaracterization of my expertise.

Q Well, I'm not trying to mischaracterize anything. I'm just telling -- I think you testified that you do not know the full effects of DOI on somatosensory perception, and you're not researching any other psychedelics. And apparently you're being offered as an expert in the effects of psychedelics on somatosensory perception. So is that a mischaracterization?

A No.

MR. MANN: Your Honor, this witness is certainly not an expert in psychedelics,

hallucinogens, drug abuse, drug addiction. He has no published works on hallucinogens. His research is only half done. It appears he's going to testify only about his project. He's not going to testify about the Eight Factor test. And based on his prior testimony yesterday, it appears he's only going to testify about the perceived difficulties he thinks he may face if DOI -- DOC and DOI are scheduled. He's not an expert on how scheduling a controlled substance affects research as a whole. He's certainly not an expert in research techniques. He's not being offered for that.

And so I see no reason here to qualify him as an expert. If he's going to testify about what he thinks the scheduling of DOI or DOC might have on his research, he could be offered as a fact witness. But there's no need to qualify him as an expert for the purposes of his testimony today.

JUDGE SOEFFING: Thank you, Mr. Mann. Mr. Phelps, your position?

MR. PHELPS: Yes.

JUDGE SOEFFING: Come on up to the podium.

VOIR DIRE

BY MR. PHELPS:

Q So, Dr. Ramos, could you explain the context of what it means that you are in training in the academic world?

A Yes. Being a scientist means that you're a lifelong learner, and so you're always learning and always in training. We're trained by people who are more senior than us, and we learn from people that are more junior than us. It's very common language in science to refer to almost any stage of your career as training.

It's even in the language of grants. You often receive grants that are called training grants because they give you the money to perform science that's going to improve your abilities. So it's really common to use the word training at almost any stage of the scientific career. Yes.

BY MR. PHELPS:

Q Okay. When did you begin studying somatosensory perception?

A I first began studying somatosensory perception in 2019.

Q 2019. And how, what -- how did you begin those studies?

A In 2019, I began studying somatosensation by working as an electrophysiology teaching

assistant with Dr. Diana Bautista and Dr. Ellen Lumpkin. Both of these scientists are incredibly renowned in the field, and I worked for them at the Marine Biological Laboratory, preparing samples of touch, itch, and pain neurons for electrophysiology experiments.

Q If you had to estimate, how many hours do you think you've spent in the lab working on somatosensory perception research?

A Gosh, I couldn't tell you, but it would be thousands.

Q Thousands over the course of the last five years?

A Yes.

Q And how many -- could you describe your review of the literature on somatosensory perception?

A Yes. I read papers on somatosensation almost every day and I've been reading papers on somatosensation since 2019. I've met several of the foremost leading experts on somatosensation in science over the last several years and maintained close correspondence with many, as well as I follow all of their work very closely.

Q How would you describe your knowledge of

the history of the study of somatosensory perception?

A My historical knowledge of the study of somatosensory perception is great, actually.

Q And how would you describe your knowledge or understanding of the most current or cutting edge research in somatosensory perception?

A I would say that I'm up to date on the latest understandings and everything that has to do with somatosensation.

Q Dr. Ramos, how long have you, either formally or informally, been studying or educating yourself about the field of psychedelics?

A I think I begun -- I first began writing down and proposing my research ideas for the study of psychedelics during the last year of my PhD as I prepared to transition into my postdoctoral research studies. And I think I completed my PhD at the end of, let me look at my CV. Yes. So I first probably began reading about and developing my psychedelics research ideas at the end of 2020, beginning of 2021.

Q Okay. And had you done any literature review about the field of psychedelics prior to it being part of your formal research proposal

process?

A Yes. So, in graduate school, there's a really common type of seminar known as a journal club, where people get together to discuss groundbreaking research occurring generally in the field of neuroscience. And in this process, in a journal club in my lab, we began to review papers on psilocybin.

Q And what is, what other research is going on out there today regarding psychedelics and somatosensory perception?

A Yeah, there's actually a lot happening out there today. So I'm aware of, there are research groups trying to understand how MDMA alters our perception of touch in humans. There are research groups trying to understand how MDMA alters our perception of pain in rodent models. There are people studying psilocybin, ayahuasca, DOI, in the context of touch and pain. And that's what I'm recalling right now off the top of my head.

Q Okay. And, can --

A It's important to recall that until recently, psychedelic research was considered incredibly taboo. And it is now that it's experiencing a revitalized effort by the

scientific community, it's important to state that a lot of research on psychedelics right now and even in the field of somatosensation is in progress. There are a lot of people like me that are currently in the middle of doing a lot of important work in the context of psychedelics and somatosensation.

Q So these other leading experts in the field, do you know approximately when they, when their studies on these topics began?

A I would say that my project is pretty representative of where the field is at. So it's probably within the last two years that people have started and everyone is probably at a similar timeline.

Q Dr. Ramos, are you familiar with the review process that takes place when you apply for either an HHMI grant or your other fellowship?

A Yes. So for the HHMI grant, what you do is you submit a research proposal. And this is, it's funny, scientists always say that's a great question. That's a great question. So when you submit a grant for, because you want to try and receive that funding, you write a research proposal. In the context of HHMI, the grant was peer reviewed by, I would say, at least 40

incredibly esteemed scientists. HHMI is known to fund some of the best scientists in the country. The Nobel Prize Laureate this year in chemistry was an HHMI investigator. These people review the grant and this grant that I wrote included preliminary data on DOI. They review this grant and then based on how promising they think it is and how promising they think you are as a scientist, they decide whether or not to fund it. So my preliminary experiments on DOI were included in my HHMI grant and reviewed by my peers at HHMI.

Q And the research that you've done, is it contributing to the scientific community's understanding of the neurochemical effects of DOI?

A Yes, sir.

Q How so?

A The fact that DOI is a psychoactive chemical and I'm administering it to awake and behaving animals and I'm recording how that changes their behavioral properties. And so in that way it could be said that I'm adding to our understanding of the neurochemical effects of DOI.

Q And is the work that you've done so far, is it contributing to -- how is that contributing to the scientific community's understanding of the

central nervous system effects of DOI?

A So DOI has effects on both the central and the peripheral nervous system. The scientists, for a long time with respect to psychedelics, have focused their research on the central nervous system. In science, it's called having a brain bias. The brain is a very attractive organ to study, and so people study it, but when they do so, and when they only study the brain, they neglect the peripheral nervous system, which is quite literally everything else.

And my research right now, when I give an animal DOI, it has an effect over their entire body. The experiments I'm working towards performing right now is actually trying to understand when I see changes in behavior that are a consequence of DOI, are they caused by DOI's actions on the central nervous system, or are they caused by DOI's actions in the peripheral nervous system? So I'm working to provide context to a blind spot that has been long overlooked.

Q Would you say at this point that the full effects of psychedelics on somatosensory perception is known?

A No, not even close.

MR. MANN: Objection. Your Honor, I think we're way beyond getting this witness qualified.

JUDGE SOEFFING: I agree. Stick to the qualifications and less on actual opinions.

MR. PHELPS: Okay, no problem. I was just trying to follow up on what he was saying.

JUDGE SOEFFING: So I sustain the objection.

MR. PHELPS: Okay, I think that's it on questions then, Your Honor. The assertion that he's going to testify on the full effects is what the Government was asking about, and that's not known. Dr. Ramos is in the midst of leading research on the somatosensory perception and how that's affected by DOI.

In regards to how that's relevant to the Eight Factors, Factors 2 and 3, Factor 2 is the scientific evidence of its pharmacological effects. So he is contributing to that understanding, as well as Factor number 3, the state of current scientific knowledge regarding the drug and other substance. Dr. Ramos has a particular expertise in a field of study that nobody else is going to be testifying to or

testifying about. And while he's not directly saying, I'm breaking down Factors 2 and 3, the testimony and information and expertise that he's providing is certainly helping the court understand those factors. And the state of current scientific knowledge regarding the drug and other substance is very broad and there's lots to be understood and he provides a particular expertise in that field. He's got one of the most prestigious grants to study this. Those go through an extensive review process. And so this isn't some backyard chemist that's just doing things on his own. This is highly structured, he's highly qualified, and we do believe that he should be recognized as an expert in the field as described in his proposed testimony.

JUDGE SOEFFING: Dr. Ramos, let me ask you, have you ever been designated as an expert or recognized as an expert in any legal proceeding?

THE WITNESS: No, sir.

JUDGE SOEFFING: Okay, so, Mr. Phelps, I guess I'm not seeing why I need to designate him as an expert witness or recognize him as an expert witness for purposes of his testimony. He was not designated as an expert witness in your original

pre-hearing statement. It wasn't until the supplemental where he was added as a proposed expert witness. I'm not sure why I would need to recognize him as an expert witness to receive the testimony that he's going to give. Is there some particular reason why that's important, that I recognize him as an expert?

MR. PHELPS: Well, yes, because he can, as an expert, it gives him some leeway to opine on the elements that relate to Factors 2 and 3 specifically, and can give a broader contextual understanding of that through his opinions, based on what he's understood of the field. He's able to put it in a broader context than just what he's talking about, than just his particular research.

JUDGE SOEFFING: I think what's at issue here is really his research. He talked about the fact that he has read a lot of what others have done, he's reviewed other people's research. But it sounds like he's really here to talk about his own research. I'm not seeing why he needs to be designated as an expert for that. So I'll receive all the testimony that was in the summary, but I'm not going to designate him as an expert witness in the field that was proposed in the supplemental

pre-hearing statement.

MR. PHELPS: Understood, Your Honor.

JUDGE SOEFFING: Okay, so the Petitioners have offered Dr. Ramos as an expert in the study of the effects of psychedelics on somatosensory perception. The Government has objected to his qualification as an expert in that field. For the reasons that the Government stated, after conducting its voir dire, as well as my own inquiries made to the witness, and because I feel that I can receive the proposed testimony without qualifying him as a witness, I will sustain the Government's objection. I will not recognize him as an expert at this time.

MR. PHELPS: Understood, Your Honor.

DIRECT EXAMINATION

BY MR. PHELPS:

Q So, Dr. Ramos, we're going to be discussing your study of DOI in the context of pain. What do you mean when you say you study pain?

A Yes. So pain, when we think about pain as scientists, it's important to understand that it has two different components. The first component is the physical detection of a stimulus. So when something that can actually hurt you makes

contact with your body. So physical, chemical, or thermal stimulus, this phenomenon of being able to recognize a stimulus and process that is painful, that's called nociception, and it's the physical processing of pain.

However, pain also has another face to it, and that's the emotional component, the more cognitive component. Humans can feel pain and can feel pain without any physical assault on their body. They could still just perceptually experience pain through their thoughts. And so pain is both nociception and the emotional component.

Because we can only study the emotional component in humans, my research is on nociception, so the physical transformation of a stimulus into a nociceptive perception. But to make our conversation easier, so I don't have to keep saying nociception, I'll be saying that I study pain.

Q And so far, your study has not been conducted on human participants. You said that, right?

A No.

Q How does the work that you're doing translate potentially into humans?

A Yes. So many of the cells that we have, many of the molecules that are in our body and the functions that they undertake, those molecules and those functions are preserved in other mammals such as rodents. So if we can understand what molecules DOI is binding to, how those molecules are changing cellular function in the context of pain, we can leverage that understanding in humans as well. This is something called translational research, and scientists are working on stuff like this all the time, everywhere.

Q And is this translational research done in other, is this specific to psychedelics or DOI, or is that in other fields?

A No, it's done across every area of medicine.

Q And could you explain why DOI is needed to study pain?

A Yes, because DOI is a highly specific agonist of the 2A receptor. It's fair to say that DOI's agonism on the 2A receptor is, makes it a very special research tool.

Q I'd like to turn your attention now to what's been marked for identification purposes as SSDP Ramos, Exhibit Number 65.

JUDGE SOEFFING: One second. Mr. Clerk, Exhibit 81 was not ever admitted into evidence, is that right?

MR. GLEASON: It was.

JUDGE SOEFFING: It was. Okay. Thank you.

MR. PHELPS: Do you have that in front of you?

THE WITNESS: Yes, sir.

BY MR. PHELPS:

Q And do you recognize that document?

A Yes.

Q What is it?

A It's a scientific research article on the expression of the serotonin 2A receptor in pain neurons.

Q And are you familiar with the contents of the article?

A Yes, I am.

Q And is the document, as it's presented in front of you, is that an accurate representation of the article?

A Yes.

Q Well, first, can you give a general, well, first, where was this article published?

A This article was published in the Journal of Neuroscience.

Q And can you tell us a little bit about that journal?

A Yes. In science, the smaller the journal name, the more high profile that journal is. So to have the name Neuroscience means that it is one of the most high profile journals in the field of neuroscience.

Q And when was this article published?

A This article was published, it looks like in 2009.

Q 2009.

A Yes.

Q And could you just summarize what this article is about?

A Yes, sir. So In this article, the authors were interested in the expression of the serotonin 2A receptors in pain neurons. So before this article was conducted, there was evidence that the receptor would be expressed in these neurons, but the exact distribution of its expression exactly where and what neurons it was in was not known. And people had not done any work to validate whether or not those neurons were pain neurons.

So in this experiment, the authors very intricately take, perform experiments to demonstrate that, in fact, this receptor is expressed in neurons that are important, that in neurons that transmit pain. And they do experiments to kind of reveal a little bit more information and the exact identity of these neurons, because there's more than one population of pain neurons, there's actually many populations of neurons that transmit painful information. And so the authors try and get an understanding of exactly which populations express the 2A receptor, because understanding which populations can give us a better understanding of the function of the 2A receptor in pain.

Q Thank you. I'd like to turn to page four, and you see figure one there at the top of the page.

A Yes.

Q Could you explain what's happening there in figure one?

A Yes, I can.

JUDGE SOEFFING: So, Mr. Phelps, I think it'd be better if you offered into evidence before we start talking about what the document includes.

MR. PHELPS: Absolutely, Your Honor. At

this point, we would move to admit what's been identified for identification purposes as Exhibit 65.

JUDGE SOEFFING: Mr. Mann, any objection?

MR. MANN: Yes, Your Honor, I'm trying to find out where in the pre-hearing statement, the contents of this article and his discussion of it has been noticed to the Government.

JUDGE SOEFFING: So your objection at this time is that there was not proper notice to the document?

MR. MANN: Yes. Well, I don't see it. That's the problem with this pre-hearing statement. There's a list of articles' names, and there's no indication as to what this witness is going to bring out of this particular article. I don't see how the Government is expected to read all these articles and solve a giant puzzle each time trying to figure out what the witness is going to take from these particular articles. He didn't write this article. He's not recognized as an expert and we don't know what he's going to take out of it. So I don't know where the Government's been put on notice as to what he's going to testify

about in this article.

JUDGE SOEFFING: Well, you had your motion in limine. I don't believe you raised this as an issue in your motion in limine which did cover other documents which were excluded by the tribunal.

MR. MANN: I understand that, Your Honor.

JUDGE SOEFFING: You've had it as part of the document exchange. So if it's as to notice, I'm going to overrule that objection. All right, so.

MR. MANN: Fair enough.

JUDGE SOEFFING: So Petitioner's Exhibit marked for identification number 65 has been offered. Over the Government's objection, it is received in the record as Petitioner's Exhibit 65. It's in. You may use it.

(Whereupon, the above-referred to document was received into evidence as Petitioner's Exhibit No. 65.)

MR. PHELPS: Thank you, Your Honor. Dr. Ramos, are you still there on page four?

THE WITNESS: Yes, sir.

BY MR. PHELPS:

Q Could you please explain what's shown in

figure one?

A Yes. Your Honor, do you see in panel A that there is a kind of black oval running diagonally across the panel against a blacker background? That oval is called the dorsal root ganglia. It's an organ that all mammals have. So both humans and mice have 31 pairs of the dorsal root ganglia, and they run down the length of your spine. In this organ live all the neurons that innervate your skin and transmit information important for touch, itch and pain. And so what you're seeing here is a cross section of the dorsal root ganglia, and the smaller circles that you see within it are the sensory neurons, important for transmitting pain information.

The dark ones that you can't really see in this picture don't have any expression of the 2A receptor. But as you can see in panel B, in a more blown up version of what's in the white box of panel A, what you're seeing here is fluorescent tagging of the 2A receptor. So there are several somatosensory neurons within the dorsal root ganglia that are very clearly expressing the serotonin 2A receptor, which is the target of DOI.

Q And can you explain the significance of

what all that means?

A Yes, it means that DOI can directly act on these pain neurons and alter their function.

Q And so what inferences can you make from that information?

A It means that DOI can be used to tell us more about pain, and it might even be able to have anti-pain properties.

Q Can you explain that connection with the anti-pain properties or what you mean by that?

A Depending on how DOI acts on these cells and the changes that it confers to them, it could change their ability to transmit pain information. So it could actually make it so that the signal that the neurons transmit to the brain is dampened and it could have pain relieving properties.

Q Now, Dr. Ramos, I'd like to turn your attention to Exhibit Number 50.

A Thank you.

Q Do you recognize this document?

A Yes.

Q And can you identify what it is?

A Yes. It's a research article where the authors aim to understand the effects of a few different serotonin 2 receptor activators or

agonists on allodynia.

Q And are you familiar with the contents of this article?

A Yes, I am.

Q And is this article, is the document in front of you an accurate representation of the article as a whole?

A Yes.

Q And is this the same – is this the article that is cited on page 31 of your proposed summary in the pre-hearing statement?

A I believe so.

MR. PHELPS: Your Honor, at this time, we would move to admit what's been identified for identification purposes as Exhibit 50.

JUDGE SOEFFING: Mr. Mann, any objection?

MR. MANN: One moment. No objection.

JUDGE SOEFFING: Petitioner's Exhibit marked for identification number 50 has been offered and in the absence of objection is received in the record as Petitioner's Exhibit 50. It's in. You may use it.

(Whereupon, the above-referred to document was received into evidence as

Petitioner's Exhibit No. 50.)

BY MR. PHELPS:

Q Thank you, Your Honor. What's the title of this article, Dr. Ramos?

A Antiallodynic Effect of Intrathecally Administered Serotonin 2 Agonists in Rats with Nerve Ligation.

Q And can you break down what that means?

A Yes, I can break down what that means. The first word, allodynia, is a word that scientists use to refer to a specific somatosensory phenomenon. Allodynia is when a stimulus that would normally be benign, such as a gentle touch, becomes painful. So when touch gives pain, when touch leads to pain, we call that allodynia.

So you can imagine, we have all probably experienced the phenomenon where we burn ourselves, and then the area where we burned ourselves is hypersensitive for maybe a few days to even the most gentle touch. That is called allodynia. And so that's what this paper is about. When touch gives rise to pain.

Intrathecal means that they're going to administer compounds, specifically serotonin 2 receptor activators, through the spinal canal. So

it's a technique that scientists use to directly deliver these drugs into the spine. And rats with nerve ligation are a model for neuropathic pain.

Q And where was this article published?

A It was published in the journal called Pain. And I'll remind the court that the smaller the name, the more high profile the journal.

Q And there's a little emblem up in the top left corner. What is that?

A That means that the article has been, it has the stamp of approval of the International Association for the Study of Pain. So this journal is recognized by scientists all over the world who study pain.

Q Okay. Could you summarize what this article is about?

A Yes. So the researchers in this article take rats, and then they do a technique called nerve ligation. So what this technique is, is they actually tie a little knot around the nerves that innervate the rat's leg. And it's a small surgery that they perform. Because they tie this knot around the nerve, what this does is it actually simulates a nerve pinching injury, and the rats develop allodynia so touching their leg is very

painful for them. So this is a model of pain in humans. So people who receive or experience nerve damage develop neuropathic pain. And this is how we're able to study this phenomenon in rodents.

So the authors perform this surgery on the animals. After the animals have recovered from surgery and have developed allodynia, they can administer different compounds. Specifically in this paper, they administered DOI and ask, does DOI relieve any of the animals' pain?

Q And what conclusions did they reach in this paper?

A In this paper, they --

MR. MANN: Objection, Your Honor. This witness is not an expert witness. The article speaks for itself.

JUDGE SOEFFING: The article does speak for itself. He is not an expert witness. He did testify that he's very familiar with the research in the area. He follows the studies. I do find that he is familiar with this particular publication. So I'll allow him to testify as to what he believes the conclusions are and I will review that, obviously for consistency, as the document does speak for itself. So I'll overrule

the objection.

THE WITNESS: In this paper, they found that DOI provides the animals relief to their allodynia. So it makes the stimulus less painful.

BY MR. PHELPS:

Q Thank you. I'd like you to turn to page three of this document. And there's several figures there. Could you talk specifically about figure two?

A Yes. So, Your Honor, I found in my experience that when I talk about data such as those that are represented in the graph, it's important for people to be able to understand the technique that underlies this data. And the tool that both scientists and medical doctors use to perform the experiments that are represented in the graph. It’s a small tool the size of a pen. And I have one of those tools with me. Would I be able to present it to the court? The court can keep it.

JUDGE SOEFFING: Let me see.

THE WITNESS: For visualization purposes.

JUDGE SOEFFING: Okay. And why don't you hold it a little higher?

MR. PHELPS: Could you hold that up and

could you explain what it is while you're holding it up so everyone can see that?

THE WITNESS: Yes. This is a Von Frey filament. It's the gold standard for assessing touch and pain in humans and rodents. So what you're looking at here is a filament calibrated to deliver a specific amount of mechanical force when it pokes. This is a small filament, so it delivers a small amount of force.

But when we do these experiments, both doctors and humans have a whole set of filaments that deliver a range of forces. So for example, if you're a human who has lost touch sensation, a doctor will evaluate you by poking you with these filaments. We can perform these similar experiments in rodents, poke them and record their behavioral response to see if they're demonstrating behaviors associated with pain. And so this is the tool that is used in these experiments and it will help to understand the data.

MR. PHELPS: And that's the same tool that's used when similar types of studies are conducted on humans?

THE WITNESS: Yes.

BY MR. PHELPS:

Q Anything else about figure two that's noteworthy for you?

A Yes. So the actual result, Your Honor. You can see in this figure there are two axes. The X axis running across the horizontal plane and the Y axes running across the vertical plane. If you look at the Y axis, the unit there next to threshold is grams. So it's referring to the amount of force. And what they're recording here is the amount of force required to elicit a response in the animal. Less force, a smaller number, means that the animal is in pain.

And so if you look at the beginning, these animals have gone through this nerve ligation procedure. They're in pain. So at time zero, the amount of force required to elicit a response is three grams. It's very little. And with a low dose of DOI that doesn't have physiological action, so that's the bottom line running across the graph, you can see that the animal's response doesn't change. It stays at three grams.

But in the white circles, after the animals received DOI treatment, you can see that the amount of force required to elicit a behavioral

response jumps up to nine. So that means the animals are being less impacted by this force so the interpretation of this data would be that the animals are in less pain following DOI treatment.

Q Anything else there about figure two that's noteworthy?

A The anti-pain effects of DOI seem to persist for over two hours. And that's very noteworthy in biology.

Q Why is two hours a noteworthy time there?

A It speaks to the fact that DOI can relieve pain for several hours.

Q And I'd like you to now go to page four of the exhibit.

A Yes.

Q And do you see what's marked there as figure five?

A Yes.

Q Okay, and this one has got a lot of bars here so we're going to break this one down just a little bit. Could you explain what is identified on each of the X and the Y? Or first, can you give a kind of broad description of what this figure shows?

Q Yes.

A So the part of this figure that is relevant to our discussion today is the second group of bars to the right where under which is the DOI designation. Those are the experiments that actually involve DOI. The Y axis, the axis running vertically, is the maximum possible effect. And so that's just showing the higher the number, the higher the number, the more of the pain response is there.

Q And so we're looking at specifically the right side of that graph.

A Yeah.

Q And what is shown on the Y axis, on the vertical axis?

A Yeah, sorry. So the Y axis is looking at the effect, the magnitude or the intensity of the DOI effect that we talked about in the previous graph. So in the previous graph we saw that DOI has anti pain properties and we see that there's a difference after the animals are treated with DOI. This is showing you the magnitude of that effect in the black bar. So it's showing that DOI drives, it's relative to the previous graph. It has an effect size, as we would call it, of 60 percent.

Q Okay. And what are the other bars in that graph showing? You said the black one is the DOI.

A Yeah. And the other bars, so the ones relevant to the 2A receptor are the -- so next to the black bar are two bars, the one that's dark gray and one that's white. That's experiments performed using something called ketanserin. Ketanserin is an antagonist of the 2A receptor. It blocks DOI's action at this receptor. So what this data is showing is that DOI acting on the 2A receptor is important for its pain relieving properties.

Q And what about the next three bars there on the right?

A Those are during -- those are experiments using other antagonists that don't target the 2A receptor, except for MDL, that don't target the 2A receptor and showing that there's no effect.

Q So in that right side, the black bar showing DOI and the one on the far right with the slanting left to right lines are almost at the same level there. What's your interpretation of that?

A That means that the antagonist that they're using on the far right is not relevant to the mechanism at study.

Q What does that mean?

A It means that that drug is not important for the underlying biology.

Q Okay, so what can be inferred from this data?

A From this data, we can infer that DOI has the ability to relieve allodynia in this rodent model and that it does so through the serotonin 2A receptor.

Q So based on these last three pieces of data, these last three figures that we've covered, what is the current state of our understanding regarding the effects of DOI on pain?

A We know that the 2A receptor is expressed in pain neurons. We have some evidence that DOI could have the ability to relieve pain in this rodent model. What we're lacking is everything that comes in between. How does it do this? We don't know that yet.

Q And so what's missing from that understanding of the knowledge?

A We would need to understand when DOI is given to these animals, what is its exact effect on these pain neurons? How does it change their function? How does it change the signals that they transmit to other neurons that they connected to

because our body is not a vacuum. It's a highly interconnected network. And so how does it change their signal, the signal they transmit to other neurons? And ultimately, how do those changes give rise to these changes in behavior and everything in between.

Q And why is this lack of knowledge important or relevant?

A This lack of knowledge is important and relevant because it 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.

Q And so how does the work you're doing through your grant shed additional light on this phenomenon?

A Yes. I'm basically working to fill that everything in between that I just discussed.

Q Can you -- What kind of work are you doing to fill that gap?

A I'm performing many different types of neuroscience experiments at several scales of biology, as we discussed yesterday, to demonstrate what exactly happens to the function of these neurons when you apply DOI. What is its effects

on it? What are the changes to the neural circuits and what are the actual -- I'm working to characterize extensively the different behaviors in somatosensation that DOI drives and the cellular mechanisms of how DOI changes those behaviors. I'm trying to provide the characterization that we need to develop novel therapies.

Q And what kind of results or evidence have you collected so far related to DOI and its direct action on pain neurons?

A Yeah, so currently in my experiments, I have found that DOI can directly act on pain neurons and activate them. What this means is that DOI binds to the 2A receptor on pain neurons and changes their function. So I have unpublished evidence of this phenomenon.

Q And what kind of evidence have you found regarding the way that DOI alters pain behaviors?

A Yes, I have found in my experiments that DOI can relieve two different types of pain in rodent models. I have found that DOI can provide relief to mechanical pain and that DOI can provide relief to thermal pain.

Q And in the studies that you're conducting, what kind of dosages of DOI are you

using in the animals?

A The dose that I'm using for DOI is one milligram per kilogram. This is a standard dose used across a scientific literature for the study of DOI.

Q And do you know how that relates to, you said this is standard across DOI studies, specifically in the field of pain studies, or DOI as a whole?

A More generally, it's specific to the study of DOI as a whole across the psychedelic literature in rodents.

Q Okay, and do you -- Are you familiar with how the dosage you're using compares to the dosages used in the self-administration studies that have been testified to previously?

A That's outside the scope of my expertise.

Q Okay. Are you aware if the dosage that you're using is an amount that causes what's recognized as hallucinations?

A In animals, the dosage that I am using causes the head twitch response.

Q It does. Okay. And so how does DOI change the animal's response to pain?

A In my experiments, animals that do not

receive DOI show more of a pain response than animals that do. So, for example, in the, in my experiments where I apply a thermal stimulus, so we're able to deliver a small pulse of heat to the animal's paw. Animals that receive saline are very sensitive to the heat. They feel like, not to anthropomorphize them, but our interpretation of that would be that they feel more of a burning sensation. Animals that receive DOI feel this less intensely.

Q And is your work on this complete?

A No, it's in progress.

Q And what's the timeline you would estimate needed to finish this particular work you're doing?

A I need two more years.

Q Two more years. And why is that?

A Biology is slow, right. These are animals that are alive. We have to breed them, we have to wait for them to get to the right age, and then we have very narrow time windows to perform the experiments that we need to perform and everything is very slow. It's not uncommon for projects in neuroscience to take three to six years.

Q And how much time do you have remaining in respect to your funding through the Berkeley fellowship?

A Yes. My funding for the Berkeley component of my fellowship expires in 2027. Since we're about to start 2025, I would say that I have two years left.

Q You have two years left of funding on that particular grant.

A At Berkeley.

Q And so after those two years -- after that section of the project is done, you said your HHMI grant goes further than that, right?

A Yes. It provides me funding for me to begin my own research lab at an R1 university here in the United States and continue performing my research, carrying out my research.

Q And how do you anticipate carrying out this particular research after that two years expires?

A After the two years expire? Well, if everything goes according to plan, before those two years expire, I will accept a job at a university and transition to a university where I will run my own research lab pursuing all of these ideas.

Q What particular ideas are those? Where do you see this research going?

A Yes.

MR. MANN: Your Honor, I don't understand why we're going on a discussion about Dr. Ramos' career path. If this has to do with the effect of scheduling on his career, we would object for the record. We understand the court's position that this evidence is going to be allowed, but we would just object that research harm evidence is not relevant to this proceeding.

JUDGE SOEFFING: So I'll overrule the objection. I don't think we're necessarily talking about his career path. As to the trajectory of the future research that may be done with DOI, which is something that I specifically allowed to be presented at the hearing. Although it may be given reduced rate weight, as I stated in my order on the motion for limine due to the fact that that's not part of the Eight Factor analysis. But I'll overrule that objection. He may answer.

THE WITNESS: Can you repeat the question?

BY MR. PHELPS:

Q Yes. Where do you anticipate the

research going after this two year window of what you have currently planned? Where do you take the research next?

A Yes. So right now my research is currently characterizing the effects of DOI in, we would call these in wild type animals. So animals that have had no specific manipulations like the nerve ligation in the previous study. The next obvious steps would be to take the understanding that I developed from my experiments and more closely probe in several animal models of pain, how does DOI exert its pain relieving effects? And so that would probably be some of the first projects that I would be running in my own lab.

Q And then ultimately, long term, how could this research impact public health for humans?

A Yes, this research, in a way, this research could inform us at a level way beyond psychedelics. So this research is about understanding what are the cells and molecules that are important for our perception of pain. And if we can understand why these cells and molecules are important in the context of pain, we can manipulate them to relieve pain. And so these experiments will create a broader understanding of how mammals

feel pain and we can leverage that understanding in the context of humans.

Q So specifically related to the timeline, you talked about going to an R1 university before. What is that?

A R1 stands for Research 1. It's very much like Division 1 in sports. It's basically the highest research division that a university can be granted in the United States. And to qualify for the R1 designation, the university needs to bring in a certain amount of funding and have a high caliber, the scientists working at the university need to be of a high caliber.

Q And what other kinds of research is done at R1 universities?

A Everything.

Q Medical research?

A Yes.

Q On humans?

A Yes.

Q And so if you were studying DOI at one of these R1 research universities, would there be an opportunity to collaborate with medical researchers?

A Yes, that's the dream.

Q Could you explain that?

A Yes. So different universities have different departments and different scientists working at them. Ideally, it would be if I worked at a university that, for example, had a medical research unit, I could collaborate with scientists in that unit to advance the findings of my experiments in humans and begin to pursue that research.

Q And so through that collaborative research, is there a possibility in the future of using DOI for similar experiments in humans?

A There's a possibility, yes.

Q So, how would DOI being placed in Schedule I affect just the timeline of your work?

A It would totally disrupt my ability to perform my experiments. From the information that I have gathered from colleagues at Berkeley, if DOI were scheduled and it became a Schedule I substance, the laboratory that I am currently affiliated with does not have a Schedule I license.

So let's say that tomorrow DOI was Schedule I. I would not be able to perform the experiments that I'm currently working on, and I would need to begin the process of acquiring a

Schedule I license at Berkeley. From information that I have gathered from speaking to my colleagues, it seems like this process can take about a year. And given my two year timeline and two years of funding and all the momentum that I would lose, it's quite possible that this scheduling would derail my entire research career at Berkeley and cause me to not be able to accomplish what I need to accomplish in a timely manner and before my funding at Berkeley expires.

Q So if you were unable to carry this on to an R1, and you said the goal is ultimately to collaborate with medical researchers, how would your inability to do that impact public health?

A It means that all, that people are not going to be able -- that means that humanity as a whole will not benefit from all of the work that I have invested in, all of the work that I've done, everything that I've done before that turns into anything good for anyone. The time that it will take for that to happen will be significantly stunted. Science is already slow as it is. This is going to make it such that before we see anything groundbreaking come out of my research, it will take much longer.

Q Dr. Ramos, you signed on as a -- you yourself filed as a petitioner in this case, right?

A Yes.

Q Why did you do that?

A Because I knew that I had standing in this case.

Q And what do you mean by that?

A I mean that I knew that I am funded --

MR. MANN: Objection, Your Honor. These are legal conclusions he's testifying to.

MR. PHELPS: We can move away from standing. I would agree that is technical term, but the why I think is still relevant.

JUDGE SOEFFING: I'll sustain the objection and let you to rephrase the question.

MR. PHELPS: Okay. Thank you, Your Honor. Why was filing this petition important to you?

THE WITNESS: Yes. I want the ability to continue to do my work as I've been doing it. That's why I'm here today. I don't want to be here. I just want to be able to do my work. That's all that I want to do.

BY MR. PHELPS:

Q If you were not sitting here with us

today, where would you be?

A I'd be doing experiments in the lab.

Q How many hours a week do you spend doing those?

A What people don't understand is that even a minor deviation, such as one day from the laboratory, can actually take weeks out of a scientist's rhythm because setting up an experiment isn't a one day thing. Oftentimes to set up an experiment, you need three weeks of preparation, and then you need the time it takes to actually perform and run the experiment and the time it takes to analyze the data. So by being here, I'm actually losing out on weeks' worth of work because I can't set up anything and I can't do anything until after I've set something up.

Q And what are the financial impacts potentially of a scheduling of DOI? How does that relate to your funding currently?

A So, what are the financial impacts? I mean, here's the thing is that my funding at Berkeley expires in two years. In two years, in 2027, I need to either transition to the next part of my grant by acquiring a job at a university and to acquire a job, I need to complete my research.

Or I would have to stay on at Berkeley and try and figure out some other alternative funding mechanism, which would be incredibly difficult because I would be a late stage postdoc, and the opportunities available to me would be minimal. And so I would have to figure out a way to support myself while I continue my work.

Q So what could be the potential professional consequences of that disruption?

A Yeah, it can make it so that I am unable to find a job and I've been working at having a job as a neuroscientist for the last 10 years.

Q So Dr. Ramos, you said your current institution is UC Berkeley, right?

A Yes.

Q And can you just speak a little bit about the UC system as a whole and UC Berkeley in particular and its standing in the academic world?

A Yes. I think we've all heard of UC Berkeley, and we've all heard – I mean people call it Cal. UC Berkeley is a giant research institute. There's so much science happening at UC Berkeley. There's so much science happening at UC Berkeley that it has a special parking lot dedicated only to Nobel Laureates, where there are like 12 to 15

spots for all of the Nobel Laureates at UC Berkeley scattered across the sciences. That's the level at which UC Berkeley performs science. There's so many HHMI investigators, HHMI awardees. There's so many science buildings and research labs that I'm only familiar with a fraction of them. It's just an immense scale of science, and it's really on the leading edge of scientific research.

Q And even as a leading research institute, you said that they do not currently have a Schedule I DEA license, correct?

A No, my lab does not. Other labs at UC Berkeley do.

Q Can you explain the relationship between other labs with those licenses and why you're not able to just piggyback on that?

A I'm not affiliated with those labs, and that’s not -- you can't just piggyback onto anything. Once it’s a Schedule I substance it becomes -- the protocols in place -- once something becomes a Schedule I license and the scientific laboratory has a Schedule I registration, that doesn't mean that people can just piggyback onto their studies. For someone to use a Schedule I substance, they would need to be a member of that

lab mentored by the principal investigator of that lab. The principal investigator is the person in charge of the research happening in the lab. And people need to be specifically on the IACUC protocol. So yesterday we mentioned IACUC. People need to be on the protocol and need to be authorized controlled substances users. And so, yeah, I can't just piggyback onto someone else's research in the lab. Not only that, my research is not a plan of the research happening in other labs. It's my research plan.

Q And you said initially your plan was to do some similar studies of this with MDMA, correct?

A Yes, I intentionally and initially wanted to do research with MDMA, and I wrote a proposal. That's the proposal that is on my CV for the Miller Institute. I was awarded this proposal to perform this research with MDMA. But because the lab that I work in does not have a Schedule I license, and because it could take me a year to get that license, and the funding was only for three years, I decided that pursuing this avenue was not the best use of my time and was not conducive to me accomplishing my goals. And so I pivoted to working with DOI.

BY MR. PHELPS:

Q So through that transition and exploring MDMA, did you become familiar with the process that it would take to obtain a Schedule I license for your lab?

A Yes, I have familiarity with the process.

Q Okay. I'd like us to walk through that process, and I think it would be most helpful to have a kind of a visual understanding of what steps need to be taken.

JUDGE SOEFFING: So let me stop you there, Mr. Phelps. I see that there's an easel that's been put up, and you're talking about visual aids. Are you planning on using that easel?

MR. PHELPS: Yes, Your Honor. This is such a complex process that a visual understanding of all the places and steps that have to be taken, I think, would be beneficial to the court.

JUDGE SOEFFING: Okay, and you're planning on putting up something that's not been an exhibit that's previously been admitted.

MR. PHELPS: No, he's going to be drawing on the board to walk us through what his steps would be.

JUDGE SOEFFING: Okay, so we need to have that placed somewhere where everybody can see it.

MR. PHELPS: Absolutely.

JUDGE SOEFFING: Okay, so the law clerk is motioning over here. Are you going to use it for this next line of questioning?

MR. PHELPS: Yes. Yes, I think so. It's what, 10:20 a.m.? I don't know what you're thinking for a morning break. I don't know if now would be an okay time and we can get it set up?

JUDGE SOEFFING: No, let's continue on for maybe till 10:45 a.m. or whenever you're --

MR. PHELPS: Okay.

JUDGE SOEFFING: Around there. Okay. Sorry to interrupt. Go ahead.

MR. PHELPS: No, no, no problem. So how would you describe the level of bureaucracy that goes into obtaining a Schedule I license?

MR. MANN: Objection, Your Honor. None of this has been disclosed in the pre-hearing statement.

MR. PHELPS: This is the impacts on his research. Let me find it in our statement.

MR. MANN: What I see here is he says he will testify if that the proposed Schedule I classification is passed, Dr. Ramos' research into the understanding of neuropathic pain and his

treatment will be significantly stunted. That is it. And now we're on a journey through DEA bureaucracy. He's not an expert in how DEA works and none of this has been forecast.

MR. PHELPS: This is related specifically -- what he is about to show, is going to demonstrate how significantly his research will be stunted. We've heard testimony before from Dr. Carbonaro that this is an easy, mundane, you send in an application process that's done in three months and an actual researcher who is familiar with this process from the applicant's standpoint can provide certainly relevant information for the court to consider and weigh against the Government's characterization of a Schedule I license and specifically how the research would be stunted.

You've heard from -- every minute he has to spend away from his lab is impacting his research. And what he is going to show through this is what the time actually takes. It's very relevant.

JUDGE SOEFFING: Well, I think he has testified as to how the need to get a registration would impact his research. I don't see anything

in here specifically about an application process and that he would testify as to what it would take to apply to get a registration. So I think that that is an overreach as to what has been disclosed in the pre-hearing statement.

So in terms of the process to apply, I don't really see that in here. If you want to continue to ask about how the need for a registration would impact the research, I think you have covered that to some extent, but I would allow you to continue to explore that. So I'll sustain the objection as to the specifics as to application process for registration because I don't see that in the prehearing statement.

MR. PHELPS: Dr. Ramos, how would this applying for a Schedule I license or having to obtain a Schedule I license significantly stunt your research?

MR. MANN: Objection. Asked and answered.

JUDGE SOEFFING: I think it has been asked and answered. If you want to refine that, but I think he has spoken in general terms as to how that would affect his research. So sustained. You can reask a more specific question.

MR. PHELPS: Dr. Ramos, based on your understanding of the scheduling process, you said you believe it could take you up to a year?

THE WITNESS: Based on my --

MR. MANN: Objection. Asked and answered.

JUDGE SOEFFING: Overruled. I'll allow him to answer.

THE WITNESS: Based on my understanding of the process, from what I've gathered from my colleagues who have gone through it at Berkeley, it could take up to a year, yes, or more.

Q Why is that?

A Because there's several levels of administrative hurdles.

MR. MANN: Your Honor, this is also, again, all hearsay.

MR. PHELPS: This is, he, so you have --

JUDGE SOEFFING: Hold on. Hearsay is not specifically --

MR. MANN: He just testified that his colleagues told him something.

JUDGE SOEFFING: Yeah, yeah. It is hearsay. I will allow the testimony. Hearsay is permitted in administrative proceedings if it has

sufficient reliability. Sounds like he had these conversations as part of his professional duties.

MR. PHELPS: I can lay a bit of a foundation there.

JUDGE SOEFFING: So I'll overrule the objection. I'll allow you to further explore.

MR. PHELPS: Okay. Thank you. Who did you consult with when you were looking into the licensing?

THE WITNESS: I consulted with other scientists at UC Berkeley that had acquired their license already and had all the relevant documents necessary to acquire the license.

BY MR. PHELPS:

Q And were those researchers working in the field of psychedelics?

A Yes.

Q What specifically?

A These specific researchers were working with psilocybin.

Q And based on that inquiry or following up with them, why would it take a year?

A There are several steps and several levels.

MR. MANN: Objection. Hearsay. Calls

for speculation.

JUDGE SOEFFING: Overruled. But we're not going to spend a lot of time on this.

MR. PHELPS: Certainly.

THE WITNESS: May I answer the question?

MR. PHELPS: Yes, sir.

THE WITNESS: Okay. So there are several levels of administrative hurdles that a scientist would need to clear. The first levels of which start at UC Berkeley and then they move on to the State Research Advisory Panel as well as the DEA. We would have to clear both through those and then circle back around to the university for final approval. And I could elucidate on some of the smaller steps in between those different administrative hurdles.

MR. PHELPS: And while you haven't done this specifically for a Schedule I license, you are familiar with the process for getting things approved through your laboratory in other words, right?

MR. MANN: Objection. Leading.

JUDGE SOEFFING: Overruled.

THE WITNESS: Yes, I am.

MR. PHELPS: And so this isn't an

entirely foreign process?

THE WITNESS: No.

BY MR. PHELPS:

Q Okay. What are those steps?

A At UC Berkeley, the first step that you need to do as a researcher to work with the Schedule I substance is be added to the laboratory's research protocol, their IACUC protocol just in general. After you've been added to the protocol, and that takes approximately three months because I've been added to my own lab's research protocol and it's a very slow process.

Once you're added to your lab's research protocol, the next thing that you have to do before you can even think about working with Schedule I substances or any scheduled substances is that you need to surrender your fingerprints to the state of California and present yourself for a background check. I've also done that process and that takes three months. So we're at six months.

After you've done those two processes, if your lab, like my lab currently does not have a Schedule I registration, you need to begin to write a detailed experimental protocol that needs to be added to your lab's current research protocol.

MR. MANN: Your Honor, we're way outside the scope of what's been disclosed.

JUDGE SOEFFING: Well, this may not have been specifically talked about, but it does give me a better understanding of the impact of the need for DEA registration and how it affects his research. So I think that broadly this is covered in the pre-hearing statement because he's talking now not just about the need for a DEA registration, but other impacts that the requirement for a DEA registration would have on his research. So I'll allow the continuation of the questioning. Overruled.

MR. PHELPS: Thank you, Your Honor.

THE WITNESS: So just to summarize, we've gone through two steps. We're about six months in. So the next thing that I would have to do once I've surrendered my fingerprints, done my background check and been added to my lab's research protocol, is that I would need to update the protocol to include Schedule I substances.

These protocols need to be very detailed, very well thought out. They need to include the exact experiments that you're proposing to do, the exact amount of the Schedule I substances that you will

use, and just in general, very detailed understanding of experiments you will be carrying out needs to be communicated. It could take probably weeks to write this protocol. And after I've written it, I would have to submit it for IACUC approval. And that the IACUC approval at UC Berkeley I think meets once a quarter. So depending on when I submitted it, it could be another three months before they review it.

Once UC Berkeley has reviewed it and if they don't have any questions, if they do have questions, we would have to go back and forth. If they allow us to add Schedule I substances to our IACUC protocol, then we could submit an application to the Research Advisory Panel of California and to the DEA. Dr. Carbonara yesterday testified that the DEA reviews its applications in three months. So we're about nine plus months in now, but the Research Advisory Panel of California is notoriously slow and meets infrequently. I would not be able to move forward until I received approval from both of these organizations.

Once I have received approval from the DEA and the Research Advisory Panel of California, then I would have to circle back around to the university

and receive final approval and authorization from UC Berkeley to be able to work with these substances.

And then we would need to perform physical modification of our laboratory to comply with diversion control measurements. And honestly, who knows how long that could take because that would require the physical alteration of the lab to install things such as a safe.

MR. PHELPS: Could you take us back to the timeline from where at this point when you're onto the physical modifications?

THE WITNESS: Yes, we're at like 12 months in here.

BY MR. PHELPS:

Q And would that be the, would the physical modifications then be the final step?

A I think that the physical modifications need to take place before we can be approved because the DEA needs to inspect these physical modifications and our diversion control measurements and approve them.

Q Have you in your, all of your general research experience, have you ever had to make physical modifications to a laboratory?

A I have never had to make physical modifications to a lab, no.

Q Okay. So you couldn't speak to what you would have to do through the --

A No.

Q Okay. So how does the characterization of getting this approval being just a letter compare to what you've understood the process to be?

A To me, it sounds like a gross mischaracterization of the process.

Q And why is that?

A Because the process is much more complicated, much more time consuming and much more involved than has previously been discussed in our proceedings thus far.

Also, I can't do it by myself. I need support from other people in my lab, from the university and from my department. It's actually not something that I can do alone.

And support from the other administrations that are involved in the process.

Q Thank you for walking us through that, Dr. Ramos. If DOI was placed into Schedule I, what steps would you take next regarding the, where

would your -- there's kind of different options for your research to go. Right?

A Yes.

Q Where would it go?

A If DOI was placed on Schedule I, was scheduled as Schedule I substance and I could no longer work with it, I would start pursuing Schedule I registration and I would have to figure out something else at work. That's the reality.

Q So I would like to move to just one other topic here. What kind of measures does your lab take to ensure that diversion of DOI is not occurring?

A Yes, I can explain the steps that we take to make sure that doesn't happen. First and foremost, every order of DOI that our lab has ever placed is recorded and we know exactly how many times we've ordered DOI and how much DOI we have ordered.

When DOI is received, the staff in our lab hand it directly to me and I place that DOI in a lockbox and only I have the key to that lockbox. And then an emergency backup key exists.

But I keep all the DOI that I've ever worked with in a lockbox that only I can access.

And when I do open the lockbox to work with DOI, the amount of DOI that I take out is I take note of the amount of DOI that I'm taking out because every experiment that I perform I record and measure the amount of DOI that I use in the experiments and the amount of DOI that I administer to the animals so we have the DOI.

The DOI goes through a strict chain of custody. It comes directly to me. It's locked up and all of the DOI that's ever used is recorded.

Q So you said the start of that process, you have to order the DOI.

A Yes.

Q Can you explain a little bit about how that works?

A Yes. Ordering DOI is amazingly simple. And great. You, as a scientist, because I have these qualifications, because I'm part of a research university that has a relationship with the companies that provide DOI for scientific research, I am able to log onto our lab's ordering system and order DOI as I would any other research chemical.

And receive it in a timely manner so that I can perform my experiments in a timely

manner.

Q You said your lab has an ordering system. What is that?

A Yes, many labs have an ordering system or use a third-party platform such as something called Quartzy. What this does is it allows you to upload your scientific credentials and then communicates those scientific credentials to scientific vendors so that you don't have to do that process for every single order.

Instead, a relationship is formed between you and these vendors. Your qualifications are confirmed and verified. And then after that, your lab can order reagents from these vendors in a streamlined manner.

Q Are you familiar with the company, Cayman Chemicals?

A Yes, Cayman Chemicals is a company that provides research reagents to scientists.

Q Have you ever ordered DOI through Cayman?

A I do not order DOI through Cayman Chemicals. I order DOI through another company called Sigma-Aldrich.

Q Is Sigma-Aldrich comparable to Cayman?

A Yes, sir.

Q And what is your understanding of what that company is, Sigma-Aldrich?

A It is a company that sells scientific reagents to scientists.

Q What are scientific reagents?

A They can be many things. They can be tools, they can chemicals. They can be anything that a scientist needs to do their work. They can be flasks, they can be drugs.

Q So any scientific equipment, not specifically chemicals or drugs.

A Yes, it depends on the specific company, but they can be pretty broad in the things that they provide.

Q And to order something like DOI, does Sigma-Aldrich verify who's ordering it?

A Well --

A Or, let me rephrase --

MR. MANN: Objection. This witness wouldn't have any knowledge of that.

MR. PHELPS: Well --

JUDGE SOEFFING: Sustained, I'll allow Petitioner to rephrase.

MR. PHELPS: I can rephrase. Dr.

Ramos, what information do you have to provide to be able to order chemicals?

THE WITNESS: I only need to provide the order information, like what do I want.

BY MR. PHELPS:

Q Yes.

A And how much I want.

Q All right. I'm sorry. Let me clarify. Do have to, to order chemicals from these companies, do you have to demonstrate that it's for a scientific or research purpose?

A I, so in labs, these administrative tasks are sometimes performed by lab support staff. I have not myself gone through the process of establishing that relationship with a scientific vendor so I can't speak to that.

Q Okay. To your knowledge, would you be able to order these chemicals without going through those channels?

A To my knowledge, no. Many 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 because I've been doing this, I've only ever done this as a scientist.

I wouldn't even know, I would not know what that looks like. I just know that if you log onto the websites without your scientific credentials, they don't let you really see much actually.

Q To your knowledge, would somebody be able to order from these chemical companies DOI for recreational use?

A I'm not --

MR. MANN: Objection, Your Honor. I think he's established that he doesn't really know how that works.

JUDGE SOEFFING: Overruled. If he knows how it works, he can answer or state that the doesn't.

THE WITNESS: To my knowledge, 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.

MR. PHELPS: Thank you. No further questions for this witness, Your Honor.

JUDGE SOEFFING: Okay. Mr. Mann, I

assume you're going to conduct cross-examination?

MR. MANN: Yes, sir.

JUDGE SOEFFING: So we will go ahead and take our morning break for 15 minutes. We are off the record.

(Whereupon, the above-entitled matter went off the Record at 10:44 a.m. and resumed at 11:06 a.m.)

JUDGE SOEFFING: All right, we are back on the record. Dr. Ramos, I remind you that you are still under oath. Mr. Mann, you may conduct your cross-examination.

CROSS-EXAMINATION

BY MR. MANN

Q Dr. Ramos, I would like you to look at Exhibit No. 65. Respondent's -- or the Petitioner's exhibit.

A Yes. I have it.

Q Now I believe you stated that a lot of your work and research is based on up and coming new studies and the most recent research. Is that correct?

A I do not recall stating that.

Q All right. Well is it based on current research?

A It's based on research.
Q All right. Not necessarily current and up to date. You'll --
A Can I get a --
Q -- agree it's --
A -- can I get a definition for what is considered current?
JUDGE SOEFFING: Yes, go and supplement your answer.
THE WITNESS: Can I get a definition for what is considered current?
MR. MANN: Well let's go the --
THE WITNESS: In this context.
MR. MANN: -- 15 years.
THE WITNESS: In the last 15 years. The thing is, that that's now how science works.
BY MR. MANN:
Q My question is, would you say that your work is based on current research?
A Yes.
Q Okay. And you'll acknowledge that this report, this study is from 2009. Correct?
A Yes.
Q And it's from France. Correct?
A Yes.

Q So a Schedule I registration would not be required to conduct this research. Correct?

A I'm unfamiliar with the laws of France.

Q Well I'm talking about the United States. A Schedule I --

A Oh.

Q -- registration in the United States would not affect this research at all. Would it?

A No.

Q Okay. All right. And I would like you to -- I would like to ask you something about this particular study, which you cited. Isn't it true that it says here and I'm quoting from the second column on Page 1, about two-thirds of the way down, it says peripheral injection of 5HT2AR agonist and that would be DOI. Correct?

A DOI is a 2A receptor agonist.

Q Okay.

A That doesn't necessarily mean that is what these authors are referring to --

Q Right.

A -- in the citations.

Q But it says significantly reduces the paw withdrawal latency to radiant heat or mechanical stimulations and hyperalgesia induced

by and I don't know how to pronounce this word, ketanserin.

That basically says in so many words that the 2A agonist increases pain. Does it not?

A That is what these authors are referring to --

Q Okay.

A -- in this sentence, yes.

Q And that the antagonist, which is not DOI, reduced pain.

A That is what the authors are referring to in this paragraph.

Q And I would like you to look at Page 6 of this same article that you cited.

A Yes.

Q The second column, DOI facilitates the capsaicin-induced release of SP and the rat dorsal horn essentially saying DOI enhances the pain.

A It's saying that DOI facilitates the release of substance P in the rat dorsal horn.

Q And that in layman's terms mean it enhances the pain does it not?

A Substance P is a molecule that can signal pain. It doesn't necessarily mean that it enhances the pain. It means that actually because

they're using the word facilitates, your interpretation is correct. Yes.

Q Okay. Thank you. Now I would like to move to Exhibit 50, which you also cited?

A Yes.

Q And I'll note that this is a study done in Japan. Correct?

A Yes.

Q Which would not be affected by the United States making DOI a Schedule I controlled substance. Correct?

A Yes.

Q And this is from August of 2000.

A Yes.

Q Now you cited this too in support of your position that DOI reduces pain.

A Yes.

Q And if you look on Page 3, I'll note that you never really discussed the effect of alpha-Methyl-5-HT did you?

A I did not discuss it. No.

Q And that actually on Page 3 if you look at that left-hand chart at the bottom, shows that alpha-Methyl-5-HT actually performed better in terms of relieving pain for a longer period of time.

Correct?

A In this experiment, that's what the data demonstrates.

Q Okay. And in your studies, have you considered using any non-controlled substances?

A Yes, sir, I have.

Q Okay, but you're not using them are you?

A I have used non-controlled substances in my studies.

Q In your current research, are you using any substances I guess we would call them, well any substances that do not produce hallucinations?

A Yes, sir. I am using substances in my current studies that do not produce hallucinations.

Q Any serotonin 2A agonists that don't cause hallucinations?

A Yes, sir. I'm using a serotonin 2A agonist called AL-34662.

Q Okay. Now your testimony and I don't want to mischaracterize it. It seems to be revolving around the idea that at one point DOI would have a currently accepted medical use.

A That is not how I think of my testimony.

Q Well your testimony seemed to revolve

around the idea that DOI might be a pain reducer.

A My testimony in my own words is that DOI could reveal novel, cellular molecular insights into our understanding of pain.

Q Okay.

A And that insight could result in the creation of novel therapies.

Q And you realize a DOI has no currently accepted medical use. Correct?

A Yes, sir.

Q Okay. You acknowledge that. And you're not really addressing any of the factors that would relate to whether DOI should be scheduled or not?

A I'm delivering my scientific understanding.

Q You mentioned that when you do your experiments with DOI, you lock up the DOI?

A Yes, sir.

Q And why bother doing that?

A Because I don't want anyone to tamper with DOI in any way.

Q Okay. Are you worried that someone might take it?

A Yes, sir.

Q Why? Because it's harmful isn't it?

A Because 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.

Q And that would be a problem wouldn't it?

A Yes, sir.

Q Now in your experiments, how do you administer DOI to the -- I assume rodents?

A Yes. I dilute the DOI in saline solution and then I inject the animals myself with DOI.

Q Is it done intrathecally?

A It is not done intrathecally. No, it is done intraperitoneally.

Q Would that be systemically?

A Yes, sir.

Q Yes?

A Yes, sir.

Q Okay. And you realize that that according to Exhibit 50 increases pain?

A In the study that Exhibit 50 cites, the authors that they're citing found that activation of the 2A receptor in those studies can cause pain.

Q Okay. Thank you. All right so there was a lot of discussion about the harm that might occur to your research if DOI is Schedule I. Are you going to shut down your research if DOI is Schedule I? Yes or no?

A No.

Q And whom have you talked to at UC Berkeley about the difficulties in attaining a Schedule I registration?

A I have talked to other scientists at UC Berkeley about the process of acquiring a Schedule I registration.

Q And who are they?

A Do I name them?

Q Yes, please.

A I had spoken to the two people in particular, I've spoken to multiple people, but two people significantly contributed to my understanding of the process, actually three people.

Dr. Hillel Adesnik at UC Berkeley, Dr. Andrea Gomez at UC Berkeley and the lab manager for the Adesnik Lab, Janine Beyer I think is her name.

Q I believe you -- Adesnik?

A Adesnik.

Q And --
A Gomez.
Q Gomez? And did you mention Lammel?
A I did not mention Lammel. I have not had correspondence with his lab regarding this --
Q Okay. And does Dr. Adesnik have a DEO registration?
A To my knowledge, Dr. Adesnik does have a DEA registration.
Q And does Dr. Gomez have a DEA registration?
A To my knowledge, Dr. Gomez does have a DEA registration.
Q Okay. Have you had discussions with either one of them about possibly doing your research under their DEA registrations?
A Yes, I talked about that with them and neither of them seemed to communicate that. That it would be a possibility. It seemed like they did not feel like they had the breathing room to add me onto their protocols.
Q So they both said no, they would not do it?
A They did not say that.
Q They did not say no?

A They did not say no.

Q So they didn't give you a yes or no answer on that?

A Correct.

Q Okay. And who are your advisors at Berkeley?

A Dr. Diana Bautista and Dr. Ellen Lumpkin.

Q All right. And who is the principal investigator?

A Both of them.

Q All right. Do you, you've said you ordered your DOI from Aldrich Sigma. Is that correct?

A Sigma-Aldrich, yes, sir.

Q Sigma-Aldrich. I'm sorry. And are you aware that Sigma-Aldrich has a Schedule I DEA registration?

A I would imagine that they do.

Q All right. I believe it was your testimony that even one day missing research can harm your project. Correct?

A Yes, sir.

Q So how long is your research going on? You've done it for two years.

A Two years.

Q And you're going to do it for two more years?

A Yes, sir.

Q Okay. So you haven't taken a day of vacation during all that time?

A Of course I do. I'm a human.

Q All right, so one day missing research does not derail your research product. Does it? Or your research project does it?

A It does, it can. Breaks need to be structured and planned.

Q Dr. Ramos, you talked about having to get IACUC approval?

A Yes, sir.

Q Okay. And what does IACUC stand for?

A IACUC is the Institute for Animal Use. It's the Institute for Animal Use and Care. Basically IACUC is a body of, is a group of people, committee at universities that evaluate whether or not the protocols are ethical and up to standards.

It consists of scientists, civilians, and veterinarians.

Q And is it safe to assume that you got IACUC approval to use DOI in this experiment?

A Yes.

Q Did you not? Okay. So you already had to go through that process?

A Yes, I believe I said that during my testimony.

Q And it's safe to say that you have not applied for a DEA registration. Correct?

A No, I have not yet.

Q And you've not spoken to anyone at DEA about the process of applying for DEA registration?

A I have not, no.

Q Okay. How much money have you received to do your current research?

A I have received, I'm currently supported by two grants. The one from the Miller Institute and the one from Howard Hughes Medical Institute.

The Miller Institute I have been affiliated with them now for two complete years. So that would include my salary for the first year and a portion of the second year.

So that's going to be $120,000 plus an extra $20,000 for extramural funds so that's $140,000 from the Miller Institute. And then the Hannah Gray Fellowship that's going to be salary

for one year so $140,000 plus $80,000, whatever that number is.

And then plus another $40,000 of extramural funds. So close to probably a quarter of a million dollars I have received thus far.

Q I think you had in your CV it's $1.5 million. Is that --

A Yes, it's administered over eight years.

Q Okay. So two places, the Miller Institute and the Hannah Gray Institute?

A Yes.

Q Okay, did I get that right?

A Yes, the Miller Institute and the Howard Hughes Medical Institute.

Q Okay.

A Yes.

Q Why did I say Hannah Gray?

A That's the name of the Fellowship Awarded --

Q Okay.

A -- by the Howard Hughes --

Q The Howard Hughes Institute?

A Yes, sir.

Q Okay. So have you informed the Miller

Institute or the Howard Hughes Institute that your research may be hampered or hindered or shut down at some point?

A I have not informed them of that because if, because I have leeway to conduct other experiments not related to DOI under the stipulations of the grant.

Q And how long have you known about DEA's efforts to control DOI?

A I have learned about them when the proposed rulemaking was posted.

MR. MANN: All right just one moment, Your Honor. That's all I have. Thank you.

JUDGE SOEFFING: Okay. Thank you, Mr. Mann. Mr. Phelps, redirect?

MR. PHELPS: Yes, if we could have just one moment.

JUDGE SOEFFING: Okay.

REDIRECT EXAMINATION

BY MR. PHELPS:

Q Dr. Ramos, the Government asked you about in one of the papers that you cited there was actually a citation to other research that DOI, in fact, increases pain.

A Yes.

Q And the research you've been working on is in how DOI can be used to decrease pain. Can you explain how both of those things could be determined in scientific experiments?

A Yes, I can do that. So biology is really complicated and messy. And the biology of serotonin is complicated and messy. There have been experimental results demonstrating that serotonin in our nervous system can both signal pain and signal against pain.

And so it continues to be a mystery amongst the scientific community of how and when it does one or the either and that's why this research is so important.

Q So that conundrum is really at the heart of the research that you're doing?

A Yes, sir.

Q And why is it, why is it important to understand that?

A If we can understand how serotonin in some instances be pro-pain and in other instances be anti-pain, that means we have a deeper understanding of how pain works and we can leverage that understanding in the development of therapies and medicine.

Q And would a further understanding of how that works be a benefit to public health?

A Yes, sir.

Q So would it be fair to say that making it harder to find that out could harm public health?

A I think that's an accurate assessment.

Q Now the Government asked you if you had spent every single day of the last two years working in your lab. Correct?

A Yes, I recall the question.

Q And you stated that was not correct. Right?

A Correct.

Q So can you explain how when every single day is, every single day away from your research can negatively impact your research, how do you balance that with the fact that you can't work in your lab 365 days a year?

A Yes, if I was working every day, I would be burnt out. If I was burnt out, my ability to perform my experiments to the best of my ability at the quality that I need to perform them would be significantly stunted.

So like every animal on the face of the planet, I also need to rest.

Q And so do how you, I guess my question is how do you, how do you structure your need to rest and take breaks around the, you know, around your research?

A Yes, so I, when I do experiments, I outline very detailed plans for these experiments and then I follow through on those plans and I also program rest and break in between those experiments.

So there are times where I am pushing projects really hard and then there's times where it's more of a slow burn and I'm analyzing the data and results from projects that I have performed.

And thinking about the next steps. Right? What people don't think about when it comes to being a scientist is that doing experiments is important, but thinking about what you do and taking time to think about it and what it means is just as important.

Q So you have to be very thoughtful in how you structure your time away from the labs to not impact your experience.

A Yes, I am very thoughtful about how I structure my time away from the lab.

Q And what is the difference between time

spent away from your lab for rest or to think back on your research versus time spent away from your lab dealing with bureaucracy?

A Yes, one of those is restful and it allows me to recharge and come back better and one of those is not restful, it does not allow me to recharge and does not allow me to come back to the lab in a better state.

Q And does the, does your commitment to the time you have to spend in your lab affect your ability to take time out for things that you sometimes would prefer to do?

A No.

Q You've never had to give something, you've never had to forego doing something outside of your lab because you had tests to conduct?

A Yes. I have.

Q And can you just explain how much having to be in your lab impacts your, what you're able to do outside of the lab?

A It has a significant impact and I could give an example. When I was a graduate student, the experiments that we conducted on animals required that they were on a water restriction schedule.

So that meant that the animals did not have free access to water. They needed to receive water at a specific time of day for a specific amount of time and an animal can't go the weekend without water because they're alive.

So throughout the entire duration of my Ph.D., I actually had to go into lab every day Monday through Monday. I had a team mate that sometimes we allowed each other to take breaks and he would do Saturday and I would do Sunday.

But for the duration of my Ph.D., I had to work throughout the week and the weekend and I had to plan my weekends. And sometimes I couldn't do things that I wanted to do because on the weekend, I still had to go in and take care of my animals.

Q And when you're working through these experiments, are you there at the lab on a standard 9:00 a.m. to 5:00 p.m. time schedule?

A That's not really how it works. Sometimes I can be in the lab on a standard 9:00 a.m. to 5:00 p.m. schedule. Sometimes I have experiments that last as long as 12 hours.

Q So it's not unusual for you to spend a 12-hour day in the lab just doing experiments?

A That's not unusual, no.

Q And the Government asked you a bit about your communications with your, with your fellowship and grant sponsors through this. So I'd like to just kind of zoom out on that for a minute.

And can you explain how your relationship with those two organizations works?

A I'm a scientist affiliated with those organizations and they fund me to do my research.

Q And do you provide them reports along the way to --

A Yes, I provide them with updates and I have the opportunity to communicate changes to my research.

Q Okay.

A Yes.

Q And have you had to communicate those changes in the past?

A When I switched from MDMA to DOI, I don't think I had to, I did not officially communicate it, but through discussion, everyone for example, at the Miller Institute knows that I work on DOI, even though my original proposal was for MDMA.

And with HMMI, I communicated with people at HMMI with someone in particular who has actually I think since then retired. But I communicated with someone that was involved in the Hannah Gray administration that I would be participating in these proceedings.

And yes, and I do give them regular updates on the work that I am doing, the research that I am doing. Yearly updates.

Q And how much do these granting institutions manage your day-to-day activities in your lab?

A They are not responsible for micromanaging my day to day or the experiments that I do.

Q And at this point with DOI not being scheduled to this point, other than the time you've had to take away from the lab to deal with this, has it impacted your ability to conduct your experiments?

A Yes, it has.

Q How so?

A We've had to prepare for these proceedings and that has taken time away from my job.

Q Okay. Looking at the job though, right now you're able to continue the same experiments with the DOI just around different time constraints. Right?

A Yes.

Q Okay. So other than letting them know maybe you're in these proceedings, you don't need to report to them that your research has changed yet. Right?

A No.

Q If DOI was to be placed in a Schedule I, would you communicate that to your grant funders?

A I don't necessarily need to tell them that DOI is Schedule I. What I would communicate is any alternative experiments that I begin to pursue.

Q Would those, would those granting institutions have any role in obtaining a DEA license?

A No.

Q Would you have any reason to communicate with them about your attempts to get a DEA license?

A I do not have to communicate with the

granting funding agencies anything that has to do with attempting to get a Schedule I license to my knowledge.

MR. PHELPS: Thank you. No further questions for this witness, Your Honor.

JUDGE SOEFFING: Thank you, Mr. Phelps. Mr. Mann, any re-cross?

MR. MANN: One second.

JUDGE SOEFFING: Okay.

MR. MANN: Nothing further, thank you.

JUDGE SOEFFING: All right, Dr. Ramos, thank you for your testimony. You are excused. I direct you not to discuss your testimony with anyone other than your attorney until the conclusion of the hearing.

THE WITNESS: Thank you.

JUDGE SOEFFING: And, Mr. Phelps, did he go to get the next witness?

MR. RUSH: Yes, he's yes.

JUDGE SOEFFING: Okay, very good.

MR. RUSH: I'll be, Your Honor, I'll be conducting the examination --

JUDGE SOEFFING: Okay.

MR. RUSH: -- of the next witness.

JUDGE SOEFFING: We're off the record.

(Whereupon, the above-entitled matter went off the Record at 11:36 a.m. and resumed at 11:37 a.m.)

JUDGE SOEFFING: Back on the record. And Mr. Rush, I understand you're handling the next witness.

MR. RUSH: Yes, Your Honor.

JUDGE SOEFFING: Okay. You may call the witness.

MR. RUSH: Your Honor, the Petitioners would like to call Dr. Harrison Elder.

JUDGE SOEFFING: Okay. Dr. Elder, please come up to the witness stand. Please raise your right hand. Do you swear or affirm under penalty of perjury that the testimony you are about to give shall be the truth, the whole truth and nothing but the truth?

DR. ELDER: I do.

WHEREUPON,

HARRISON ELDER

was called as a witness by Counsel for the Petitions and, having been first duly sworn, assumed the witness box, was examined and testified as follows:

JUDGE SOEFFING: You may be seated. Please state your first name, your last name and

spell them both for the record.

THE WITNESS: My first name is Harrison, H-A-R-R-I-S-O-N, last name Elder, E-L-D-E-R.

JUDGE SOEFFING: I thank you. Counsel, you may inquire.

MR. RUSH: Thank you, Your Honor. Good day. Thank you for taking the time to provide testimony to us today. Would you please reference Exhibit 74?

THE WITNESS: Thank you.

DIRECT EXAMINATION

BY MR. RUSH:

Q Would you please identify what the document is?

A It is my CV.

Q And is this a CV that you drafted?

A I did.

Q And you prepared this?

A That's correct.

Q And is it accurate?

A It is. It might be a little bit out of date depending on when it was submitted. But it is accurate to the --

Q Were your --

A -- best of my knowledge.

Q -- qualifications, it's there, there's nothing materially missing?

A That's correct.

MR. RUSH: All right. Your Honor, I would like entered into evidence Exhibit 74.

JUDGE SOEFFING: Mr. Mann, any objection?

MS. ATTANASIO: No objection, Your Honor.

JUDGE SOEFFING: Okay. So who's handling this witness for the Government?

MS. ATTANASIO: I will be, Your Honor.

JUDGE SOEFFING: Okay. Please identify yourself for the record.

MS. ATTANASIO: Alexis Attanasio, A-T-T-A-N-A-S-I-O.

JUDGE SOEFFING: Thank you. Okay so no objection. Petitioner's Exhibit marked for identification No. 74 has been offered. In the absence of an objection, it is received in the record as Petitioner's Exhibit 74. It's in, you may use it.

(Whereupon, the above-referred to document was received into evidence as

Petitioner's Exhibit No. 74.)

MR. RUSH: Thank you, Your Honor. We're going to walk through your resume now so we can get a full understanding exactly of your experience and competencies and qualifications to present at this hearing.

Your educational background, would you please describe any degrees that you have?

THE WITNESS: Absolutely. So I received my Bachelors of Arts in Biology from the University of Virginia in 2016 where I first began my research.

After graduating from the University of Virginia, I obtained a post-baccalaureate certificate from Northeastern before matriculating into VCU, Virginia Commonwealth University in Richmond where I earned my Ph.D. in Pharmacology and Toxicology.

BY MR. RUSH:

Q Are these accredited universities?

A They are.

Q And you received degrees from each of them. Correct?

A That's correct.

Q As part of your Ph.D., did you have to

provide a dissertation?

A I did. And defended it.

Q And you defended it?

A That's --

Q And you defended it successfully.

A That's correct.

Q What was the topic of that dissertation?

A Well the title here on the CV is Modulation of Opioid-Induced Respiratory Depression by Stimulants and their Associated Monoaminergic Receptor Mechanisms in Mice Using Whole Body Plethysmography.

Q Now regarding your training and course work that you've undertaken, would you please give an overview of what type of coursework that was?

A Absolutely. I mean aside from my general Bachelor's in Biology for undergraduate where I learned the basics of cellular and in vivo biology during my Ph.D. work, I took many courses on biochemistry, chemistry, neuropharmacology, the basics of pharmacokinetics and pharmacodynamics among many other courses.

Q Were you trained in any sort of methodology regarding how to evaluate data and

analyze data as part of your education?

A Absolutely. I took many courses on statistics and data analysis.

Q Okay. And you've taken courses on what are the standards for evaluation of, you know, research.

A Yes.

Q Thank you. Now I see you worked at -- what's your current position?

A So over the last year, I completed a post-doc, post-doctoral training at Johns Hopkins University School of Medicine in their Behavioral Pharmacology Human Behavioral Pharmacology Unit.

I very recently, I have left Johns Hopkins to begin employment in the private industry.

Q And with whom are you currently employed?

A I am currently employed by DeFloria Biosciences, but I am here on my own behalf and not representing them today.

MR. RUSH: We understand that.

JUDGE SOEFFING: Let me ask, when did you leave Johns Hopkins?

THE WITNESS: Roughly a month ago,

month and a half ago.

JUDGE SOEFFING: Okay, and when did you begin the new employment?

THE WITNESS: About six weeks ago.

JUDGE SOEFFING: Okay. Thank you.

THE WITNESS: Yes.

BY MR. RUSH:

Q And what's involved in your current employment?

A I'm the Senior Manager of Clinical Development for the company. So I help to develop, bring drugs through the clinical development process Phase I through III trials and all the regulatory documentation that's needed to successfully get a drug approved.

That's essentially the core components of my job. Including designing research and trials and things like that.

Q So it has a compliance aspect of it as well as analyze and research studies, things like that?

A Absolutely. It's made me quite familiar with the regulations surrounding controlled substances and drug development.

Q All right, let's go to your previous

position. Where was that at?

A Prior to graduate school?

Q Prior to your current, no prior to your current job that you currently have. Your most recent one.

A Oh, that was, so when I was a post-doctoral fellow as Johns Hopkins University's Behavioral Pharmacology Research Unit. Yes, that was my previous position.

Q This research unit, John Hopkins, is this regarded, how is this regarded generally in academia or popular, yes, in your, in the sector of, you know, scientific research?

A I can confidently say without bias that it's considered to be one of the top human behavior pharmacology labs in the country, if not the world.

Q Are there any notable alumni from John Hopkins University School of Medicines Behavioral Pharmacology Research Unit?

A Certainly. Roland Griffiths for one. Matt Johnson, another psychedelic researcher, Ryan Vandrey who is my advisor is another alumni who is but one of the top cannabis researchers in the world as well as the Government's witness, Theresa Carbonaro. Dr. Carbonaro is I believe an alumni

of this program as well.

Q And will you please describe what type of work were you doing at John Hopkins?

A When I was a post-doc at Hopkins, the majority of my work was related to human laboratory studies of drugs with abuse potential. So primarily cannabinoids and other phytochemicals from the cannabis plant.

But also working with the psychedelic group that was there and conducting outside of the human laboratory trials that I helped to develop and conduct and publish, I also did a significant amount of surveillance work, if you will, drug surveillance work.

Q Would you please explain to us what you mean by drug surveillance work?

A Absolutely. So there are at least two projects during my time there that are still actually ongoing that were involved with determining the availability of various cannabinoids and their analogs to the public through retail and other means.

Purchasing those products and having them analyzed for their contents. I also undertook projects similar to that for psychedelic

compounds, unscheduled and scheduled and their availability in the community and ratio locations and online as well.

JUDGE SOEFFING: Mr. Rush, can you adjust the microphone to get that a little bit closer to you?

MR. RUSH: Oh, sure. Absolutely.

JUDGE SOEFFING: Where you're speaking. Thank you.

MR. RUSH: Is that better? Oh.

JUDGE SOEFFING: Hold on a second. We're having a little bit of a technical difficulty with the reporter.

THE WITNESS: Is this loud enough?

JUDGE SOEFFING: You're fine. Yes, we're off the record.

(Whereupon, the above-entitled matter went off the Record at 11:47 a.m. and resumed at 11:48 a.m.)

JUDGE SOEFFING: Okay, back on the record.

BY MR. RUSH:

Q I see on your resume it indicates that you have experience. It looks like read surveillance studies, product chemical

composition to identify safety risks. What does that mean?

A So what that entailed was I'll just give an example. For the first part of the study, we went, we randomly selected various smoke shops and other retail locations to go and purchase cannabinoid products that were labeled with various cannabinoid analogs, psychedelic analogs, bought those products, sent them off to a lab for analytical chemistry, to determine what chemicals were in those products and at what concentration and what dose.

So that's determining their safety for consumption by the general public.

Q Okay, so we're working as a research fellow at John Hopkins, you were as part of your position, you conducted an analysis of illicit use of the version of drugs.

A You could say that yes.

Q Okay, I've seen that it says you aided in writing, reviewing, submitting regulatory documentation for clinical research studies for investigational new drug applications, clinical protocols and IRB documentation.

What did that entail and what was the

purpose of that?

A Most of that was regulatory documentation to ensure that the clinical trials and clinical studies that we were running were safe, were approved by HHS or at the FDA as well as the DEA because we were running studies on Schedule I through V drugs.

So much of that documentation was documenting the safety of those scheduled drugs that we were testing or we were proposing to test in clinical laboratory studies.

Essentially due diligence on the safety of our protocols and the purpose of the research.

Q And you, did you evaluate the legitimacy of the research involving the potentially controlled substances?

A Absolutely. I mean, as someone who had a background in pharmacology and toxicology while many of my colleagues were more in the psychometric side of things, I was tasked with ensuring that the toxicological data on scheduled substances was accurate.

And proved that the drugs that we were looking at would not be a safety risk in the laboratory when administered in a controlled

setting.

Q And you were responsible with rendering that determination?

A I was responsible for writing it up, but these documents were then obviously reviewed by various boards like our Institutional Review Board, the IRB and HHS DEA so I wrote them up and yes, and submitted them, but they were reviewed by other agencies and groups.

Q And is that a difficult process that you would, that they would, there's multiple levels with this that this would be submitted through?

A Yes, that's very typical.

Q Okay. Thank you. Was your work group viewed by any senior people to you there?

A Oh, certainly. I wasn't the principal investigator on the grant so the PI of those grants would review those, that documentation before submission.

Q And the people senior to you supervised you, did they approve your analysis?

A Yes.

Q Okay, I see here you've listed independently authored critical reviews of scientific literature in the field of clinical

pharmacology. Would you please explain what that means and what that entailed?

A Certainly. One of the first projects that I undertook at Johns Hopkins was to write up a comprehensive review, which is just a large research paper where you search the literature for published studies and then summarize them in a large, in a review paper to communicate the current state of some topic in science.

So specifically, I was looking at the human behavioral and clinical pharmacology of cannabinoids, their analogs and related phytochemicals.

Q And when you were conducting these reviews, if for example, if you were conducting a review of a substance say like heroin, a Schedule I substance, would a person who opines on that as part of your analysis be restricted to only people who have conducted actually heroin research?

Or could it be people who have conducted all sorts of research if it's relevant and reflected in the science overall?

A I wouldn't say that it's restrict to someone that's, I'm not sure I fully understand the question, but I wouldn't say that only people

who've conducted research with certain drugs are restricted, are the only ones that can publish and opine on them in the peer reviewed literature.

For example, I undertook this review to familiarize myself with the cannabinoid literature as I had previously worked mostly with monoaminergic drugs. So that's a common practice I would like to say.

Q So typically people are in your position, they can educate themselves and they typically do educate themselves on a variety of topics without actually conducting laboratory research themselves?

A That's correct.

Q All right. Thank you. Let's move onto your next position here. I see content, a writer at Psychedelic Science Review. What is Psychedelic Science Review?

A That is an online publication for public readership.

Q And what type of topics are covered there?

A The topics on Psychedelic Science Review are essentially reviewing current psychedelic science and happenings in the field of

psychedelic science so talking about new advances, new published papers, potential legal issues, things of that nature.

Q I see also it looks like you have indicated that current topics also involve abuse liability.

A That's correct, yes.

Q And that abuse liability, how many do you, what did that involve the abuse liability identifying?

A So the purpose of my work with Psychedelic Science Review was essentially scientific communication to the public. It was something I felt that needed, we needed more of.

And so one of the articles that I wrote, one of the last articles that I wrote was an article explaining what an Eight Factor Analysis was in simple terms, simple lay public, going over each factor of an Eight Factor Analysis, what it meant and how it might be applied to a drug like MDMA.

This was back before MDMA had been fully submitted to the FDA for approval so I essentially was explaining how an Eight Factor Analysis may work for new and novel psychedelic or inactive inert drugs so that was the gist of that paper or

that article I should say.

Q Okay. Thank you. Did you, did you analyze any papers there on hallucinogenic substances?

A Certainly. I mean, every article that I wrote for the Psychedelic Science Review was well cited with the published peer reviewed scientific research that's out there.

I didn't just opine. I mean, it was, they were well researched articles that I had written for them.

Q Well let me ask you about that. Your comment you've opined, you've evaluated these articles. What's the standard that you go by to do this? Is there a standard that research is evaluated under?

A I mean the quality and legitimacy of research is typically evaluated on being peer reviewed and then published in journals by reputable institutions and researchers.

Most of that article was based on a published article by Dr. Jack Henningfield who is another drug policy advocate and consultant who wrote a peer reviewed and published paper outlining the process for evaluating psychedelics under an

Eight Factor Analysis. I believe it was published in 2022.

Q And peer review, that said peer review is kind of the standard that you would work with and that's generally what you could, was that the accepted methodology of them for analyzing and qualifying the validity of research?

A Yes, I would say that that's the general gold standard for what constitutes the research, a published research paper.

Q And when you're evaluating these things as part of your positions, do you look for errors in the papers?

A I do. I tend to be a little bit, scrutinize the papers a little bit more if I'm skeptical of their findings, but I absolutely read through papers that I cite.

Q But generally in the, in your experience, there's established standards and generally accepted methodologies that are applied?

A That's correct, yes.

Q And you applied those yourself?

A That's correct, yes.

Q Were you ever, did you ever not apply those?

A Not to my knowledge.

Q Now I see you were a Project Manager and Clinical Liaison; Misuse, Abuse, and Diversion Drug Event Reporting System, MADDERS at Analgesic Solutions, LLC. What is Analgesic Solutions, LLC?

A Analgesic Solutions, LLC was a company that I worked for after graduating with my bachelor's from the University of Virginia up in the Boston area.

And the company was founded and this was a small company that was founded to improve the quality of analgesic clinical trials of pain medications.

And the product that I was in charge of was this, the MADDERS system, which was what you just stated, the Misuse, Abuse, and Diversion Drug Event Reporting System, which was designed by myself and the owner of the company, Dr. Nathaniel Katz, to capture, evaluate and report instances of misuse, abuse and diversion of investigational drugs.

So let's say a new opioid or a new chemical entity that was being looked at for pain relief, we would implement this MADDERS system and the clinical trials of it to assess misuse, abuse

and diversion of those new unapproved investigational drugs.

Q Would you call this kind of an emerging drug threat?

A I'm sorry, I don't know if I understand the question.

Q Well I, I asked if you determined or you assessed whether there were, you know, the likelihood that there is a new threat emerging from drugs based upon your analysis of diversion, misuse?

A That's correct. We would provide essentially an abridged threat analysis on these investigational drugs to determine if they posed a threat to public health if they were to be approved let's say as a pain medication.

Q And in your analysis here, did you, did you look at only scheduled drugs?

A Most of the drugs that I was evaluating with the MADDERS system were unscheduled or uncontrolled at the time because they were investigational drugs.

That was part of the reason that we were monitoring them is to see if that would later be necessary.

Q So as part of your duties, you were tasked with monitoring and evaluating whether there is misuse, diversion of non-scheduled drugs.

A That's correct.

Q Thank you. What is the adjudication committee at Analgesic Solutions?

A So the way that the MADDERS system would work is as I'm sure some of, you know, large Phase III clinical trials are run at multiple sites.

We would train site staff who were running the study on various ways to identify misuse, abuse and diversion. We would train them on how to write up a narrative and collect information around instances where they suspected any of a number of triggering events as we called them.

And I would collect those reports from the sites and bring them to an adjudication committee that I had convened of key opinion leaders and experts in the field of addiction medicine.

I would convene the adjudication committee maybe once or twice a month to go over any reports that we had received from the sites, any narratives and reports from the sites of

misuse, abuse and different potentially diversion related activities.

And then I would gather their opinions and make a judgment on whether or not that report from the site truly constituted an instances of misuse, abuse or diversion.

Q So you were working with your team then looking at clinical research if something was being inappropriately diverted, inappropriately used, that's what your team would sort of meet, collect on and provide an opinion on whether it was improper. Is that --

A That's correct. And then those results would eventually be written up for submission with the new drug application to both the FDA and I believe the DEA.

Q So these reports that you would generate these -- I see it says clinical trial safety monitoring pharmacovigilance of use liability assessments and outcomes. And these you reported to the FDA?

A That's correct. Yes, we reported them to our clients, which wrote them up in their NDAs, documents that are submitted to the FDA and DEA.

Q I see here it says you published

manuscripts on clinical abuse liability, clinical trial design for peer review journals, present findings for trial safety monitoring and international scientific conferences. And that was for psychoactive substances typically?

A Yes, I believe one of the papers that we published on clinical abuse liability was on an investigational opioid drug developed by Nektar Pharmaceuticals.

And we actually did find several instances of abuse and diversion in those trials, which is why we published the data. And then I had also presented much of the data that I collected with the MADDERS system that international conferences and other scientific meetings.

Q And what was the result of your work? Did you have any accomplishments, successes of providing this liability, abuse liability data. I see here it says you submitted with -- what is this drug, Epidiolex?

A Yes, actually so that I would say was one of the greater successes of the MADDERS system while I worked there. Epidiolex otherwise known as cannabidiol, CBD, was being developed by GW at the time and we had implemented the MADDERS system

in their trials to demonstrate that CBD had little to no abuse liability, which it does not.

And that was actually a success because of the negative result. We didn't find any instances of abuse or diversion of CBD that was put into there, that was reported to the client.

And that their drug was eventually approved a year or so later with the inclusion of some of our negative data from the MADDERS showing a lack of abuse potential.

Q When you were working in your evaluation compliance capacity there, was cannabidiol -- what Schedule was that?

A The status of CBD is a little convoluted over the past several years. CBD I believe was at one point considered a Schedule I substance as a component of cannabis.

The Farm Bill from 2016 I believe it was, a U.S. Agriculture Bill, reclassified hemp-derived CBD as an unscheduled substance. I don't really know that the specifics of the legislative ins and outs of CBD's controlled status, but at the time it was considered to be noncontrolled if it was from hemp.

But it had previously been considered

to be a Schedule I substance as a component of marijuana or cannabis if you will.

Q So basically you, part of your experience involved looking at a substance that was previously Schedule I and Schedule V now?

A That's correct. Actually, yes, that's correct.

Q And you also worked as an associate product manager, it says MADDERS at Analgesic Solutions, LLC.

A Yes, the following few positions on my CV are simply the previous positions that I held before being promoted and taking over various aspects of the company to manage.

Q Okay. Well we need to know what you did there and what your responsibilities were.

A Certainly.

Q What was your obligations under the MADDERS system? What was your employment duties?

A Prior to managing the MADDERS, when I was an associate, I would essentially do all of the activities that are required to implement the system so flying to sites, training site personnel in how to spot misuse, abuse and diversion-related events.

Collecting those narratives and reports, convening the adjudication committees, helping to do data analysis on those MADDERS reports and data, helping to draft up the manuscripts, things of that nature.

It was more of an assistant role, but essentially all the same duties I had as a manager.

Q And so it was kind of an establishing the methods and procedures to establish the validity or compliance?

A Yes, that's correct.

Q What is KOLs? I see up here identified and liaised with KOLs.

A It's an acronym for Key Opinion Leader so a doctor, researcher, physician who is considered to be an expert in their field by their field.

Q So your work, a Key Opinion Leader, that would be kind of the expert in the field on that?

A Yes, an expert from the field, yes.

Q And you liaison with them, worked with them and they approved your methodology?

A Yes, I would say that they approved of the methodologies. Some of them were involved in our Scientific Advisory Board as well whose purpose

was to review the validity of the methods.

Q And you also looks like trained clinical site personnel in compliance?

A I did, yes.

Q What is the accurate paying reporter and placebo response reduction?

A Those were earlier products developed by Analgesic Solutions to improve the validity and the accuracy of the pain reports that we, that subjects in clinical trials would give to site personnels.

So, you know, early on we were working on some Phase IV efficacy and surveillance trials that were actually mandated after many of the Purdue and OxyContin lawsuits.

And those were developed to improve the reports that patients were giving as patients sometimes, or subjects are sometimes not the most well-versed in how to report their pain on the scales that are used in clinical trials.

Q What's a focused analgesics selection testing device?

A That was a device that is related to those two trainings that would be placed on a subject's forearm. It would heat up. It had a

thermal component, would heat up on their forearm to a painful degree, various different settings of painful degrees.

And it was used to train subjects and patients on how to accurately feel and report their pain. So let's say if it heats up to 100 degrees Fahrenheit that might be a 2 out of 10.

If the device heated up to 150 degrees Fahrenheit for a second, you know, we were trying to get them to report that accurately or see if they could report it accurately. That was what the device was used for.

Q Okay, so it's a device used to evaluate pain?

A Yes.

MS. ATTANASIO: Objection, Your Honor. Can we restrict the questions of these to this matter? We're kind of going outside the scope here about what his expertise is.

MR. RUSH: Your --

MS. ATTANASIO: About these different things.

JUDGE SOEFFING: I'll give some latitude because he is being offered -- I assume this is a lead up an offering him as an expert

witness?

MR. RUSH: Absolutely, Your Honor. We're trying to establish that he has the qualifications to represent himself as an expert to this court and we need to explain what those qualifications are.

JUDGE SOEFFING: Sure. I'll overrule the objection. I will say that we are spending a lot of time on this. So to the extent that it's not specific to what he's being offered an expert in, I think that would yield us some time savings.

MR. RUSH: Understood, Your Honor.

JUDGE SOEFFING: Let me ask since we have this little break here, Dr., again what is your current title since you've left Hopkins at the new job?

THE WITNESS: I'm the Senior Manager of Clinical Development.

JUDGE SOEFFING: Okay. And the name of the company again?

THE WITNESS: DeFloria Biosciences.

JUDGE SOEFFING: Can you spell that please?

THE WITNESS: D-E-F-L-O-R-I-A, Biosciences.

JUDGE SOEFFING: Okay and where's --

THE WITNESS: And again, they're in Littleton, Colorado outside of Denver. I don't know if I could give you the street address off the top of my head, but again, I should state that I'm here as a private citizen and not as an employee of them.

JUDGE SOEFFING: Do you work in Littleton, Colorado or you work remotely?

THE WITNESS: I work remotely at the moment.

JUDGE SOEFFING: Okay, thank you. Go ahead, Mr. Rush.

BY MR. RUSH:

Q Thank you, Your Honor. Would your undergraduate research assistant position entail cocaine self-administration? Please tell me about what that --.

A Certainly.

Q Briefly.

A Yes, that was when I was an undergraduate. It was my first introduction to research. I worked with Dr. Wendy Lynch, who was a well-renowned psychostimulant and monoamine researcher.

And I was an undergraduate laboratory assistant, running cocaine self-administration studies with rats, not assessing abuse potential, but assessing actually treatments for substance abuse disorder and stimulant use disorder.

Q Okay, thank you. Have you published any academic papers?

A I have published many academic papers, yes.

Q Approximately how many?

A Approximately 12 to 16. I haven't counted recently. There's several that are being reviewed.

Q Understood. And those were peer reviewed publications?

A That's correct, yes. Looks to be about 15.

MR. RUSH: Your Honor, we would like to move that Dr. Elder be certified as an expert in pharmacology, chemistry, substance abuse, and compliance.

JUDGE SOEFFING: All right.

MR. RUSH: Regulatory compliance.

JUDGE SOEFFING: So that's different than what was put in the prehearing statement. Can

you give me that again?

MR. RUSH: Pharmacology, chemistry, substance abuse liability and regulatory compliance.

JUDGE SOEFFING: Pharmacology, chemistry, substance abuse liability, and regulatory compliance?

MR. RUSH: Yes, Your Honor.

JUDGE SOEFFING: Okay. In the Supplemental Prehearing Statement, it stated he was going to be offered as an expert in the study of respiratory depression and substance use disorders.

Specially, the use of monoamines including psychedelics as modulators of respiratory depression. Do you not wish to enter him as an expert in that field or as this designation?

MR. RUSH: I would add that to the designation that we are seeking. I just want, what I'm trying to do is I'm trying to be broad because it's -- or at least I'm trying to capture a definition that reflects what he's truly an expert of.

And not have it put into a very sort of

narrow -- that's kind of pedantically limited structure based upon verbiage.

JUDGE SOEFFING: Well that is the purpose of the prehearing statements is to state what the person is going to be offered as an expert in and you're talking about different categories of science than what was disclosed in the Prehearing Statement.

MR. RUSH: I guess I would, let me look at his what the supplemental statement, but the --

JUDGE SOEFFING: The Supplemental Prehearing Statement.

MR. RUSH: Yes.

JUDGE SOEFFING: Let me ask Ms. Attanasio, what the Government's view is if you're willing to stipulate to him being an expert in these fields or what's the Government's position?

MS. ATTANASIO: No, Your Honor. We would object to that because we've had no notice of this and they've had months to tell us or to change, make a motion about changing his expertise here.

JUDGE SOEFFING: Okay. What about, what's your position or would you like to conduct voir dire on the disclosed subject matter for which

he was to be proposed as an expert in?

MS. ATTANASIO: Oh, we would voir dire that.

JUDGE SOEFFING: Okay. All right, well you know, I don't think there was sufficient notice to the Government of these other areas in which you're now proposing to have him admitted as an expert in.

So we will stick what was disclosed in the Supplemental Prehearing Statement. Mr. Rush, I assume you still want to offer him as an expert in that?

MR. RUSH: Well, yes. I believe that the respiratory depression disease fall under the category of pharmacology so we would expert in pharmacology also.

And you know, it's my understanding that the purpose of this is to provide notice to the Government that they're not surprised and they were adequately able to prepare.

And the Federal Rules of Civil Procedure are more flexible here. It seems that there's, based upon what was in the, you know, our first description of what Dr. Elder would testify, our initial Prehearing Statement explained to the

Government what this, you know, reflecting what his actual experience and expertise is and provided them with notice.

There's not a surprise that's occurring based upon what's been provided to them between his resume, the description in our initial Prehearing Statement as to what he would testify to and then the Supplemental one is the supplemental. It's additional to --.

JUDGE SOEFFING: Right. Well, the subject matter certainly that was disclosed to the Government, you know, he can testify to, but I do think it is a bit of surprise.

It's a surprise to me that you're listing, that what you're offering him as an expert in initially here is completely different than what was put in the Supplemental Prehearing Statement.

There's no mention of pharmacology, chemistry. There was a discussion about substance use disorder, but there's no mention of regulatory compliance.

So I think, you know, if you want to stick with what you have in Supplemental, I'll allow the Government to conduct voir dire and then, you know, I'll make a ruling.

MR. RUSH: Well I --

JUDGE SOEFFING: It's not going to affect, you know, if it's been disclosed he can talk about it through subject matters, but I'm not going to designate him as an expert in something that the Government was not given prior notice about.

MR. RUSH: All right, yes, well that would be he can testify to the issues on his personal knowledge and experience, but the -- so what exactly is the --

JUDGE SOEFFING: Well what I have and what was written in the Supplemental Prehearing Statement is that he would be offered as an expert in the study of respiratory depression and substance use disorders, specifically the use of monoamines including psychedelics as modulators of respiratory depression.

MR. RUSH: May --

JUDGE SOEFFING: Is that what you wish to enter?

MR. RUSH: May I confer with my --

JUDGE SOEFFING: Sure.

MR. RUSH: -- co-counsel, Your Honor?

JUDGE SOEFFING: Sure.

MR. RUSH: Thank you.

JUDGE SOEFFING: And let me just add, Mr. Rush, this was discussed at the first Prehearing Conference over the summer when we discussed the parties' Prehearing Statements and at that point, none of the proposed witnesses for the Petitioners were disclosed or offered as expert witnesses.

And we discussed that and that's why in the Supplemental that the Petitioners filed, that Supplemental Prehearing Statement identified each of the witnesses as an expert in that particular area, which are very specific and highly technical.

So I think there's been, there certainly was a lot of discussion about this in the prehearing proceedings and ample opportunity for the Petitioners to think about exactly what they wanted to offer these witnesses as experts in so here we have to say.

MR. RUSH: All right, Your Honor. I would just like to as he here will testify as an expert in say respiratory depression substance use disorders specifically the use of monoamines, including psychedelics as modulators of respiratory depression.

And it would be my understanding that

is pharmacology, but and, but so we will, we will accept your, the previous --

JUDGE SOEFFING: Okay, well I will now ask the Government if they want to stipulate to pharmacology or not based on that description, but so you'll offer him as an expert in what was disclosed in the Supplemental Prehearing Statement with potentially pharmacology being added to that if the Government is agreeable.

MR. RUSH: Yes, Your Honor.

JUDGE SOEFFING: Okay. All right, Ms. Attanasio, you may conduct voir dire now or we can break for lunch and you conduct it when we come back.

MS. ATTANASIO: We can break for lunch.

JUDGE SOEFFING: Okay. Let's go ahead and we'll break for lunch and we will return in one hour. We're off the record.

(Whereupon, the above-entitled matter went off the record at 12:26 p.m. and resumed at 1:38 p.m.)

JUDGE SOEFFING: Okay, we are back on the record, Dr. Elder is on the stand, Dr. I remind you you are still under oath, and Ms. Attanasio you may conduct your voir dire.

MS. ATTANASIO: Thank you, Your Honor. Good afternoon, Dr. Elder.

THE WITNESS: Good afternoon.

BY MS. ATTANASIO:

Q So I believe on direct you briefly mentioned respiratory depression. What is respiratory depression?

A Respiratory depression refers to the slowing of breathing induced by disease or drug.

Q What kind of drugs cause respiratory depression?

A All manners of drugs can cause respiratory depression in various assays, but most commonly opioids such as fentanyl and oxycodone, those are typically what's held up as an example of respiratory depression, but many different drugs, alcohol included, can depress respiration.

Q So I believe you mentioned respiratory depression earlier, you were talking about your dissertation. Can you go into a little more detail about what your dissertation was?

A Sure thing. So I spent several years in a pre-clinical laboratory working with mice and rats. The dissertation work I did was looking at fentanyl specifically, fentanyl's depression of

respiration that typically leads to fatal overdoses in humans. My dissertation work was predicated on a finding of mine early in my research where I saw that combinations of fentanyl with psychostimulant drugs like methamphetamine, amphetamine, cocaine, tended to have a very interesting interaction whereby higher doses reverse that respiratory depression and lower doses actually exacerbated it.

And so my dissertation work focused on looking at the various monoamines, so dopamine, norepinephrine, and serotonin receptor targets of amphetamines to determine which of those were contributing to this bidirectional effect that I saw. Over the course of that research and what that research included was looking at numerous agonists of monoamine receptors, including DOI as an agonist of 5-HT2A to determine what their influence was on respiration and behavior and if they could reverse fentanyl induced depression, and that was the dissertation work that I did.

Q Have you studied any other psychedelics, specifically as modulators of respiratory depression?

A As modulators of respiratory

depression? None that I would say are pure psychedelics if you will. MDMA is somewhere in between, it's an amphetamine and it has some psychedelic mechanisms of action but I wouldn't call it a psychedelic, it's more of an entactogen.

Q Do you still have Petitioner's Exhibit 74 in front of you?

A I do.

Q I want to turn to page three, where we talk about your publications. Specifically can you talk about the serotonergic psychedelic modulation of opioid reward and behavior?

A Yes, that's a review manuscript that I put together with Dr. Jaster kind of combining some of the findings that we -- some of the results that we obtained during our graduate work as well as a review of some of the literature on how psychedelic 5-HT2A agonists modulate opioid reward, so the reinforcing effects of opioids, and how psychedelics interact with respiratory depression to ameliorate that effect, as well as an in depth mechanistic discussion of how psychedelics activate the 5-HT2A receptor, the circuits that hey activate, the regions of the brain that are impacted by psychedelics and things of that nature.

That paper was submitted, it's under review, it's currently, I don't believe published yet.

Q What experience do you have in substance use disorders?

A My entire research career has essentially revolved around substance use disorder and substance abuse. So my first research experience at the University of Virginia with Dr. Wendy Lynch was looking at treatments for stimulant use disorder, SUD, in rats who are self-administering cocaine. I previously described my experience looking at misuse, abuse, and diversion of investigational new drugs, both scheduled and unscheduled. The T-32 training grant from NIDA that I obtained my PhD on that I was funded by was granted by NIDA, the National Institute of Drug Abuse, and I believe the title of it is Pharmacology of Drug Abuse. So my entire PhD training revolved around substance use disorders and drug abuse, psychoactive drugs.

MS. ATTANASIO: Just one moment, Your Honor. Looking back at your paper that you said has not been published yet that you were working on with Dr. Jaster, can the Witness be shown Petitioner's Exhibit 17?

THE WITNESS: Thank you.

BY MS. ATTANASIO:

Q Is that exhibit from the paper you were discussing before?

A This looks to be a figure from some of Dr. Jaster's work on extinction of oxy preference in male and female mice.

Q Yes, but is that part of the paper we were discussing before about the --

A It's part of the results that are included in the paper, I'm not sure if this figure finally made it into the paper, the final version of the paper.

Q Okay.

A Yeah. They tend to be edited after peer review, so.

MS. ATTANASIO: Your Honor, the Government doesn't object to Dr. Elder being an expert, but only in what was put in the supplemental prehearing statement, respiratory depression and substance abuse disorder, specifically the use of monoamines including psychedelics as modulators of respiratory depression.

JUDGE SOEFFING: Okay, all right, thank you Ms. Attanasio. Mr. Rush, do you still

wish to offer him as an expert in additional areas besides what the Government is not objecting to?

MR. RUSH: While we believe he does have expertise in that, we'll agree to that.

JUDGE SOEFFING: Okay, so we'll stick with what he was testifying as an expert in, in the Petitioner's supplemental prehearing statement. So the Petitioners have offered Dr. Elder as an expert in the study of respiratory depression and substance use disorders, specifically the use of monoamines, including psychedelics, as modulators of respiratory depression. In the absence of any objection by the Government, the tribunal accepts the Witness as an expert in that area. And you may ask your next question, Mr. Rush.

MR. RUSH: Thank you, Your Honor, if I may have one moment, please. Would you describe the classes of drugs you studied and which of those you have the most pharmacological knowledge of?

THE WITNESS: Certainly. I've spoke a little bit about my dissertation work and the research that I did in undergrad and in the years following my undergraduate studies. I would say that the vast majority of my work in graduate school with animals was done with opioid agonists,

psychostimulants such as amphetamines, and also psychedelics, I spent at least two out of the three rotations I did as a student rotating through labs working with various psychedelic compounds under Dr. Steve Negus and Dr. Jaster's lab as well. Although I do have experience with most classes of abused drugs I would say, it's just that psychostimulants, opioids, and psychedelics tend to be the central ones. I currently work extensively with cannabinoids, although those are scheduled and unscheduled.

BY MR. RUSH:

Q Okay. When you say a psychedelic drug, is there a defined list of drugs that are psychedelics, or can it mean many things?

A It really depends on who you ask. There are multiple different definitions of a psychedelic in pharmacology. The definition that many people accept and one that I typically subscribe to is psychedelics must activate the 5-HT2A receptor or 5-HT2 subtypes in order to produce the psychedelic action. I mentioned before things like MDMA act as an amphetamine, but they also do have effects at 5-HT2, which makes them somewhere in between, they kind of have a unique

mechanism of action. Some people would call MDMA a psychedelic and others would not. Some people would also lump things like ketamine, NMDA antagonists into the broader classification of psychedelics, ketamine and GCP, but I personally tend to subscribe to the 5-HT2 theory.

Q But there are people who are recognized experts also who would call something as ketamine to be a psychedelic?

A Yes, that's definitely not a settled issue, there's many different drugs with various mechanisms of action that experts, people with PhDs who study this field might consider psychedelic drugs. Another way I've seen them classified are prototypical or classical psychedelics, and then psychedelics as a whole, so prototypical psychedelics like the LDS, psilocybin, mescaline, whereas ketamine might just fall under the greater classification of psychedelic or hallucinogen.

Q Those psychedelics, do they encompass only scheduled drugs or do they also encompass unscheduled drugs potentially?

A They could potentially encompass unscheduled drugs in things like dextromethorphan, DXM, it's an NMDA antagonist with other

serotonergic effects, if taken at the right dose it can produce dissociative and some might call hallucinogenic psychedelic effects.

Q Now these monoamines, what is a monoamine?

A The monoamines, at least in the way that I'm referencing them in my publications and on my CV are considered to be dopamine, serotonin, norepinephrine, adrenaline could also be considered a monoamine, as could others, but the three primary monoamines in the central nervous system that mediate behavior, addiction, things like that are dopamine, norepinephrine, and serotonin, or at least that was my focus.

Q Okay, so the drugs that effect serotonin -- I'm trying to understand this because it's fairly complex for a layperson. So this monoamine, so a drug that effects serotonin or dopamine, that's a monoamine potentially?

A Yes, that would be a monoaminergic drug, yes.

Q Okay.

A So psychedelics would be considered monoaminergic drugs, or an agonist of a monoamine receptor, if you will.

Q So if I understand correctly, it sounds like that monoamine class of drugs is a fairly broad class of drugs.

A Yes, it's very broad.

Q Okay, thank you. And in your personal experience, in your professional experiences as you testified, you do have experience with assessing the diversion of controlled substances?

A I do, yes.

Q And for monitoring for these what you typically see as problematic behavior, yeah, noncompliance?

A That's correct.

JUDGE SOEFFING: So Mr. Rush, less leading.

MR. RUSH: Yes, Your Honor. Do you have knowledge of the acquisition of DOI for research?

THE WITNESS: I do, yes, I've acquired DOI previously for my studies, my research.

BY MR. RUSH:

Q How is DOI typically acquired?

A When used in a legitimate purpose, as it usually is in the laboratory, we simply reach out to a chemical supplier such as Sigma-Aldrich

or Cayman Chemical that we have a prior registration with. Most of the companies that provide scheduled and unscheduled compounds for research tend to have us registered with them, and then you simply just order it to the lab like another research material. They tend to be quite expensive as they are right now, but I've acquired them through these commercial suppliers previously, yes.

Q You stated that part of your experiences analyzing illicit use and diversion from a compliance -- have you see acquisition of this from any non-regulated chemical companies?

A So as part of my work, both on my dissertation with the respiratory depression and in other surveillance work I've had to look through, I've 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. I personally have never come across DOI from any of these vendors that would sell to the general public, it's just not something that seems to be widely available.

Now, I can't say if it's available in other black market sources, but I've never seen --

it doesn't seem that DOI is widely available to the general public, I would personally say, and I haven't seen it diverted from the lab or heard of anyone ever asking to buy it or take it out of the lab. There's not a lot of interest in it, I guess I'll put it that way, when it comes to diversion.

Q Have you even seen one instance of illicit offers of sale of DOI?

A I don't believe I have.

Q In your review of medical literature, scientific research literature, have you encountered any information regarding that there is human use of DOI?

A In the medical and scientific literature, I actually looked last night, I don't believe that there are any case reports of human use of DOI published in peer review journals. There are obviously forums and online drug discussions where people claim to have taken it, but I've 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.

Q Now you've testified that you have extensive experience in evaluating and critiquing

the legitimacy of research and the validity of research, if I'm correct.

MS. ATTANASIO: Objection, Your Honor, that's not his expertise.

JUDGE SOEFFING: Sustained.

MR. RUSH: You've commented that you have experience evaluating, rendering part of your -- it's like the psychedelic review and some of these other plans you work on for peer review publications and analyzing these, would evidence from one of these social forums generally be considered the type of evidence that would be in one of those type of publications or as valid evidence?

THE WITNESS: Typically those would be considered anecdotal and potentially spurious. I've seen them published as a part of, I don't know, a narrative, I guess, to say -- they can be included as certain types of data but with caveats and limitations, but no, you would never be able to publish those because they're uncorroborated reports, anyone can write anything they want on the internet. So they can be collected and published as part of a larger study, but the accuracy and validity of that information typically requires

limitations and stipulations.

BY MR. RUSH:

Q So this anecdotal social media forum type of evidence, is there any verification process in that, if it would be offered?

A No, there's no way to verify if people's posts on Reddit or Bluelight or any of these other sites is accurate or if this person took the drug that they're claiming to have taken. Any number of things could be incorrect about that, which is why they're not considered to be reputable scientific information. They might be used to provide color or background for an actual study, but they wouldn't be considered evidence.

Q Would Erowid be an example of one of these types of sites?

A It would, yes.

Q Would Reddit?

A Reddit would be, yes.

Q Would the comments on Facebook?

MS. ATTANASIO: Objection, Your Honor, we're still going outside of his expertise.

JUDGE SOEFFING: Overruled.

THE WITNESS: I guess you could consider a comment on Facebook to be a forum, a post

about drug use on a forum, it wouldn't be typical, and I don't know if you could really -- if you read a comment on Facebook about somebody taking DOI, it doesn't have face validity to me.

MR. RUSH: What would you view as valid, verifiable evidence of the use of DOI?

THE WITNESS: Verifiable evidence to me would be a report from an emergency department of someone reporting in of a drug testing center reporting finding DOI in a blood or urine sample, a study that's done, a survey even of psychedelic users that they brought it could be used as evidence, but there's many different types of evidence that could corroborate human use of DOI and there really is not any. A case report even of someone just of medical personnel encountering someone intoxicated on DOI would be good evidence of that.

BY MR. RUSH:

Q Have you encountered any incident of that?

A Just did a search last night on PubMed and nothing came up.

Q Thank you. What has been your experience with epidemiology of drug overdoses?

A So in order to -- the background for my dissertation work on fentanyl induced respiratory depression necessarily required me to do an in depth analysis of overdose deaths, the epidemiology of overdose deaths in poly-drug use, the prevalence of drug use in the United States, the types of drugs, so I have extensive experience researching epidemiological topics, especially as they relate to overdose. And when I was -- in several aspects of my career I've had to do epidemiological work as both background rationale and justification for some of the studies that we've run. So I'm fairly familiar with the epidemiology of drug overdoses.

Q And in doing that work, what did you learn about illicit and grey market drugs for your research?

MS. ATTANASIO: Objection Your Honor, he's not an epidemiologist, or at least he wasn't offered as one as an expert.

JUDGE SOEFFING: Well he's not been qualified as an expert in epidemiology, yes, but to the extent that he has worked in that area or published, I think he can comment and discuss what work he has done in the area, so overruled.

THE WITNESS: I believe the question was about my knowledge of illicit and grey market substances, is that correct?

MR. RUSH: Yes.

THE WITNESS: As part of my research, my background research and rationale research for the fentanyl overdose and respiratory depression work, I did an extensive and exhaustive search of -- I don't know how to put it, grey market vendors of various chemicals and drugs, so things like fentanyl analogs, other opioid analogs like nitazenes, also psychostimulants and various psychedelics that are offered by grey market vendors, so I had 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, it allowed me to get a fairly clear picture of what is available to buy to the general public.

BY MR. RUSH:

Q And when you analyze this research that you conducted, you looked at different classes of drugs?

A I did, it was in order to evaluate a vendor of these grey market, illicit but analog

chemicals, you necessarily had to go through their whole catalog, which showed me the types of offerings that these vendors had, and I ran into dozens of different chemicals that were offered over the years, between 2019 and 2023. I never once came across a vendor offering DOI in that time, but you know, I don't know if there's anything else to say on that point, yeah.

Q Were there different classes of drugs that were more popular or less popular with these vendors?

A Oh absolutely. The novel benzodiazepines and novel fentanyl analogs and opioid analogs were by far the most popular and most dangerous drugs that were being offered, whereas most vendors carried a smaller number of psychedelic drugs or psychedelic adjacent drugs that seemed to be less popular and less discussed on forms and things of that nature.

Q What type of psychedelic drugs did you encounter with these vendors?

A All classes of psychedelic drugs, so modified analogs of LSD, tryptamines, base tryptamines and substituted ones, substituted phenethylamines that are illegal in this country

but not in others, various classes.

Q You're going to have to help me out a little, I don't know what a substituted tryptamine is. So give us a few examples of what type of drugs those are?

A Sure thing. So these grey market vendors would offer things like 4-hydroxy-methyl-ethyltryptamine, which is similar to psilocybin but is unscheduled, or they would offer something like LSD, 1 butyl LSD, which has a butoxy group on it or butynol group on it, excuse me, rendering it not LSD but a prodrug of it, things of that nature.

Q Did you come across these, I've seen them referred to as DOx class of compounds? First, let me make sure I understand what DOx as it's referenced means.

A Sure thing. I believe the terminology DOx was coined by Dr. Shulgin, referring to the dimethoxy nature of the series of amphetamines, so two methoxy groups on it, di, the D, oxy, O, and then the final substituent on the molecule is the x, right, and that's either B or I or C, to denote various homologues of the series.

Q And when you looked at these illicit

drug vendors, was that class of drug a very popular class of drug among psychedelic drugs for sale, or less popular that the other psychedelic drugs that are there?

A They're exceedingly rare, some of them would be available every so often, but they're a rare class of drugs because they're not popular recreationally due to the duration of their onset, their duration of effects, their general unpleasantness, but that's me opining a bit on their effects, they just don't seem to be very popular with the vendors so not many of them carry any of the DOx series. If they can at all, many are scheduled as we've spoken about in court previously.

Q And your research looking at substance abuse, what features have you found to be common in drugs that have a high potential for abuse?

A So generally in the field, drugs of abuse and drugs with an addictive nature -- I'll stick with drugs of abuse for now. Drugs with a high potential for abuse tend to share some common core features, specifically a rapid onset of action, many of them involve effects on the dopamine system to produce their reinforcing,

rewarding, and euphoric effects, as well as a quick offset of action and many other features. I think really what's core to most abusable drugs is effects on certain neurotransmitter systems like the opioid system specifically, the mesolimbic dopamine system, the GABAergic system, and their pharmacokinetics, so the speed of onset, the time to peak effect and then the duration of peak effect and the time, how long it takes to offset, so the half-life of the drug. Those are common things, shorter pharmacokinetics, more condensed pharmacokinetics are more typically seen in drugs with a high potential for abuse, things like heroin or cocaine or other drugs that engender addiction and are abused.

Q Do you find these sort of characteristics to be present in DOI?

A No, that's one of the reasons I believe that the DOx series is not very popular, it lacks those characteristics specifically, no effect on the mesolimbic dopamine system in the way that addictive drugs do, an extremely protracted onset and duration of action that people find -- that reports tend to say is extremely unpleasant, as actually the opening statement that the Government

made included a quote from Dr. Shulgin himself that stated that the effects were not very pleasant.

Q And DOC would also be a drug that had the same --

A Yes, they're quite similar in their pharmacology and their pharmacokinetics and pharmacodynamics. So the time course of their effects and the type of their effects.

Q How prevalent in your research did you find abuse of Schedule I psychedelics to be in the U.S.?

A When I was looking through the epidemiology of drug overdoses and ER admissions, ER presentations, psychedelics drugs were among the least prevalent drugs in ER admissions and not present in almost any overdoses, a very small number compared to other classes of drugs. They make up a very small proportion of drug abuse related to mortality and injury.

Q When you say overdose of a psychedelic, would that necessarily mean death?

A An overdose is not necessarily fatal, no. For example --

Q Oh, sorry.

A Just to clarify, if you will, 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. Might require monitoring, but not life-threatening.

Q And in your experience, does this tend to be a permanent type of injury?

A I don't know if I can speak to the permanence of the psychiatric effects of psychiatric drugs, they tend to resolve when treated correctly. I know there can be lasting unpleasant memories and maybe comfortability with those memories, and in some cases people might describe it as trauma, but there are few reports of lasting injury and disability from psychedelic use or over dosage. I'm not saying it can't happen, but I'm not an expert on the long term toxicology of psychedelic overdose.

Q Okay. These adverse effects that you've described that sometimes can be impactful as you described if I understand, in your review of the literature have you found any evidence that they sometimes actually can have a beneficial effect?

A Certainly, I think that's why many of us are here, the long term effects of psychedelics are being studied and have been studied for the treatment of various psychiatric morbidities. It's been shown in the literature through gold standard double-blind placebo control trials that psychedelics can have positive effects long term, that's correct.

Q Do you think, is it your understanding, what might be described in some contexts as an adverse event may be in the context of psychedelics may have a different sort of outcome or

A There are published reports of people having challenging experiences on psychedelics that they later come to feel were instrumental in their growth in moving past certain psychiatric difficulties. Let's say someone has a very difficult trip on a psychedelic, they have a very difficult experience, it's very unpleasant for them in the moment, they're scared or anxious and really having a difficult time with it. It's been reported many times that maybe weeks or months down the line that person may come to feel that that experience was while very negative and uncomfortable it helped them to get over some sort

of difficulty either psychological or otherwise.

Q You indicated that you worked on new drug applications and you have an understanding of these, I guess these adverse events with a scheduled drug in one context may be viewed as an adverse event but possibly could have a different broader meaning?

A I'm not sure I understand the question.

Q I'm sorry, I'll try to rephrase it better. I guess I'm trying to understand here that I see lists of harms that are cited and drugs sometimes have negative effects, even prescription drugs, and that sometimes there might be negative effects, but there may be an overall net positive, I guess that's my question, is have you seen evidenced of that?

A Yes, when you're developing a drug there's necessarily a risk benefit, or benefit to risk assessment in evaluation to determine if the benefits outweigh the risks. There's obviously benefits of DOI that we're still discovering and these psychedelic drugs that we're still researching. I'd say that that the risks are comparatively to other drugs, many drugs that we tolerate the risks of for their benefits are

comparatively quite small, actually. The toxicity of psychedelics and DOI, DOC, is minimal compared to other commonly abused or commonly used therapeutics, I would say.

Q How frequent is it to find death from these classical psychedelics?

A It's exceedingly rare for someone to die primarily because of the use of a psychedelic drug.

Q In your survey of all the data and literature, have you seen incidents where people who overdose use more than one drug?

A Yeah, polysubstance use I would say is the rule rather than the exception when it comes to drug abuse, at least with substance abuse disorders, that was a part of my dissertation work was looking at psychostimulant and opioid co-use, and I would say that co-use or poly drug use is quite common.

Q So a person who overdoses maybe using a psychedelic and a different drug, is that correct?

A That's correct, and typically a medical examiner, when they would go to report the cause of death would indicate what the primary cause of

death was. Let's say that there was fentanyl and psilocybin in someone's system, a good medical examiner would report on the death certificate that it was a death caused by fentanyl or primarily attributable to respiratory depression from fentanyl and then note that there was psilocybin found in the system. This is just a scenario I'm, you know, creating here, but that's typically how that's done. So yes, 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.

Q So if the person's abusing something like say amphetamines or something and a classical psychedelic, it's more likely that it would be not the psychedelic?

A That's correct, it's more likely that the other drug is the primary contributor, yes.

Q And sometimes when statistics are gathered, is there a potential that those two drugs could be conflated and not distinguished which one had the greater likelihood of resulting in death?

MS. ATTANASIO: Objection Your Honor, I think we're going farther outside his expertise at this point.

JUDGE SOEFFING: I think we are straying away from that, there's also a lot of leading going on here. So I'm going to sustain the objection.

MR. RUSH: What drugs have you seen with similar pharmacology to DOI?

THE WITNESS: Let's see, there are, I mean we've already discussed previously in the hearing some Schedule I psychedelic drugs that share commonalities with DOI.

JUDGE SOEFFING: So I'm only interested in your testimony, not what anybody else has said in the hearing, just what you want to testify to in terms of the answer to that question.

THE WITNESS: Thank you for the direction. So again, as I said, 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 psychedelic compounds in the sense that it's very selective for receptor subtype. There are other 5-HT2A agonists that are not scheduled, not considered abusable, and actually I think the drug lorcaserin is an agonist of 5-HT2C receptors and can cause hallucinogenic effects at a certain dose, and that

was an approved therapeutic drug, I'm not sure if it was withdrawn for other reasons, but it was an approved drug used to treat obesity.

MR. RUSH: Do you know if that was in one of the classes of scheduling?

THE WITNESS: You know, I do believe it was intended to be scheduled and a lower schedule, IV or maybe III, but I do not recall the specific schedule. I do know drugs like lisuride activate 5-HT2A in a non-hallucinogenic way, completely unscheduled drug there as well.

BY MR. RUSH:

Q Have you found similar pharmacology in any scheduled substances?

A To DOI?

Q Yeah, a difference, a non-Schedule I, I guess is what I'm asking, if there's -- yeah.

A Like I said, drugs like lorcaserin can activate some 5-HT2 receptors. I'd honestly have to think and reference various classes of drugs, but there are many drugs that activate 5-HT2 receptors that are approved and scheduled in schedules other than Schedule I.

Q Now you've worked on designing drug studies, is that correct? Or research studies?

A That is correct, yes.

Q Why is DOI important in research?

A So 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 I believe. Its selectivity for those receptors means that it's a very accurate tool for assessing the effects of those receptors, and specifically how they're activated to -- receptors can be activated in different ways, right?

I mentioned lisuride as a 5-HT2A agonist drug that doesn't cause hallucinogenic effects. Serotonin in our bodies doesn't cause psychedelic or hallucinogenic effects, so DOI being an unscheduled, available, and selective compound for these receptors has been extremely important for determining how those receptors are activated to produce psychedelic effects, and the specific contributions of that receptor subtype, whereas drugs like psilocybin, LSD, mescaline, dimethyltryptamine are much more promiscuous and hit numerous receptor subtypes. So DOI has been instrumental for teasing apart the differential contributions of the different receptors to

psychedelic effects.

Q So does DOI act differently than those other psychedelic drugs?

A So I almost went down that kind of line of thought in your previous question. DOI is quite different from those classical psychedelics in the sense that it has no affinity for 5-HT1A as LSD and psilocybin and MDMA do and has very little affinity for dopamine or other monoaminergic -- so it's very selective for this one receptor, so it's very different from other psychedelic drugs which tend to be promiscuous, they bind with a lot of different sites and cause a very complex array of effects, whereas DOI is very selective and a little less promiscuous, a lot less promiscuous in its binding, so it acts differently.

Q In your understanding of the available evidence, have you -- I'm sorry, one second, present my question. That difference in the receptors, the way it's targeted is that it's specific, and you indicated that these other psychedelic drugs are more I believe you said promiscuous with the other receptors. Since DOI is specific or more specific it seems to the 5-HT2A receptor, is it likely then that it would have

different pharmacological effects on the person?

MS. ATTANASIO: Objection, Your Honor, outside his expertise.

MR. RUSH: Your Honor, he's testified this is a -- he's commented on monoamines and he would comment specifically on substance abuse and monoamines.

JUDGE SOEFFING: So I'll overrule the objection, I do think we are kind of getting outside what was disclosed in the prehearing statement too, I think as I'm looking through it, we've covered most of what's in there, but I'll overrule the objection and allow you to continue.

MR. RUSH: We also -- just because Dr. Carbonaro's certification as an expert, she was allowed to opine on things that were --

JUDGE SOEFFING: I'll give you some leeway.

MR. RUSH: Okay, thank you Your Honor.

THE WITNESS: I can answer that question then, if that's allowed?

JUDGE SOEFFING: Yes.

THE WITNESS: It would be likely that the effects would differ from those more promiscuous serotonergic agonists in their

subjective character and pharmacological effects, correct.

MR. RUSH: So it's just not possible to say that because this is in the same class that it would have the same effects, likely?

THE WITNESS: No, just as it would be incorrect to say that any drug that -- any psychostimulant is the same because they all are indirect agonists of monoamines by releasing them or inhibiting their reuptake. Methamphetamine is quite different from phentermine, which are both approved drugs, they're very different but their core mechanisms of action are exceedingly similar, they're essentially the same.

BY MR. RUSH:

Q What are like, those drugs, what's a risk of those?

A What type of risks?

Q I guess like what would if it was your greatest danger with those type of drugs that you just referred to?

A The psychostimulants can be addictive, they can be lethal in overdose, they can cause psychosis. There are a number of toxicities related to psychostimulant use, abuse, and

addiction. I mean, you could also look at opioid drugs, many of them share the same core common pharmacology of activating u-opioid receptors, some like heroin, Schedule I, some u-opioid agonists, they all share the same one mechanism of action.

Like codeine and certain preparations is a schedule 5 drug, dextromethorphan, an unscheduled drug, also has a metabolite that is a u-opioid agonist. So just having the same mechanism of action doesn't necessarily mean that the effects or the level of the effects are the same or that the character or quality reinforcing nature, desirability, just having that same mechanism of action can be altered in many different ways, as the opioid and psychostimulant examples kind of illustrate.

Q When you're looking at research then, would you tell me what in vitro research is?

A In vitro research tends to be with cells, it means in glass, essentially, it's not in whole animals.

Q And how about in vivo?

A In vivo means research with live, whole animals.

Q And to assess the pharmacological effect of a substance, which one would be more determinative?

MS. ATTANASIO: Objection Your Honor, we're still talking about pharmacology here and that is very broad compared to what he's been put in as an expert.

JUDGE SOEFFING: Yeah, I'm not seeing where you're going with this Mr. Rush, I think we're way off what was disclosed in the prehearing statement and what he's been admitted as an expert in.

MR. RUSH: I guess what I'm trying to get at is these mechanisms I guess, he talked about respiratory depression through monoamines, things like that, I'm trying to understand the mechanisms of the different drugs with substance abuse, and so many substances are also monoamines as he described, so I'm trying to figure out I guess what the risk is, things like cardiac risk. You know, is there a cardiac risk with DOI that's equivalent to these other drugs that frequently cause overdoses?

JUDGE SOEFFING: Yes?

MS. ATTANASIO: Your Honor, I mean,

what he's trying to figure out isn't necessarily relevant to what's going on in this case.

JUDGE SOEFFING: Yeah, I'm not -- can you show me in the prehearing statement where you're talking about that? Because I'm not sure what it relates to.

MR. RUSH: Give me one second to review, please, Your Honor. I guess I'm looking to investigate abuse liability as it was described in the -- can I borrow this for a second? In the prehearing statement we identified he would testify that there's very few verified documentations of individuals taking substances, he will testify to give the nature of the drug and its pharmacological effects, its self-limiting nature, its structural aspects relating to mescaline or DOM, duration, and how these qualities sufficiently separated to make abuse potential comparisons impractical.

JUDGE SOEFFING: I think he's covered most of that, I didn't hear anything about, you were just talking about cardiac.

MR. RUSH: Well I guess --

JUDGE SOEFFING: So there's nothing there about --

MR. RUSH: Well the -- I guess I was trying to get to the pharmacological effects. I mean we're trying to find out whether at the core whether this is dangerous and how dangerous it is, and I'm trying to figure out what the pharmacological effects are, how dangerous it is, as part of the factors in our eight factor analysis, and trying to ascertain is this dangerous, and if it is dangerous, how dangerous is it?

JUDGE SOEFFING: Well you can ask a couple more questions, thought I think you need to wrap it up and move on.

MR. RUSH: Understood Your Honor.

JUDGE SOEFFING: So I'll overrule the objection and I'll allow limited additional questions on this.

MR. RUSH: I'll move on to implications with research, potentially as we said he will testify on the negative impacts potentially on research. In your experience in reviewing, designing, assisting with research protocols, do you have input into selecting which substances might be used in those studies?

THE WITNESS: If I'm understanding the question correctly, you're asking whether or not

the scheduling status of a research tool has any bearing on whether or not I use it in my research and if it makes it more difficult, is that what you're asking?

BY MR. RUSH:

Q Yeah, that would be a fair assessment.

A I think that it's pretty fair to say that yes, the scheduling status of a drug absolutely has bearing on which drugs you choose and have access to for your research, just due to the onerous regulatory, financial, availability issues, there are many different hurdles to go through when you work with Schedule I drugs, and I know that some might say that they're not there but they 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, as I was in one, my advisor, Dr. Patrick Beardsley, had a Schedule I license, conducted heroin research for many, many years, did work with fentanyl analogs and fentanyl, many of which were placed into Schedule I during my work in the lab on respiratory depression, which was, I got to see firsthand, very onerous to deal with the collecting, measuring, and reverse distributing

all of these chemicals that were not Schedule I that came in, and scheduled halfway through our research. I got to see the whole process of that and it was quite onerous, and the infrastructure to handle Schedule I drugs is quite onerous, so I chose not to use Schedule I drugs in my dissertation work precisely for many of those reasons.

Q Have you seen instances where people may opt for a different drug because of the cost factors?

A Absolutely, it's one of the reasons that people have opted to use DOI, but I've seen it elsewhere as well. I used for example oxycodone many times in place of heroin in respiratory depression and other behavioral assays because heroin was just too difficult and expensive to obtain for the lab, and oxycodone was similar enough.

Q And it's more difficult to acquire and work with a Schedule I substance from what I understand you saying, so do you believe if DOI was added to Schedule I it would be more difficult to work with?

A Absolutely, there's no doubt. I think that the amount of research with DOI would fall off

considerably until some other unscheduled psychedelic was validated for many of those assays, at which point that might be scheduled too.

Q In your review of the evidence in research that is occurring out there, what type of research have you found DOI to be involved in, used for?

A I actually think that's another really important part of keeping a drug like DOI unscheduled. The research on DOI is quite diverse, right, it doesn't just relate to treating psychiatric disorders. There's recently been a body of evidence that's been gathered on the anti-inflammatory effects of DOI that would have never have been discovered if it was a Schedule I drug, you don't kind of go looking around for other interesting effects with precious Schedule I research materials, so that entire anti-inflammatory line of research on phenethylamine psychedelic was spurred by the availability of DOI in many different labs, and labs that would not have the Schedule I license. So if you're looking at other body systems other than the central nervous system, as I have, I've been focused on the central nervous system so my

labs had Schedule I through 5 licenses, but a pulmonary lab, a cardiac lab, labs with other focuses wouldn't have those licenses and it would limit the scope of research that could be done with DOI. So I guess that would be my answer.

Q Do I understand you then correctly that research with a Schedule I drug tends to be very, looking for one specific area, not more general?

A That's correct, you have to submit your proposal for why you want to use that Schedule I drug to the DEA and if it seems frivolous or if it seems like too far out there that won't be approved. So yes, research with Schedule I drugs is very directed and targeted, it's less exploratory.

Q What is mechanistic research?

A Mechanistic research can mean a whole bunch of things depending on the level that you're talking about. Mechanistic research in terms of brain circuits, so neurological circuits involved, in some drugs' action the cellular mechanism is involved, the receptor mechanism is involved, there's many different levels of mechanistic research.

Q Would it be research to design a specific drug class for treatment?

A Oh yes, structure activity relationship, SAR research is important for medicinal chemistry and the design of new and improved drugs. Like I mentioned before, there's many drugs that are slightly modified versions of others that are improved versions.

Q Just general fundamental basic research in understanding these systems, how they work, would that be mechanistic research?

MS. ATTANASIO: Objection, Your Honor. Again, where are we going with this? We're still outside his expertise.

JUDGE SOEFFING: Yeah I'm not sure, and you're asking a lot of leading questions, I'm not going to be able to give much weight to it anyway because you're asking leading questions that suggest the answer.

MR. RUSH: Okay.

JUDGE SOEFFING: So I'll sustain the objection, you can ask your next question.

MR. RUSH: Okay. Could I have a second to confer with my counsel?

JUDGE SOEFFING: Sure.

MR. RUSH: What is reverse distribution?

THE WITNES: reverse distribution of a

drug is when a lab has to send back their controlled substance for the DEA for destruction, or usually destruction not redistribution, but you don't just get to dispose of controlled compounds however you choose, there's a formal and lengthy reverse distribution process to divest yourself of controlled substances as a lab or as a researcher.

BY MR. RUSH:

Q And have you experienced that with when a drug switches to a Schedule I status?

A I have, when my laboratory was researching a series of fentanyl analogs, like I said before, they were scheduled in the middle of that process and we had to account for all of them, the amounts of all of them, post facto, and then reverse distribute them back to the DEA once we were done using them or could no longer use them because of the protocol change. The same thing happened when one of my advisors retired and the Schedule I license was under his name, many of the Schedule I and Schedule II drugs that were registered to him had to be reverse distributed, and after a 45 year career in research there was a lot, there were many drugs to be sent back to the DEA, it was a many month process reverse distributing them.

Q And what happened to the research when that occurred?

A That didn't impact the research that had already been done, but it definitely had a cooling effect on any of using the fentanyl analogs in any future research, just due to the administrative difficulties.

MR. RUSH: That's all the questions I have, Your Honor.

JUDGE SOEFFING: Thank you Mr. Rush. Ms. Attanasio, do you have a cross examination?

MS. ATTANASIO: Yes Your Honor.

JUDGE SOEFFING: How long do you think that would be?

MS. ATTANASIO: Longer than 10 minutes.

JUDGE SOEFFING: Okay. Why don't we go ahead and break for the day since we need to end at 3:00. So Dr. Elder, you're dismissed from the stand for today, you are technically still on the stand, I'm going to direct you not to discuss your testimony with anybody until we resume tomorrow, and we'll be back tomorrow at 9:00 a.m. We are off the record.

(Whereupon, the above-entitled matter went off the record at 2:50 p.m.)

C E R T I F I C A T E

This is to certify that the foregoing transcript

In the matter of: Schedules of Controlled Subtances

Before: US Drug Enforcement Administration

Date: 11-14-24

Place: Arlington, Virginia

was duly recorded and accurately transcribed under my direction; further, that said transcript is a true and accurate complete record of the proceedings.

Neal R Gross

Court Reporter