00:00:00.000 --> 00:00:03.110

And I'll let you know as soon as the recording has started.

00:00:04.430 --> 00:00:22.640

Alright so the recording has begun wanna welcome everyone today to LCD 's deliberative dialogue session 3 concerning evaluation of THC compounds and begin a discussion around how we might determine and define? What is and is not impairing today?

00:00:23.750 --> 00:00:24.410

Ohm.

00:00:25.280 --> 00:00:28.930

I'll go over the agenda really briefly and then move into our slide deck.

00:00:29.580 --> 00:00:38.390

Umm I'm just gonna have a brief introduction here for the next 5 or 10 minutes or so going through uh panelist roles. My role as moderator.

00:00:39.150 --> 00:00:50.670

Uh participant listener roles and then our meeting format and we'll have a brief introduction of our panelists today and then begin our our uh moderated panel discussion.

00:00:51.310 --> 00:01:00.500

Uh and then we'll have uh open question section starting at 2:00 PM and then we'll wrap up at 2:25, so we can stay on time today.

00:01:02.500 --> 00:01:04.190

Ohh me see if I could.

00:01:06.340 --> 00:01:08.150

All those right into that.

00:01:20.040 --> 00:01:50.580

All right, so I just like to set the stage for today's meeting. Our goal today again is to build an understanding of how we might determine and define what THC contents are and are not impairing our intentions today are the same as many of our deliberative dialogue sessions. But here we'd like to continue a platform to share and discuss plant chemistry perspectives increase opportunity for respectful and moderated dialogue between offer.

00:01:51.710 --> 00:02:02.650

And continue the sessions that we started last summer, so that was last set of June and July about these issues to inform future rule and policy development.

00:02:04.470 --> 00:02:10.930

So why are we here Umm I'm sure many of you are familiar with why we're here, but we'll go over it again just in case.

00:02:11.580 --> 00:02:23.340

Uh the agency issued a policy statement last year concerning THC compounds other than Delta 9 and we adopted a new rules section. Uh effective February 5th of this year.

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Uh around the evaluation of THC compounds and we defined terms, such as additive solvent ingredient alphabet most rules.

00:02:35.160 --> 00:02:53.680

2022 legislative session uh came and went and uh didn't result in any changes or any definitions that we could advance in rules. So we'd like to continue a discussion and concerning cannabis plant chemistry to inform future rule and policy development.

00:02:54.570 --> 00:03:17.080

With all of our deliberative dialogue sessions comments that are received are added to an Excel workbook or a table or organized by theme and analyzed and then we share those with both the public and the board to inform us decision making moving forward. We also as I noted record. These sessions and put them up on our website, so everyone can view them.

00:03:17.600 --> 00:03:22.070

Uh at a time of your convenience or for additional information.

00:03:24.470 --> 00:03:53.980

Alright so meeting protocol for today. Uh we have 4 fantastic fan panelists that are rejoining us from our sessions from June and July of last year. I'll be your moderator today on Kathy Hoffman policing rules manager for the agency and then we have all of our great guests who join us today and you'll be our participants and listeners and hoping that you can stay in participant and listener mode until 2:00 o'clock and we start taking questions.

00:03:54.680 --> 00:03:55.200

Uh.

00:03:57.410 --> 00:04:26.810

And then I would like to to just briefly touch on what deliberative dialogue is although many of you are familiar with us because you've joined us for other deliberative dialogue sessions began just running really emphasize that this is an opportunity for us to all think together to listen deeply to other points of view explore new ideas. We're really looking for points of agreement and examine assumptions that we might have about these particular issues.

00:04:30.000 --> 00:04:49.320

Umm and then just again just to emphasize the difference between deliberative dialogue and debate, and I'm gonna focus here on the the? What deliberative dialogue is again. It's a way for us to find common ground to listen and find meaning and the subjects that we're addressing here.

00:04:50.170 --> 00:05:03.840

Uh consider alternative UM and then move the conversation forward so just again. Gonna gonna concentrate on the positives of deliberative dialogue for this session today.

00:05:05.240 --> 00:05:35.190

We do have a few ground rules. I'm not going to go through all of these because again I know many of you have already seen these but again, I just want to emphasize that there is no right answer here. This is not an opportunity for us to debate each other, or seek points of diversion really we're we're here to find common ground so that we, we can move the conversation forward around. What impairing and non impairing might mean if we even use those words at all.

00:05:36.490 --> 00:05:44.860

Again, this is a public work session, it will be recorded and and uh. We'll put that up on our outward facing website when we're done today.

00:05:46.110 --> 00:06:16.270

So uh a little bit about the format. UM, I'll introduce the panel here in a few small a few moments and each panelist will introduce themselves give a little bit of background and then we'll begin the moderated panel discussion so that's where participants solution to the panel discussing issues amongst themselves and then I'll try to ask a few questions and we're hoping for a really good dialogue around this.

00:06:16.360 --> 00:06:46.770

The topic today and then once that discussion is over and again. We hope that that will be concluded around 2:00 PM, then we'll have uh a question and answer or discussion session and so, if you would just kindly raise your hand use the hand raise function in teams and then either Jeff or Audrey will call on you in the order that you hand was received or it was help.

00:06:46.850 --> 00:06:48.580

Help help I guess is the best way to say it.

00:06:49.460 --> 00:06:58.010

Uh I just wanted to take a brief moment here and uh introduce who from LCB is uh helping to make this.

00:06:59.000 --> 00:07:22.050

Flashing happened today, we've got our rules coordinators. Jeff Kildall in Audrey Basic, joining today. Our administrative professional Tierney. Hamilton steel and our policy and rules director Justin northern them and I just wanted to stop here for a moment and ask Justin if there's anything that you wanted to add or say before we get started today.

00:07:24.520 --> 00:07:50.570

Thanks Kathy I think you covered everything really well. The only thing I would add is please. Keep in mind. You know, we're we're planning on a number of these deliberative dialogues, so this is not going to be the only session for feedback and and on topic. So we are planning additional deliberative dialogues in the near future, so not everything is going to be covered today and so, if you have interest in those please. Watch out for those particular topics so thank you.

00:07:51.320 --> 00:08:02.870

Tastic things Justin and uh when we conclude today, I do have a slide with the tentative dates for our future deliberative dialogues. There's one scheduled in May and June.

00:08:04.140 --> 00:08:20.900

All right, so I'm going to do 2 things at once here. If you feel compelled. Please share uh who you are if you're affiliated with any association if you wish to share that in the chat box and maybe give a little brief sentence.

00:08:21.850 --> 00:08:27.890

2 about why you're interested in this topic, and then I'd like to call our great panelists to come on camera.

00:08:29.260 --> 00:08:35.780

Uh and we'll go ahead and start with introductions and notify since you are already on camera. We'll start with you.

00:08:37.050 --> 00:08:47.040

OK, thank you so yes, I'm Nephi Stella. I'm a professor in pharmacology and psychiatry and behavioral sciences at the University of Washington.

00:08:48.950 --> 00:09:03.280

Thank you Nancy and Jessica Uh my name is Jessica Tonani. I'm CEO of vertebra research. We have a research license in the state of Washington and we focus mostly on molecular biology. The plant and a metabolite analysis.

00:09:04.690 --> 00:09:07.750

I said thank you Jessica and Brad.

00:09:09.110 --> 00:09:19.480

Hi everyone, Brad Douglas organic medicinal chemist by training, and professionally have been involved with regulatory affairs, namely FDA affairs for the last 1520 years.

00:09:20.300 --> 00:09:21.070

Great to be here.

00:09:22.170 --> 00:09:24.820

Thanks Brad and David.

00:09:25.870 --> 00:09:38.560

Hi my name is David Gang. I'm a professor at Washington State University in the Institute of biological chemistry. And I'm also the director of WSU Center for canvas Policy Research and edge.

00:09:39.910 --> 00:09:58.500

OK, thank you panelists for joining us today and if you weren't here for a previous deliberative dialogue sessions. This is our original uh panel so we're just really glad that you're able to join us to kick us off on this sort of new discussion. We're having around what is and is not impairing?

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So we're right on schedule and really happy about that.

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Umm I'd like to go ahead and kick us off with our overarching question and that is.

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How might we determine and define? What is and is not impairing?

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Umm and I don't I I think when we, we've thought about this concept. Certainly it was something that uh

came up during the legislative session things that I think about when considering what is and is not impairing? What is it about the interaction or the brains interaction with cannabinoids that we're trying to get at when we're thinking about what is and is not impairing?

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So maybe that is a starting point, and I'm gonna turn off the screen. So the focus is on our discussion and not the screen.

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I I I think I'll I can kinda kick off things a little bit and then kick it over to other people. I think that one of the biggest things that we've had as a panelist in our discussions is defining the word, and pairing whether we use the word impairing or intoxicating or psychoactive or there's not really a good word to define what we all kind of know is the.

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As the unknown so you know, there's an interaction that happens in the brain that makes people are the probability that they could be high and that that probability that they could be high. I think is what we're defining and so the word, and pairing. I think people have you know potentially a an immediate negative response to the word impairing as it may not be perfect. But I think you know, I would like to propose for that discussion. Today, that we use the word impairing even though we know it's not perfect.

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With that caveat, I don't know if anybody else, has any other comments on that the start.

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Sounds good how many agreement.

00:12:08.980 --> 00:12:33.620

You know, I I would I would love to hear from from nephew being the pharmacologist of of our bunch here, UM regarding? What is it on a receptor level or pharmacological pathway level? What is happening when the C or similar molecule is making somebody feel high is causing impairment?

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OK, I'll I'll I'll try I'll try to uh to decorticate this and so I I'll I'll agree with uh with using the definition of Impairing. I think it's uh. It's a good one just to kind of set set the state.

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Uh and it's a good way to actually start with the pharmacology so the so when individuals take cannabis based products and we'll be focusing mainly on the impairing properties of THC because CBD has a completely different bioactivity.

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Uh THC will eventually reach the the brain and interact with the cannabinoid receptors that are expressed in multiple areas of the brain.

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And I think the the fact that it's in multiple areas of the of the brain is very important because what the the way people talk about the the activity of TC on the brain is what we say, Polymodal, it does many, many different things and therefore right off the bat. I think we should differentiate the euphoric effect, which is what people actually refer to getting high to the impairing effect.

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And the impairing effect is going to be hard to define because it'll depend on the type of task that the individual are are are performing so in the cannabinoid field. When we start talking about impairment. We start thinking about motor impairments, so this is already the connection with driving? Are we going to have some motor impairments. Are we going to have is our reaction times going to be different.

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Is the decision making going to be affected or is our ability to focus being going to be affected so those are all the type of of questions that people think about when we use the word impairing and in terms of the pharmacology. It's because we have these receptors in the different areas of the brain and they are activated by C and therefore, that's why this area of the grade is affected and therefore you might have.

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Euphoria from one side motor impairment lack of focus and all these different effects. So I think Impairing is the is a multiple.

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Uh there's multiple aspects in Impairing and it'll depend on the type of task that the individual is performing if they are truly impaired.

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That's my my first bill cancer.

00:15:18.850 --> 00:15:30.440

And it's it's my understanding Nappy that the CB one. Receptor mediates the euphoric effects does it cost generally mediate the impairing effects or is that lately?

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Absolutely so the so the THC is going to to interact with the cannabinoid CB one receptors on neurons

that control attention in one part of the brain on neurons that are in the Cortex and that's the sensory awareness.

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We uh music is enhanced colors and is enhanced sounds or enhanced that's the euphoric effect enhanced the sensory awareness and then there's other receptors in the more deeper parts of the brain and what we call the basal ganglia that are involved in other types of function which is mortar mortar coordinations mortar precision. So the fact that these receptors in all these areas of the brain are interacted by THC will affect all these different behaviors.

00:16:19.010 --> 00:16:25.850

But it's all through CB one receptor. The difference is that CB one receptors is expressed in distinct part of the brain.

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And I think one of the things that we struggled with a little bit last legislative session is kind of defining the fact that that it's not just Delta 9 that there is Delta 8, Delta 10.

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Uh a wide variety of these nephew can you address it all the fact that that you know some of these other compounds?

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Still, buying the CB one receptor at least in affinities and can cause.

00:16:57.030 --> 00:16:59.450

Uh you know impairment for lack of a better word.

00:17:00.160 --> 00:17:30.850

Yeah, absolutely uh so yes, so the uh that would be the primary compound. It would be Delta 9. Delta 8 and Delta and Delta 10. They all have similar activity or comparable activity at the CB one receptor. According to the results that we have at this day, the field has just started to actually pay attention and start to study Delta 8 and Delta 10. So we're gathering new results on how comparable is the activity of Delta.

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Later, Delta 10 to Delta 9 so.

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Uh the the current understanding is based on older literature, but it's being confirmed today, so these 3 initial panels will have comparable activities on this. I think another way. One recent hypothesis that has risen in the field is that you know when when individuals take use. TSC then it actually is going to be metabolized by the liver and the first metabolite of GCC is going to be live and hydroxy.

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OK and that's actually used for uh pharmacokinetic drug testing test in here and and things like that to understand them.

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Well, the field is actually starting to realize that because 11 hydroxy. THC is also active at the CB one which chapter that went individuals are actually taking THC.

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The effect of teaching is not stopped by its metabolism. Because the first metabolite 11 hydroxy. THC is still active at the CB one receptor and that actually might be one of the reason why even though when TTC goes up and down in the body individual are still concerned.

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Yeah, feeling doubt cycle, Tropic effect. It's because there's a lingering of the 11 hydroxy that is still activating the the CB one receptor and that same hypothesis of Delta 9. Being Metabolized D 11 hydroxy. We actually have no idea what is the metabolism of Delta 8? What is the metabolism of Delta 10 and those metabolite might also have some bioreactor?

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But I don't so in terms of go ahead. Just quick follow up question does the mode of ingestion change the metabolism at all nothing?

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You need at which it's Metabolized, Yes, so as individuals are using it through the lungs inhaled either smoking or vaping. Then it goes directly into the lungs and then and directly through the heart and to the brain so there's no.

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I just muted I just muted. Sorry.

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Let me repeat so there's a as the as the molecule goes in as the THC goes through the lungs it goes. It goes directly into the blood through the heart and then directly through the brain so This is why the effect of inhale. THC is very rapid the the the the psychotropic effect is very rapid when it's taken or and

then eventually as it comes out of the brain. It goes back into circulation and then it goes to the liver and starts to be metabolized so when it's inhaled.

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There is no first pass metabolism. It goes directly to the right whereas when it's taken orally. Then it goes into the gut. It's actually digested we probably lose a lot of the compound with the acidity of the bank and then it goes into our bloodstream through the liver and it has the first pass metabolism. So actually the THC that is absorbed through the oral route. There's only a fraction of it. That is going to reach the brain because it's already metabolized by the liver.

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You know, I've heard that the in in the literature. There's been estimates that they'll Lebanon Droxies. THC can be. You know significantly more psychotropic and pairing. Perhaps then Delta 9. THC itself do we do. We know receptor binding affinity? Where the CB one. Receptor versus Delta 9. THC absolutely yeah. We do, and it actually this. This has been known since like the 90s where we know that delta.

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The 11 hydroxy or even the Delta 8 can bind to the receptor, but in pharmacology. There's 2 components that we need to pay attention to the first component is the binding of the molecule to the Receptor and that's the affinity and that's where we, we start talking about this is a very potent compound and things because very low concentration of compound can activate the receptor so that's the first part and we understand that pretty well.

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Since the 90s, however, now we actually are understanding that these cannabinoid receptor. Once they're activated by different compounds. They can do slightly different things. On on the neurons and therefore at this day. We actually have very little understanding. Besides the fact that 11 hydroxy or Delta 8 or Delta 10 can bind to the Receptor. We actually do not really understand how well it activates the Receptor and that could be linked to what you're actually suggesting that.

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Maybe 11 hydroxy could be more potent.

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Meaning it could bind the same way as Delta 9. THC on the receptor, but the effect later on the receptor might actually be more of those are all I'm pushing the science a little bit too far right now because I'm basing this what I'm saying right now on what we understand on the binding that is 20 years old, and just on the recent novel experiments, so I think there's a tiny bit. There's probably a little bit of more research, to be done to actually solidified.

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But yeah, so this is so those are the 2 things that we have to consider one is where are the receptors expressed in the brain in terms of impairment meaning it'll change this? This brain function versus this brain function. Then the second thing we need to consider is the molecule that is going to reach the Receptor Delta 911 hydroxy 8 and Delta 10. How precisely is that receptor going to be activated is it is Delta 9 going to be a weaker agonist than 11 hydroxy.

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We actually don't just don't.

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And I think one of the one of the discussion points. We had kind of in the prep is you know, I think as a society. We're so used to alcohol, which is kind of a direct correlation and this is a little bit more.

00:23:53.380 --> 00:23:53.860

You know.

00:23:54.580 --> 00:24:11.430

A little bit more difficult to make that direct correlation from level to impairment and that's why I think there's been such an active debate about how to define the molecules. I don't know if anybody else, you know, David have comments on that, but it it seems.

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Difficult.

00:24:14.550 --> 00:24:14.860

General.

00:24:15.550 --> 00:24:21.450

Yeah, I would agree with that and I was gonna ask David if you had any anything you wanted to add so far.

00:24:22.210 --> 00:24:48.760

Ohh, I've been happy listening to nephew talks great, UM No. But yeah, actually something like that. I thought of that. Jessica you're your question is kind of leads into exactly what I was gonna say. And that is that when you when you think about what he just said. You know, we, we this is an important thing to point out to everybody. That's listening, Delta 9. There's there's one version of it the negative. They're isomer of it right the negative optical rotation stereo isomer of it that's the active.

00:24:49.490 --> 00:25:22.280

That's the version that's active same goes for the delta and the Delta 10. So there's a single molecule in the single version of these modules and we talked about this in the previous delivery dialogue right that that the the versions. We're talking about is kind of like are left. Right hands right so let the S version is like your left handed version. That's the one that's active and it's binding to like the receptors kind of like a glove that fits over your hand and it fits it has to fit just right for it to get in there, if it's if it's if the receptor only has a place for 4 fingers and you got 5 fingers your hand doesn't go in very well.

00:25:22.530 --> 00:25:29.240

Right or if you have a big, Big Floppy Mitten that you put your hand into it can go in, but it doesn't stick very well.

00:25:29.920 --> 00:25:40.050

And that's kind of like how the receptor binding might be viewed you know as a maybe an OK analogy there. But what's what's the important thing is, is that that molecule that goes in that hand that goes in is.

00:25:40.810 --> 00:25:47.220

It's like dentical, it's the same exact chemical entity every single time. But what's different is the glove.

00:25:47.840 --> 00:26:19.070

And each person each individual that's going to take this compound one of these compounds by smoking or ingesting it. You know swallowing. It whatever their bodies are all different from each other. We have different gut microflora that are gonna metabolize and and work on those compounds differently or livers are different. We have different enzymes. We know what some of the enzymes are now that are involved in that detoxification of the compound that's really it's a detoxification pathway that are liver does that converts. These foreign molecules into a form that can be eliminated from the body that's how it gets eliminated out.

00:26:19.320 --> 00:26:23.030

And each person has slightly different versions of those enzymes.

00:26:23.740 --> 00:26:54.530

Right because we all are genetically not identical so the you know enzymes are proteins. And there may not have DNA. They're coded by DNA made out of amino acid sequences and those vary a little bit from individual to individual and those slight changes in the amino acid sequence of those proteins changes the structure. Just a little bit. Sometimes it can change it more than just a little bit so different individuals are going to respond their their enzyme their receptor. The enzyme and deliver that changes it to the receptor is could potentially be a little bit different from somebody else.

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So that means that and then those receptors are on their neurons. Those neurons were developed differently because we all have different brains. All of those factors come into play when you take one of these and so each person can have a different response. Now it's in general, very similar right. It's not completely different.

00:27:11.260 --> 00:27:40.970

But it's different enough that it's very that's one of the reasons we're having this conversation. It's different enough that it's hard to define where it is that somebody gets affected enough that everybody else in society starts to get worried about it. I mean that's really talking about here right. It's like drunk driving any kind of impairment or under the influence. It whatever words you want to use there is we get worried about somebody else, taking this doing something that could then impact somebody else like me or you or

00:27:41.270 --> 00:27:42.560

our children or whatever right.

00:27:43.190 --> 00:27:51.370

That's why we that's why we get concerned about this. That's why we're having this conversation. And because everybody's a little bit different. We're all gonna respond a little bit differently.

00:27:52.160 --> 00:28:18.710

UM and these molecules also they hang around in the body differently than alcohol does. Alcohol is a very, very simple molecule right very, very, very simple. The cannabinoids are not the more complex so they're metabolisms more complicated. It's more difficult. The timing it takes longer. All of those things come into play. And that affects how somebody is going to respond to this that affects and also we know that the body gets changed away from me. Give me one minute.

00:28:46.190 --> 00:28:51.580

And it makes it much more difficult to try to figure out OK. When does somebody become effective enough.

00:28:52.420 --> 00:28:57.980

That we need to worry about it, but we obviously do because everybody thinks these need to be regulated.

00:28:58.800 --> 00:29:29.690

But the challenge is where do you draw that line? How do you figure out what that line is? When do we know that this is an issue So what I think I'm hearing. You say is that different enough can be different.

For every person that's what I think I just heard you say the data seems to show that you would there have been studies done with people looking at trying to figure how you measure. This like nothing mentioned you know, people we've looked in urine samples. We've looked at blood samples and if you try to look at doses that you give to different people versus those results. There's not a very strong correlation with alcohol there's a nice correlation.

00:29:30.240 --> 00:29:38.000

Between ingest you know how many beers you drink? How many ounces of Scotch, you drink whatever versus the blood alcohol level there's a pretty good correlation there.

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But with the cannabinoids and THC that doesn't seem to be the case.

00:29:43.370 --> 00:29:44.480

And I think you know they?

00:29:45.300 --> 00:30:15.650

The extra thing and this is the fact that not all cannabinoids do this so it well. That's another thing we're going to get yeah, so it's it's one of those things that we have to figure out how to you know define the cannabinoids that do these effects versus the cannabinoids that don't and what level should they be. You know deemed impairing I guess so it's almost 2 things of you know, and I think that's why we've led to some degree of a structure as to have a structure of a cannabinoid.

00:30:15.860 --> 00:30:19.490

But it also has to have the function of binding to the receptor I don't know if.

00:30:23.050 --> 00:30:27.640

Yeah, because it seems that that combination is really important for it to have the activity, we're talking about.

00:30:29.540 --> 00:30:37.550

You know just because we we, we put the word cannabinol as a cannabinoid as a classification doesn't mean they have the same function.

00:30:39.160 --> 00:30:54.110

You know something that's got the word alcohol for example, in it doesn't mean that it's the same thing right so alcohol that you drink versus a sugar alcohol like sorbitol. It's chemically defined as an alcohol, but you add sorbitol to you know lollipops.

00:30:54.760 --> 00:31:03.870

And it's a solid and it has no impact on your brain or anything right. It's complete, but it's an alcohol. But it has no impact on impairment. It doesn't do any of those kinds of things at all.

00:31:04.830 --> 00:31:09.580

But chemically defined you can call it an alcohol right that there's a whole bunch of those we come up with.

00:31:10.310 --> 00:31:11.160

But yeah, it's

00:31:11.930 --> 00:31:16.520

sometimes terms that we use to classify things can also kind of muddy the waters a little bit.

00:31:19.260 --> 00:31:50.050

Maybe I'll I'll build a little bit on what was said the UM. I think probably the impairing effect and should not be focused on the the compounds, but uh but rather on what activates the CB one receptor because this is what actually is because you have some artificial cannabinoids that are in spice compounds. Spice products that don't have the same chemical structure and they're very potent at the CB one receptor and therefore will be very impairing.

00:31:50.400 --> 00:32:21.250

So truly impairing will be associated with activation of the CB one receptor uh to build on what David was saying about the diversity and the individuals not only there's a genetic defect uh difference. But there's really a history difference deliver is as as David was saying, is main goal is to detoxify foreign compounds, the more you're exposed to these molecule the more liver will actually upregulate these enzymes to degrade them.

00:32:21.390 --> 00:32:51.960

So a person who's actually been exposed to THC for a long amount of time. We'll have have actually a very active liver that metabolizes because it's been exposed. It's been upregulated so that might be another difference between individuals. The amount of THC that this person has taken will change the liver metabolism or even somebody who actually has a liver disease will metabolize so then there's the health aspect of the individual that that comes in.

00:32:52.240 --> 00:33:23.050

So that's in terms of deliver there's exactly the same phenomenon at the level of the brain at the level of the receptor which is called tolerance. The the first time individuals use. TC all the receptors are there ready to go and they get activated and the psychotropic effect is gonna be pretty pretty strong. However,

the more the individuals are actually exposed to the cannabinoid compounds and activate the cannabinoid receptors, these receptors will undergo tolerance.

00:33:23.280 --> 00:33:53.410

Meaning they're not going to be working anymore. The image might be removed from the neurons so that's why actually there's this phenomenon of individuals who get high. The first time when they start and then it doesn't work as well. And they need higher concentration and they escalate in the amount of THC. So the level of impairment. This is what people call the the functional impaired person right This person who's been using THC for so long that they're so tolerant.

00:33:53.490 --> 00:34:23.400

They can use very high doses of THC, even before getting uh impaired. So I think the the diversity in how individuals are gonna be responding is very, very uh is is gonna be very vast. The other thing I want to emphasize is the link between alcohol in line with what Jessica actually was saying there is and and David there's a there's a there's a well established relationship between the amount of alcohol in the blood.

00:34:23.970 --> 00:34:35.140

And the type of impairment that it does will do the little test and things like that because alcohol has a very different impairing activity than THC.

00:34:36.960 --> 00:34:40.800

The the typical uh stories we hear are.

00:34:41.600 --> 00:34:51.290

People that are drunk are going to be are very aggressive and will will drive very fast, whereas people that are high or very paranoiac and will drive very slowly.

00:34:51.870 --> 00:35:19.090

Uh very rarely are firemen have these stories that very rarely are fire is started by a person who was high because they're very relaxed. It's mainly an accident because people were were drunk. So the behavioral impairments between alcohol and THC are very, very different and this is where the field is going. This is what we're doing in in in in our lab actually we're trying to understand the Impairing.

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Properties of THC and our little mice. How do they are are their movement impaired is their focused impaired. All these things so that we can maybe translate that and have a better understanding of what's happening in in in humans?

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But we already know that the The The The Impairing effect of THC and alcohol are completely different. The type of question the papers that we're currently reading on THC induced impairment in humans.

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In 20 years ago, the questionnaire is how do you feel do you feel high right now a little bit medium high so very basic description of the psychotropic effect now. The field understand that there's a need to better understand the impairing effect in humans and therefore we're creating new questionnaires that are more tailored to the TC, impairing properties and even devices to be able to actually correlate how much.

00:36:19.270 --> 00:36:30.720

PHP corresponds to this impairment so that we can try to reproduce something similar to what the alcohol field has done with the the the the the testing and the finally.

00:36:31.420 --> 00:36:31.870

Uh.

00:36:34.150 --> 00:37:03.520

The fact that these cannabinoids are actually hydrophobic so very greasy molecules compared to alcohol, which is volatile so alcohol makes sense. It's volatile it will be excreted by the lungs and we can have a Breathalyzer and we can measure precisely? How much alcohol is corresponds to the blood but because THC and cannabinoids are lipophilic greasy molecules. They're not evacuated by the lungs and therefore the idea of the.

00:37:03.620 --> 00:37:26.910

Developing a breathalyzer for THC is going to be very, very challenging. Probably the route to go is going to be to actually measure the amount of THC or their metabolites in blood in a very acute session and then we might actually start getting a better correlation between the amount of THC in blood and the behavioral impairments lots of concepts.

00:37:27.650 --> 00:37:57.410

Can I ask you a little bit more about that Nephi with with the advances now in functional impairment and tying that to THC levels or metabolites in the blood? Do you think that the animal models that are currently available to assess the impairment or the activity at CB one are still useful as a proxy for assessing impairment.

00:37:57.590 --> 00:38:08.240

Or as I have there been enough advances in humans and in the work that you're doing, and others that the things like the tetrad test are not necessarily as useful.

00:38:09.860 --> 00:38:40.750

Yeah, that that's a good question so the field is now working in parallel the with the animal models and the humans and we're communicating to try to identify? What is impairment in humans and in in in animals so there are things that are easy to test in a mouse? Which is motor impairment focus. All these really basic functions, but decision making time perception. All these other things that are really important in humans are much more challenging to to test it in rodents.

00:38:41.000 --> 00:39:12.170

So we can help until a certain limit, a certain amount of behaviors, but then the final uh stretch will have to be done in. In in humans. There's some really interesting work that is coming out now in in testing the bioactivity of TC in humans. We're doing actually functional imaging of the brain try to even understand which part of the brain is actually affected when THC is used and there's a really big focus currently on the prefrontal cortex.

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Which is truly the decision making?

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Chess players have a fantastic Prefrontal Cortex because they can strategize and things like that, so but if you're under the influence and you're if you've taken teach C and you're impaired and your prefrontal cortex that will be a decision making impairment. I don't think that's much harder to actually test in in mice, so the good news is the field is actually working hard in parallel. I'm seeing the papers come out and there's some there's some good communication here.

00:39:49.000 --> 00:40:04.630

Is it? Is it fair to say I know we had this discussion sort of in the backroom and we are in a state that has a Percy blood level for THC. It is it fair to say that there is not good.

00:40:05.380 --> 00:40:16.400

Correlation between blood levels breath levels. You mentioned Nethy urine levels. Whatever the case may be and any sort of functional impairment in humans.

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Is is that the state of the art currently?

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That's yeah, we don't have a definite answer right now. People are working towards we have initial ideas of of of and what direction it's going to be, but I agree the.

00:40:32.530 --> 00:41:02.380

The current correlation between the drug levels in blood and the human impairment are not actually validated. There's still quite a bit of validation and and if if the impair if we're thinking about impairment in terms of driving which is a simple way of thinking there are some research now where individuals are actually administering THC to individuals and then they do virtual driving and they play. These video games and then you kind of see how they drive really slow for example.

00:41:02.590 --> 00:41:35.100

Uh and they're trying to understand what is the type of impairment that you can get in a video game and that will definitely be translated into the route, but again, it's about what is what is the task in at stake here and being a fart command cologist it's always about the dose? How much has actually been taken and what's the prior history. Some people might take a you know a couple puffs on a on a joint and be completely impaired and another individual who's.

00:41:35.170 --> 00:41:47.230

Has much more experience than is much tougher and can smoke out on more a whole joint and not be as impaired so that's another aspect that needs to be considered.

00:41:49.800 --> 00:42:03.680

Would you like to stop here just briefly and and reach out to Justin because I know you're probably taking notes along with me. Just in are there any questions that you'd like to pose to the panel that have come up for you?

00:42:06.840 --> 00:42:10.980

Sure, what? When we're when we're discussing the impairment issue. I think one of the important.

00:42:12.100 --> 00:42:41.430

Dynamics that we get questions on uh, especially from you know legislators and and and others is you know how do you? How do you tell the difference not just by the chemical compound but you know, and I agree with the stuff. I've I've I've listened to and and read. I can understand where you're coming from when you're talking about the the CV, one receptor activity, but how do you differentiate and impairing product versus a non impairing product at a threshold and and as the example?

00:42:42.490 --> 00:43:12.280

When we think about alcohol anything that is above 1/2 of 1% alcohol. By volume is considered to be an alcoholic beverage. Therefore regulated and age restricted so that's a really low threshold to be alcohol. So So what would a threshold look like in a cannabis type of product because we know that there's you know entourage effects when you're introducing 2 cannabinoids together. One can have an effect on the other so.

00:43:20.310 --> 00:43:36.240

Justin and this is Jessica I think one of the first important things is defining what an impairing cannabinoid is and then you can look at what should a serving size limit be packaging. You know that that kind of thing, but I think that.

00:43:36.890 --> 00:43:37.270

You know.

00:43:38.020 --> 00:43:39.360

One of the biggest.

00:43:40.110 --> 00:43:57.020

Things I think we need to do is define how do we define? What an impairing cannabinoid? Is and and there's a decent? List of them? I think today? But people are pretty creative with chemistry. So if we can come up with a definition of a chemical structure and a binding the CB one. Receptor then we can look at.

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How much of that UM leads to impairment but I think?

00:44:03.560 --> 00:44:05.870

To a large degree right now, we don't even have.

00:44:07.200 --> 00:44:19.110

I I guess we have the CSA in in the state of Washington that list. A number of these but we really don't comment. LCB perspective have that list that I that I know of I don't know if anybody else on the panel has feedback on that.

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Not really, and I I'd say that nobody really does, but I will introduce a concept that we think about from a medical chemistry standpoint and that's

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structure activity relationships. We know with whatever pharmacological compound, or classic compounds that are active somewhere in the body that changing small parts of these classic molecules either enhances effects or can these effects, so with TC like molecules you know, there's a couple places on these molecules that if you change you tweak them that you're gonna still have the impairing CB one agonist?

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Activity and I think if we're putting a list together compounds that may be impairing. We have to focus on these particular pharmacophores. These particular areas of these THC like compounds that are known to retain high inducing or impairing activity.

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Yeah, for example, we, we mentioned earlier at 11:00 hydroxy form right so if you put a hydroxyl group on that position, you don't lose activity.

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Maybe it actually enhances it in some in some cases in some individuals. But if you take a molecule. That's similar in structure. Uh for example, CBD that's when everybody talks about all the time and you try to show that it has the same activity as the TC 's and you find it doesn't.

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Right you don't get high no matter how much you give somebody they don't get high. It doesn't impair the driving the same. It doesn't impair the decision making process the same way it doesn't do any of the same things that THC does so and most of the structure is I is very similar if not identical to the C but it's got a few changes that are pretty significant that make it a different subclass and therefore it and it has a very different activity and there's a whole bunch of you know, most of the I. I think we could say the vast majority of the other cannabinoids fit that definition too. They don't have the same impairing effect.

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If we're gonna use the word impairing whatever that means they don't do the same thing to the body to the brain and they don't function the same way.

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But they might make you a little bit more relaxed or if given at a high enough dose they might make you a little bit sleepy, but you know, there's a we, we had a conversation about this in a previous deliberative dialogue. You can come up with a list of any number of compounds food. Additives whatever that if you take it off of they do the same exact thing and none of those are regulated.

00:46:52.430 --> 00:47:11.440

So right So what where do you draw the line about? What is that we're back to that point like Justin was saying, you know? The point about with alcohol. There's a level and that's because we wanna make sure we can regulate it because we know that once you exceed that threshold. You get to a certain point, it starts to become a problem and if somebody drinks enough alcohol at low enough dose.

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I mean, a lot of concentration, then you know, especially if they're.

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Don't drink it much before then, they could potentially be affected.

00:47:19.710 --> 00:47:25.360

But if you switch categories you switch it to a different molecule that they eat or drink or whatever you're not gonna have the same effect.

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So and I think that's important too. David here you know back to your question Justin that with ethanol alcohol. We're dealing with one molecule so it's easier to set limits or concentration limits on what's an alcoholic beverage or not with cannabinoids, although some of these tthe molecules are very similar molecularly. They can have different impairing effects and and vastly depending on the dose and I'll give you an example, Delta 9 THC.

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Has a 5 carbon alkyl chain, UM off of the resource and all molecule or moiety. You add 2 carbons 2 methylene groups 2 that you get a molecule called Tetrahydrocannabinol. Floral this was recently discovered to be found naturally in cannabis a few years ago that can have a significantly greater impairing effect significantly greater agonist activity at CB one receptors, so it's very important. I think that we

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we don't seek out a one size fits all dose ranging you know, and and impairing definition for all of these compounds, they have to be addressed individually.

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Which makes it challenging? Yeah, I I? Can I can see from from some perspectives. I guess uh from a uh lay policy kind of perspective that we need to be able to tackle is how do business owners? How does the general public when they look at a package they know that yes, this is or no this isn't likely to to cause impairment for me and we know that there's you know go back to your CBD comment. We know a combination or or it's.

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You believed their combination of CBD to THC in the right ratio is gonna diminish the impairment impairing effect, whereas that same amount of THC may be impairing and so when you're looking at those things we have to be able to say, Well, it can't just be a molecular compound. Nobody's gonna

know how to how to regulate that and and see that in a store. How is a reasonable person supposed to understand that and so I guess that's kind of the threshold question that we're looking at on you know it's not one size fits all totally agree with you on that, but

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I'm trying to figure out how do we get to a commonality in in that range and so that that's really the The The struggling question that we have around these because we're not interested in and and nor is anybody else interested in having you know organizations or regulators regulate non impairing products. That's that's that's food or whatever. That's somebody else 's thing and and what we're trying to respond to is those public health and safety issues and so. When does it become an issue and that's you know, kind of that threshold that we're looking at.

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So let me maybe I'll go for it right.

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Yeah, that's something I'll say quickly. I think that if we can define the affinity, which which we think about you know below which people will get high on a receptor level that you know.

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We can then package you know figure out what the labeling is on packaging. I think that that you know from a consumer safety perspective. Right now, we haven't even defined. What those impairing cannabinoids are and if we can you know from today like? Are you know working forward in the future to find what the impairing cannabinoids are then that becomes a? How do you inform consumers on the packaging perspective or what are the thresholds but I think?

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We don't even have that? What are those molecules yet and then I'll I'll let Nephi go?

00:51:04.160 --> 00:51:04.450

Sorry.

00:51:05.370 --> 00:51:36.180

No, that's OK, I will it was exactly in line with what I was thinking when you uh? What we talked about right now is only one part of the equation, which is the molecule acting on the receptor what we're what we don't know is what impairment moves and if I understand well in the alcohol field. We have a very good understanding of this level of alcohol in the blood will create this impairment. I cannot touch my nose anymore. I cannot walk on the line anymore.

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And if I remember well uh the alcohol drug testing by the road is 2 items. One is the Breathalyzer. So I can get a level and then the second thing is, are you truly impaired. Can you still aim for your nose. The thing is that when you're impaired impaired with cannabis depending on the individual touching your nose is not going to be the behavioral impairment that we're looking for. We don't know what it is so until we're able to actually establish this level of TC, just if we focused on one molecule.

00:52:10.210 --> 00:52:40.360

Delta 19 C this level of Delta 19 C in the blood corresponds to this specific impairment, which is dangerous for driving until we have that it'll be actually hard to establish that limit on the package because we don't know what it is, and it's gonna be challenging we that's fine. We can just work really hard, but it's going to be challenging because of the diversity and response between individual if I if we had to look into our crystal ball and predict the future.

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I think that the diversity and behavioral impairment that we're gonna get with THC is gonna be broader than the behavioral impairment that you get with alcohol because alcohol is a very simple molecule. THC is a very complicated. Set of molecule that has that that varies quite a bit in its bioactivity in individuals for example, some individual gets anxiety and they're gonna be scared when they're they're under using THC and other people 's not at all.

00:53:11.150 --> 00:53:15.540

So very different types of of of responses between the individuals.

00:53:16.570 --> 00:53:46.780

So so last question Kathy on the molecular structure, so one of the the things that we see that's recognized as impairing, Umm from a number of articles and and and Whatnot and industry is you know something similar to Hexahedra Cannabinol. So it's supposed to have that same type of molecular structure as as tetrahydrocannabinol without the double bonds. And so when these types of cannabinoids get discovered? How do you? How do you work those into this equation on being able to identify?

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That and of course, obviously you're you're gonna go back to the the CB one agonist activity, but Umm how how do we know those as these new evolving cannabinoids are discovered? How does that fit in the picture so and I'll stop there Kathy.

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Well, maybe we could describe how the DA puts molecule on the schedule one license.

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The way you do that is, you see the new molecule and you don't know if it's a cannabinoid agonist. So the first thing probably is the chemist they try to figure out the chemical structure. The second thing. They do is does it act does it bind and activate the CB one receptor that's the second so we know it's a cannabinoid CB one agonist and then the 3rd thing. They do is they ask our little mice because our mice are really good our being able to discriminate between having access to THC.

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Versus not THC, so there's these mice and and Richards Triangle on the East Coast that every day self administer a little bit of THC by pressing this lever and this lever. We know it's not THC in the next day. It's the other way around so they're able to know which level is THC and then suddenly, the DEA arrives with a new molecule puts it into the experiment and it's the mouse that is going to say does this molecule feel like THC or not, that's the level of.

00:55:10.230 --> 00:55:41.740

Of Psychoactivity and it's not impairment. It just feels like THC for a mouse and that's sufficient for the drug to go into the schedule one license. I don't argue that this is the right way to to go. I think we actually really need to improve this, but the the the process figuring out the chemical structure, so that we know what we're talking about second step does it activate the CB one. Receptor Yes, 3rd step does it create the bio activity?

00:55:42.350 --> 00:56:01.380

The psychotropic effects that were expecting from THC is it more than that's regulated such is it less than that's regulated such would be one way to think about it. So we need a behavioral input output a behavioral readout beyond the CB one receptor.

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Yeah, and one thing to add to that is that to kind of reiterate some said. Earlier, too, is that each one of these molecules is a different chemical entity.

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And and just you're absolutely right there's gonna be different interactions between those specific compounds and other compounds like you said the THC versus CBD ratio that has an impact. I mean, we see that with alcohol and other pharmaceutical drugs that people sometimes take you know prescriptions that they get that some you know there. There's warning labels don't take this, if you're taking alcohol or don't drive or you know, there are other things. There's lots. We know about drug interactions. All the time. There's lots of those that document. It's something we always have to be worried about but in the case of the cannabinoids and.

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As new ones like you mentioned the hydro cannabinol that are are identified.

00:56:48.930 --> 00:57:14.890

We kind of have to treat each of those as a new molecule. They're not exactly the same thing as something else that we've seen before be nice. If we could be nice. We would say OK, you know it. Looks sort of kind of like a bird there for all birds. We're gonna regulate the same well but they're not all the same right. You got chickens. You got Ducks. You got storks. You got whatever Penguins. They all do different things and the cannabinoids are kind of like that, too. Some of them are gonna be the problem. Some of them aren't. But you don't know until you do the things that the nephew just described and so even though that's

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a challenge, I think and it's there. There's it's gonna take effort and it's gonna be costly probably somebody 's got to do the work for that to figure that out, but

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we do need to figure out which ones actually have these functions.

00:57:28.220 --> 00:57:47.750

And and you can't just treat every single one because it fits into a general chemical class is the same you know, we're already talked about the same language. I just want to make sure that we're all on the same page with that, but it is. It it does make it difficult and I. I wish that I thought about this a lot. I wish there was a way to think of an easy way to define these things so that we, we could just say OK. Here's what we do. Here's how we regulate them.

00:57:49.840 --> 00:58:01.630

But I think it's I I think we can say well. Once we can put it into the bin of being something we wanna regulate then it's pretty straightforward how we regulate it right. The question is does it fit in that bin or does it fit in a different bucket?

00:58:02.430 --> 00:58:05.330

How do we know which one where it goes I think that's the challenge?

00:58:07.980 --> 00:58:37.440

And that's where I would say that the functional test that Nephites describing not just receptor binding. The functional tests allows whatever framework. Whatever policy framework for judging impairing allows it to be future proof. So instead of doing something like schedules schedule one for DEA or even using the Analog Act, which is strictly structural if you have a good definition of impairing of a functional test, something new comes along that fits in that.

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Structural class then you can evaluate is HC impairing well. If we have a very well defined, functional impairment. Classification then it could be an immediately. In this bucket or not in this bucket. If you don't have that functional test. You're kind of stuck like the DEA is found or you know, federal policymakers. They play a game of cat and mouse. You say OK this molecule is new, we have to address it and go through multiple years of sort of policy to kind of add it to a list and that.

00:59:10.680 --> 00:59:12.950

That just doesn't create clarity for anybody.

00:59:14.670 --> 00:59:16.520

And in the last.

00:59:17.940 --> 00:59:37.510

Uh. Sorry it's gonna say the other thing I think is is it's important to uh as nephew brought up. I think earlier. Artificials are in kind of their own little bucket and so you know this. This what we're attempting to do right now is about cannabinoids that naturally occur anything that doesn't naturally occur is kind of in its own little.

00:59:38.360 --> 00:59:44.700

Blocking off side, UM and I think that that's you know super important for people to.

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Understand and acknowledge is that people can create artificial cannabinoids, but that you know any definition. That's been put forward so far has had artificial cannabinoids in their own little bucket, not allowed and so.

01:00:00.180 --> 01:00:07.580

You know, we, we are really only talking about natural occurring cannabinoids and there's still large class of those but I think that that's important to?

01:00:08.200 --> 01:00:08.870

Articulate.

01:00:10.540 --> 01:00:14.450

Ohh. I wanna move into the UM.

01:00:15.130 --> 01:00:33.780

The section at the question section from our audience. We've learned a little over a kind of suspected

that would happen, but that's all right. It's been a excellent conversation and let's see if we can make it better by some additional questions from our participants so calling on Jeff and Audrey.

01:00:35.220 --> 01:00:36.820

I think perhaps.

01:00:37.610 --> 01:00:41.090

The 2 of you have been monitoring the chat box.

01:00:41.830 --> 01:00:45.900

Umm and then we'll also entertain uh hands being raised.

01:00:46.830 --> 01:00:48.800

So inviting Jeff and Audrey to.

01:00:50.230 --> 01:00:59.340

Let us know what's been going on in that chat box and whether or not hands are raised. Hi Kathy, Yeah. This is Audrey. There's no hands at the the moment OK.

01:01:00.130 --> 01:01:01.250

We did receive.

01:01:02.720 --> 01:01:04.390

2 questions in the chat.

01:01:05.490 --> 01:01:07.970

Umm the first question was.

01:01:08.930 --> 01:01:17.560

From Gabriel Picard asking where we could if we could share the links for past deliberative dialogue recordings. So we'll have to follow up on that.

01:01:20.130 --> 01:01:25.270

And I didn't I don't think Gabriel 's currently on. But if you are, and you had more to add please go ahead and raise your hand.

01:01:25.980 --> 01:01:26.380

Uh.

01:01:27.070 --> 01:01:35.030

The the second question, we, we got was from Shonda Nay and I am Sunday. If you wanted to just speak to your question.

01:01:35.960 --> 01:01:38.330

Please feel free to unmute.

01:01:39.210 --> 01:01:39.820

Go ahead.

01:01:48.610 --> 01:02:09.760

OK, I'll just read it out loud and Sean if you want to raise your hand and follow up. Please do so. So Sean wrote is there research on how minor cannabinoids in parentheses. CBG CBN Etcetera consumed in isolates at significant levels greater than 10% affect the endocannabinoid system.

01:02:13.990 --> 01:02:18.940

That's a very exciting question actually the field is really starting to pay attention to that.

01:02:20.400 --> 01:02:51.050

The short answer is probably well CBN is thought to actually interact with the cannabinoid CB 2. Receptor so CBN might actually have more therapeutic anti-inflammatory properties. CBN does not interact with the CB one receptor and therefore it's not going to be producing any of the psychotropic effects. CBG is the new fascinating compound in the cannabinoid field. We know that it has some interesting very different bio activity.

01:02:51.120 --> 01:03:10.660

Profile so it does different things. So we know that it doesn't interact with the CB one receptor. It does not interact with the CB 2 receptor on immune cells so now the field is starting to ask So what is the receptor that it's interacting with and what are the biological functions that it's going to regulate so?

01:03:12.070 --> 01:03:34.360

As the field has grown we focused so much attention on THC and then CBD showed up and we started to understand. I predict that CBG is going to be the next cannabinoid that people are going to start to study but it doesn't appear to have any impairing effects that are similar to THC because it has a different molecular mechanism of action.

01:03:35.890 --> 01:03:39.830

The follow up on that uh nothing conclusive yet, though.

01:03:41.040 --> 01:04:11.850

Still I think I heard you say it may well, we well well. We know what it doesn't do. We know that. CPG does not interact with the CB one receptor and therefore it's not going to be affecting the endocannabinoid signaling pathway because the endogenous cannabinoid signaling pathway works through CB one and CB 2, so because CBG is acting through a different receptor. We don't know the Receptor and we don't know what endogenous pathway is is affected by that.

01:04:12.330 --> 01:04:14.340

OK, thank you, you're welcome.

01:04:15.320 --> 01:04:18.150

So so one clarification on that on nathy.

01:04:19.040 --> 01:04:50.130

Knowing that CBG and CBN do not are not agonist at the CB one. Receptor is it fair to say that we could classify both of those individual compounds as not impairing in a TC like way correct. Yeah, that would be my my conclusion absolutely the same as CBD CBD. Actually doesn't is not an agonist that the CPU one receptor actually it is called there's 2 hypothesis of how CBD can.

01:04:50.340 --> 01:05:19.900

Can moderate the effect of THC on the CB one receptor the first hypothesis is that CBD binds to another binding site, which is called the negative allosteric binding site and therefore, that's what it does it tunes down the activity of CB one receptor even though it's activated with CHC so that's the first hypothesis. The second hypothesis is CBD acts on another receptor and that Receptor has a signal transduction pathway that.

01:05:20.290 --> 01:05:36.200

Down regulates the CB one receptor so either it's a direct interaction of THC and CBD on the same receptor on CB one or it's on 2 receptors and it's an interaction in the signal transduction pathway fascinating actually area of research.

01:05:43.210 --> 01:05:49.480

Alright Audrey Uh, it looks like we, we had a uh several questions pop up in the chat box.

01:05:52.870 --> 01:05:53.810

Audrey or Jeff.

01:05:54.810 --> 01:06:00.420

Yes, Hi Kathy, Uh Audrey again so it looks like our next question came from Jim McRae.

01:06:01.030 --> 01:06:06.100

And Umm I think there's multiple parts to it, so maybe Jim if you just want to.

01:06:06.810 --> 01:06:10.260

I saw you sent a second message elaborated on it if you want to unmute and.

01:06:11.360 --> 01:06:13.770

Explain your question go ahead.

01:06:28.270 --> 01:06:35.900

OK, Umm I'll I guess I'll read it out, then if folks are having trouble unmuting 2. Please put that in the chat because you should have the ability to.

01:06:36.520 --> 01:07:02.110

To unmute but Umm OK, so Jim writes you mentioned the variation across individuals in their reported experience with cannabis one of the well known and very wide variation in effects across different strains of cannabis does the breadth of impact across 20 plus percent delta 9. THC strains not suggests complex cross cannabinoid impact on drug effects and then.

01:07:02.790 --> 01:07:05.810

Second part to expand on where my question was targeted.

01:07:06.950 --> 01:07:21.630

While reductionism is convenient, it's not possible is is it not possible. Excuse me that the entourage effects often mentioned in describing the medicinally of cannabis are also at play in the expression of impairment and cannabis.

01:07:22.560 --> 01:07:30.780

Might not some cannabinoids for example, be protective of Delta 9. Medicated mediated impairment excuse me so I know that was.

01:07:31.570 --> 01:07:32.400

Multiple parts.

01:07:36.850 --> 01:07:58.490

There's the famous word entourage effect, which was such a good word that was, but truly the definition of entourage effect is the definition of drug drug interactions is the fact that when you actually have 2 drugs. They're going to produce something different than only when you have one drug so the.

01:08:08.110 --> 01:08:30.900

Drug drug interaction 2 drugs that are actually producing a different effect than a single drug uh. I I would say that the uh tempering effect of CBD on this THC CBD. One response is. One of the most exciting areas of research right now that people are looking at how can we and we don't know if it's only because it will simply?

01:08:32.540 --> 01:08:48.910

As my my previous explanation, the mod 2 molecules are acting on the same receptor and therefore it's simply tuning down or if it's a more complicated. I would call it even therapeutic effect, where CBD is actually tempering the effect of the entire signaling pathway.

01:08:49.550 --> 01:09:04.380

Umm and I think CBD is a great molecule, but I think the medicinal chemist that we have can probably optimize it and we can have even more potent CBD molecules that might actually have even more, promising therapeutic effects.

01:09:06.430 --> 01:09:33.860

One thing to add to that to the question also talked about other cannabinoids as well. And I mean. What nephew just described is what's known for CBD. None of that is known for any of these other compounds that are cannabinoids. It's also true that the plant produces many other compounds terpenes for example, are one that everybody's familiar with most most people are familiar with, but there's other classes of compounds that it produces as well. Flavonoids and some other things we don't know what any of those do.

01:09:34.800 --> 01:10:05.630

Umm and as you change the concentration of these compounds relative to each other or as was discussed. You know very large range of THC levels. You throw in very large range of differences of all these other different compounds and that drug drug interaction. That never was just talking about there's it's probably infinite possibilities of what could happen. It's gonna be very difficult to tease that all apart to be honest with you when you're talking about a you know when you're when you're ingesting, especially a raw extractor of the especially the raw plant material. You know it's not one compound. It's it's hundreds of thousands of compounds that you're testing.

01:10:05.830 --> 01:10:06.390

Or inhaler.

01:10:07.600 --> 01:10:09.170

And that's a very complicated mix.

01:10:10.570 --> 01:10:11.680

Red you're gonna say something too.

01:10:13.410 --> 01:10:35.520

No, I think you covered it. I was gonna say David I was we're gonna recognize that Jim 's question recognizes the layers of complexity that are at work here and we're just honestly. We're just peeling back some of the first layers of the onion. You can go so deep on this with Polypharmacy and drug drug interactions and we're not even really talking about, Is Everybody.

01:10:36.360 --> 01:10:57.330

At a similar level of impairment or lack of impairment as individuals. I mean as everybody's baseline the same. We could go down that rabbit hole too. So all this complexity really makes it challenging to find a starting point for? What is what is impairment? How do we define that functionally for policy purposes and it's certainly a challenge?

01:11:00.370 --> 01:11:08.370

Thanks for those questions Jim and I also see a couple hands raised am I seeing that correctly Audrey and Jeff.

01:11:09.810 --> 01:11:19.180

Yeah, I'm seeing one hand raised right now, so should we go ahead and call on Gabriel instead of going OK perfect go ahead Gabriel.

01:11:25.080 --> 01:11:25.550

Hello.

01:11:28.500 --> 01:11:29.170

We are you?

01:11:30.440 --> 01:12:00.290

Yeah, hello my name is uh Gabriel I'm uh. I work for the uh the federal regulator in Canada, so at the office of Cannabis Science Veillance. I meant it's 530 here so I'm in the middle of kid pick up so I'll I'll try my best to to to to ask my question and I apologize that I may have missed some some some parts of the conversation. So I'm happy that they're recorded and I'll appreciate the the links, but yeah, so this is so really fascinating.

01:12:00.360 --> 01:12:30.360

Topic and this is office also something that we're thinking about in Canada, particularly because you know, we have a very strict in it on the the TTC limit the quantity in in in the edible cannabis. We

obviously don't have this kind of same extent, the an issue because of of the define our definition of hemp, but it's definitely you know something that we're starting to see more and more in the in the the regulated market and you know, I'm not a farm, a pharmacologist so maybe maybe this is.

01:12:30.500 --> 01:12:50.520

This will sound a little naive for for the the the the academics on the on the call. But I'm just wondering like if in in in if this is something that would be possible. You know, I I've I've seen that in in in the the the field of toxicology where one molecule you know that is.

01:12:51.450 --> 01:13:13.920

More or less you know well understood can be kind of sets as the as the baseline and then other molecules are kind of compared to it, and and you can you know derive in the equivalency factor for it, you know I think I forget? What molecule does it might be digoxin or or some other other chemicals and obviously I think those are simpler molecules and cannabinoids but?

01:13:14.570 --> 01:13:32.380

Do you think that it would be possible or do you think that you know there could be you know a studies that would be could be like developed in a way that you know? Our our our our just for that. You know for you know you. You you could compare other you know whether it's Delta 8 or Delta 10 but you can compare other.

01:13:33.150 --> 01:14:03.130

Umm cannabinoids that that act on the CB one receptors and you could kind of compare it back to to Delta 9. That's well understood. You can look at you know equivalency factor. So you know for for regulators when you're trying to let's say that you're trying to keep the total like you know the the the CHC equivalent under 10 milligrams. Then you can kind of easily do the math or look at it has 9 milligrams of of of Delta 9. So we shouldn't allow more than another one.

01:14:03.220 --> 01:14:08.560

Equivalency you know that might be a little naive but as a regulator that would be that would be perfect.

01:14:09.090 --> 01:14:10.510

Umm so yeah.

01:14:11.460 --> 01:14:12.850

I'll leave it leave it to you.

01:14:15.510 --> 01:14:33.300

I might respond first Gabriel. Thank you for being here from north of the border. We certainly appreciate

you being here, asking the question and I think here in the states. We we could learn a lot from what you and Health Canada have done in terms of how they're regulating cannabis.

01:14:34.010 --> 01:15:04.180

What I would suggest and you know nephews probably a better person to answer this, but if we have a solid functional test, then we can have relative ratios or the sort of equivalency that you're you're describing Gabriel and another example. There is sweeteners. All your artificial sweeteners have sucrose or sugar equivalencies and I think if you do have a solid functional test. You can create that system of equivalences.

01:15:07.950 --> 01:15:10.900

And that works if they function similarly.

01:15:12.420 --> 01:15:29.740

So if if they get enough modifications to the molecules that they still have some of that effect, but then do something else as well. Then it starts to get a little complicated. You know, we don't. I know we don't really want to hear that but that's it'd be nice if everything was simpler, but it's not.

01:15:30.450 --> 01:15:32.140

Anyway, if you want to add to that or

01:15:33.490 --> 01:16:04.080

no, I think both of you did a good job on outlining the the it's a good idea to actually find figure use a benchmark for bioactivity and then figure out equivalency something that would be twice as potent could be regulated and and and half of the amount. It's a really good idea once we have actually the entire equation. This molecule of TTC does this behavioral impairment based on this reference we might actually have this.

01:16:04.220 --> 01:16:07.500

This approach very interesting idea. Thank you for sharing that Jim.

01:16:12.610 --> 01:16:14.690

Yeah, thank you thanks everyone for the answers.

01:16:22.630 --> 01:16:39.820

Go ahead and UM we're running out of time here, so I'm focusing in on questions that pertain to our discussion today and that's about what's entering and not impairing if you have questions about LCB packaging and labeling, please reach out to that program.

01:16:40.500 --> 01:16:45.270

Umm because I see uh uh collection of questions some that have.

01:16:46.080 --> 01:16:56.960

Have to do, perhaps with other things beyond the the conversation today, but I want to. Here's a question from Annie and we've only got about 4 or 5 more minutes here.

01:16:57.420 --> 01:17:18.840

Umm if the cabin, Noid is naturally occurring in cannabis, but not at high enough levels needed for products in the market. But it can be artificially synthesized from a different cannabinoid and is the exact same molecule as the naturally derived molecule CBN for example, how is that artificial?

01:17:19.020 --> 01:17:34.140

Umm how is that artificial requires it to be in a separate bucket and not allowed when it is the same molecule with the same effect or impairment and I think that might be going into the what's artificial and what's not?

01:17:34.900 --> 01:18:04.770

Yeah, we got conversations about that. Yeah, I think that how I like to explain it to people is you have. Let's say grapes can be turned into wine and you know, so if you look at this, you can take a naturally occurring cannabis and turn it into something that is naturally occurring and that synthesis synthesis and whether or not, that's allowed and is a longer term rulemaking. You know, I don't think that's part of it and then you have things that.

01:18:04.870 --> 01:18:10.850

Like a jolly rancher that's never seen a great plant and those are completely artificial cannabinoids, so you have.

01:18:11.610 --> 01:18:14.670

You know natural you can have a noise you can produce.

01:18:15.560 --> 01:18:20.180

Natural cannabinoids through the synthesis as well, and then you have artificial that are just.

01:18:22.230 --> 01:18:25.960

Never really been natural occurring, I don't know if somebody else has a better.

01:18:27.440 --> 01:18:27.670

I.

01:18:30.720 --> 01:18:36.850

Yeah, I've been using this actually differentiation between phytocannabinoids that are produced by the plant.

01:18:37.780 --> 01:19:07.960

Versus artificial cannabinoids, which are not produced by the plant. However, we can synthesize phytocannabinoids in the lab and we can synthesize artificial cannabinoids in the lab so the word synthesis. Synthetic cannabinoids is not a really good word because that just means that we're building it in the lab. I prefer to use phytocannabinoids produced by the plant and artificial cannabinoids that are not produced by the plant so.

01:19:08.090 --> 01:19:14.650

But in this particular example. CBN, which, if I remember well is actually a degradation product.

01:19:15.370 --> 01:19:29.220

Uh is is a phytocannabinoid even though it's been degraded and we can probably synthesize CBN. The Phytocannabinoid in the lab, but it's not an artificial cannabinoid be the because it exists in the plant.

01:19:30.910 --> 01:19:31.380

OK.

01:19:32.770 --> 01:19:44.960

What had bad uh I was gonna say any great question it's could serve as the basis for at least one more deliberative dialogue probably 5 more so, yeah, excellent question.

01:19:46.950 --> 01:20:18.680

All right, so we, we truly only have 5 minutes left and uh. There's one other additional question here that I wanna touch on and then I. I need just about 2 minutes to close this out because I have some additional information. I want to share but with that in mind, Shannon Vito. VE TTO asks can this panel defined in parent impairment for regulatory purposes and an individual cannabinoid level for the following list of CBD.

01:20:18.730 --> 01:20:20.520

TVG Delta.

01:20:21.230 --> 01:20:23.400

8 Delta 9 and others.

01:20:25.040 --> 01:20:26.880

And I think that's what we're trying to do today.

01:20:28.240 --> 01:20:29.600

Or at least start the combo.

01:20:31.830 --> 01:21:02.160

Yeah, I think the answer to that, Shannon is is yeah, so if the known cannabinoids. Also on the panel could say yes impairing or no impairing so you have Delta 8. Delta 9 as part of the question things like HHC. We talked about 11 hydroxy. THC similar THC analogs like TCP and B probably put those all in the impairing bucket CBD. CBG CBN non impairing. I think that's relatively easy to do well. We'll put that in air quotes.

01:21:02.620 --> 01:21:23.910

It's what we don't know or the compounds. We aren't aware of yet that's the challenge. How do you? How do you define policy to incorporate those that maybe discovered or produced by cannabis tomorrow and you know could be produced by somebody in the laboratory and be placed into cannabis products that's the real challenge.

01:21:25.000 --> 01:21:43.830

And I think the the impetus for all this is because of what happened with Delta 8 right. We we knew it existed, but it wasn't studied very well. It wasn't being used because it's only produced at very, very low levels in the plant, but then somebody figured out how to make it in the lab from other compounds from the plant and then all of a sudden, it was very available.

01:21:45.030 --> 01:22:06.060

And how do we deal with the next one of those that's the question that everybody 's concerned about when the next something like Delta 8 pops up. We wanna be able to jump on it, and you know the big here think question here is everybody's concerned about our children, especially right. We wanna protect children and others. How do we make sure that we can do that and how do we give the authority to those that need to regulate it the authority so they can.

01:22:08.710 --> 01:22:09.430

Yeah, absolutely.

01:22:11.860 --> 01:22:12.420

I agree.

01:22:14.250 --> 01:22:23.160

All right, so on that note. We've got 3 minutes left. UM we'll go ahead and uh conclude the discussion for today. What I'd like to do.

01:22:23.710 --> 01:22:40.770

Uh is uh offer for questions that we might not have gotten to Umm during this discussion today. Uh if I can reach out to the panel with those questions and perhaps you can, we can develop some responses and add them, with our recording.

01:22:41.540 --> 01:23:08.210

Of this session that we put on our website. If that's all right with the 4 of you. I just wanted to run that past you before, I said, we would do it, OK, so uh so there's that, if you have additional questions. Please send them to rules that's are you LES@lcb.wa.gov you can also find that on our rules website.

01:23:09.610 --> 01:23:13.050

I'm at uh on our LCB outward facing website.

01:23:13.890 --> 01:23:21.320

Umm the other thing I wanted to offer is Umm. Some additional deliberative dialogue gates. I'm gonna share my screen really quickly here.

01:23:22.140 --> 01:23:22.640

Umm.

01:23:24.410 --> 01:23:38.980

So we currently have 2 additional deliberative dialogue sessions scheduled one for May 31st of 2022 and the next for June 21st of 20227. I'll leave that up there for a second or 2.

01:23:39.890 --> 01:23:49.760

Umm that and we wanna make sure that we're approaching this topic from a lot of different perspectives, so if anyone in the audience would like to suggest.

01:23:50.250 --> 01:24:16.240

Umm someone for a future panel. Please don't hesitate to reach out to the rules staff. UM we're happy

to take a look at your suggestions and do some reach outs to Umm in panel our next sessions, so again. You can send those suggestions to lules at lcb.wa dot Gov messed up sharing.

01:24:21.130 --> 01:24:28.000

Alright so turning it back to the panel really quickly, we have one minute left anything else you'd like to share before we close.

01:24:32.250 --> 01:24:34.250

I guess just thanks everyone for listening.

01:24:37.300 --> 01:24:55.790

Thank you for the questions that discussing right if I think the deliberative dialogue. Format is important that we have these discussions. It's it's important that you have them probably with people that you don't agree on them with, but I think that's that's what I'd say a lot of this stuff needs to be figured out and it'll only be figured out through these sort of.

01:24:56.760 --> 01:25:00.010

Intelligent discussions and and learning from each other.

01:25:03.150 --> 01:25:03.920

Absolutely.

01:25:06.020 --> 01:25:13.180

All right, thanks to y'all Sir. Uh you're on camera if there's a question that you'd like to send us at rules.

01:25:13.720 --> 01:25:18.440

Umm uh we'd be happy to answer but we need to close the session for today.

01:25:19.490 --> 01:25:21.470

So thanks very much for joining us.

01:25:23.170 --> 01:25:37.660

Uh and with that I will go ahead and uh. We're going to go ahead and stop recording thanks everyone for your time. Today, you can look for this session again recorded on our outward facing website and wishing everybody a great day take good care of everyone.

01:25:38.360 --> 01:25:39.010

Bye.