Question 1: What are the three general categories of cannabinoids?	
Nick Poolman	This is a pretty open ended question for the group, what are three general categories of cannabinoids and then I think we have a lot of specificity to go into here but let's start, let's start broad.
David Gang	So, as we were thinking about this, how to answer this question, we decided that maybe a little diagram like this might be helpful for people. There's actually three categories there, one is called phytocannabinoids. It's also we added 'phyto' to the beginning to indicate these are the compounds that came from the plant originally, they're produced by cannabis sativa, then there's endocannabinoids, those are produced in, for example, the human body that are the natural endogenous compounds in our bodies that bind to the cannabinoid receptors naturally and it's that interaction between that endocannabinoid receptor and these compounds that does the normal natural physiological process that our bodies normally are involved with. And it's that process that gets kind of hijacked by Delta 9 THC when it comes into play and binds to that receptor. And then there's also another group of compounds called artificial cannabinoids. The top two, the phytocannabinoids and endocannabinoids, these are natural compounds. They are produced by a biological system. Endocannabinoids are by human bodies or other animals and also by some plants. Phytocannabinoids compounds that are produced by plants. I think the traditional definition or term was just cannabinoids, but because of a lot of discussion and kind of confusion in this space, we decided to put that prefix 'phyto' on the beginning of that to make it a little bit clearer to people so this would be more readily understood across the board. Examples of phytocannabinoids are things like minus trans Delta 9 tetrahydrocannabinol, minus trans Delta 8 tetrahydrocannabinol, CBD or cannabidiol, or a whole bunch of other compounds, there's about 125 of these or so they'd have been identified in the plant species of cannabis sativa. I want to point out that they have not been identified or demonstrated to have been identified into any other plant species so far, and I've been doing some more looking on that just to see and I, I still can't find any evidence for that. They seem to be specific to this one species. They're not even found in the cousin hops. Hops are in the same plant family, in the cannabaceae as cannabis sativa, but they don't produce these compounds

	either. They seem to be pretty specific to cannabis sativa, which is pretty interesting actually, but that's the plant that makes them. It could be that other plants do make them. That is possible. We've only scratched the surface in characterizing what plants make. Plants probably make about a million, at least different types of chemicals. We've only identified about a couple hundred thousand of those. It's possible that, and we've only looked at about five, to maybe ten percent of the plant species, less than 5% in any detail maybe ten percent have been looked at a superficial level. So it is possible that some other plant species might make these compounds, but it doesn't seem very likely. The endocannabinoids, on the other hand, those are produced in animal systems, they're produced by plants. An example of that is anandamide, that is one that most people are most familiar with. It's the signaling molecule that plays an important role in our physiology and helps brain function, things like that. Those are natural compounds that are produced by biological systems. It's also possible that they can be synthesized chemically in the lab. That's why those little circles overlap into the synthetic section down below. Synthetic compounds can either be these endocannabinoids or phytocannabinoids that have been synthesized in the lab, it's the same exact molecule, Delta 9 THC, minus trans Delta 9 THC, if you make it in a lab, or extract it from hemp or from recreational or medicinal cannabis it's the same exact molecule, it's the same thing. It just comes from different sources. You can also synthesize it in the lab. There are other compounds that are like the plus version. It's like, we, in our previous version we talked about handed versions, the minus and the trans. If you think about hands, it might be helpful. One of the versions, the trans, the minus trans versions, is like the left handed version. The plus version would be like the right handed version. They're really similar, but they're not superimposable exactly, right? You can't put a glove designed for your left hand on your right hand. It doesn't work very well, especially if it's a well-fitting glove. So they're not exactly the same molecule, they're similar, but they're not the same. If you synthesize these compounds in a lab, most of the chemical syntheses that are involved in making them are not specific for handedness and so you get a mixture of both left and right handed versions. Okay, so it's kind of like the gloves, if you're a glove factory that makes left handed gloves and another one that makes right handed gloves. If you do the synthesis, the way that these are made and can be made in the lab it's like mixing those up and you don't know which handed you're going to get. You get equal mixture of those. The synthetic compounds, those are different. Those are things that are, I'm sorry, in this event there’s also group down there in red called artificial cannabinoids.

	These are molecules that bind to the receptor. For example, things like K2 and Spice fit under this category, they're artificial molecules. They're not found in natural systems. They're not made in the human brain. They're not made in plants. They were made in a chemical lab, and they are (unintelligible), but they do have activities that might overlap with the activities of the endocannabinoids and the phytocannabinoids. So these are things that are one hundred percent only produced synthetically. They're not natural, they're artificial. Delta 9 THC is not artificial. It's a natural compound. Now you may make it synthetically in the lab, or you may extract it and I know I'm repeating myself here a little bit, but I kind of want to make sure everybody's clear on this. Right? So, you could make it synthetically in the lab, or you can isolate it, but it's not an artificial cannabinoid. It's a true cannabinoid that's made by natural systems. So those are the three kinds of general categories.
Jessica Tonani	And David, I think one of the things you brought up that is kind of important is the handedness, and kind of the fact that these molecules interact with receptors in the body. And that handedness, it's kind of like, if you inverted a key, it might not work in the lock anymore, or might work too well or not as well in the lock and key system. And that's why that handedness is important as it may interact differently with the receptors in the body, than the left handed version may interact different than the right or inversely.
David Gang	Yeah, and we know for example, that the cis versions or the plus versions. So those have been tested for activity versus the minus trans versions, and there's a like a hundred fold more difference in activity, much, much, less potent or if at all. So, it's exactly what you said, they don't function the same. So, they're not in the same molecule, even though they may have a really similar name. They're not the same molecule.
Jessica Tonani	I think one of the things that we talked about kind of in our pre-meeting was the fact that something could be a synthetically synthesized phytocannabinoid, that they're not exclusive, you can synthesize phytocannabinoids and they are still the same molecule.

David Gang	Right, right. You're exactly right. So that minus trans Delta 9 tetrahydrocannabinol, if you synthesize it in a chemical synthesis, I mean, and Brad can talk about this. He's a synthetic chemist, right? If you synthesize that in the lab or you extract it from the plant, it's the same exact molecule. Now, an important point here is that synthesis is not always one hundred percent efficient. And there's going to be side products, there's going to be side reactions that occur in that synthetic process, you're going to get other compounds that are byproducts of the synthesis that are not natural compounds. And it's possible that depending on how that's done, you may or may not have higher levels of some of these contaminants in a synthesis process, so that is something that is important to consider. Right, Brad?
Brad Douglass	Definitely agree. David, one thing I would add in talking about synthetic and natural that I've found is useful to overcome the ambiguity of the term synthetic is to refer to compounds that are produced by chemical synthesis, rather than just synthetic. If some people start conflating with artificial, I'd like to refer to synthetic cannabinoids as we're using them here as cannabinoids produced via chemical synthesis.
Nick Poolman	I guess one of my own curiosities is have you seen much chemical synthesis of endocannabinoids, like 2-AG or anandamide?
Nephi Stella	Yes, we can actually synthesize these endocannabinoids in the lab, and if I remember well, most of the synthesis is actually quite simple. It happens in 2 to 3 steps, so yes, it can be synthesized in the lab so that's why we can have this in the Venn diagram, the endocannabinoid blue circle. That's why we can have some endocannabinoids that are in the synthetic portion, I guess one thing to maybe also emphasize is something that we will be talking about a little bit later, is that this Venn diagram is really based on the chemical structure of the compounds, whether this compound has that chemical structure, and it's produced by natural, by the plant, or in the lab, but it's a classification based on the chemical structure. There's no indication in this Venn diagram of the

	functionality. What is the bioactivity of the compound? And that will be what we'll be talking about in the third question.
Jessica Tonani	And Nick, also I think, for example, truffles produces cannabinoids, so there is some actual production as well outside of the human by natural sources of endocannabinoids.
Nephi Stella	Maybe I'll just add to that. It appears that evolutionary, actually, the endogenous cannabinoids have been used very early on by multiple organisms and it's a molecule that allows cells to communicate between each other. So, one cell will produce the endogenous cannabinoid, and the other cell will have the receptor and therefore, we'll know that there's been some endocannabinoids that have been produced, so it's a means of communication between cells in our body. And it's been used very early on in very primitive and simple organisms already. And it's been perfected during the evolution, and today in the human body, the endogenous cannabinoids are produced in the brain, because we think about how cannabinoids will affect our brain function. But endocannabinoids, it's actually hard to find cells in our body that do not produce endocannabinoids and do not express cannabinoid receptors, so it's a very fundamental system that the body uses to communicate, and as David was saying, I believe the way to think about it is while we have our endogenous cannabinoid system, what the phytocannabinoids and the artificial cannabinoids will do is hijack that system, and act on the same receptor, and we'll come back to that. And I think one of the big differences, when you start thinking about functionality, is that these molecules don't act the same way on the receptor. So the bioactivity is going to be different.
Brad Douglass	That leads to another point I want to emphasize too, and that is that in the class, for example of phytocannabinoids, like I said, there's about one hundred and twenty-five of these have been identified from cannabis sativa, very few of them have the biological function that Nephi was just talking about. Right? Only like a handful. Most of them do not interact with that receptor at all. Most of them don't have

	any, as far as we know, kind of function that affects the brain at all. Most of them are pretty benign or innocuous as far as the human body is concerned. A few that may affect other pathways, right? There's been claims and some evidence that suggests, for example, that CBD is involved in maybe some anti-inflammatory properties, that might help your body deal with inflammation, right? The completely different process from what we're talking about with the endocannabinoid system and that receptor, completely different. So it's possible that a plant can make multiple compounds that have different activities that are beneficial or medicinally active in the human body, and this pathway, the phytocannabinoids, fit that description very well. So, only a very few of these compounds in this class and its chemical structural classes as Nephi said, and I think that's important to emphasize, very few of them are actually active in the way that we think is important as far as the LCB should be concerned, right? In terms of being able to impair somebody or anything like that. I want to emphasize, I've said that several times. I think it's important to emphasize, right? Most of the compounds out of the one hundred and twenty-five, I'd say probably one hundred and twenty of them, have have no impact whatsoever on a discussion related to how somebody's brain functions, as far as we know. Now it's possible some of them do something that haven't been tested yet. But it doesn't seem very likely that they're going to be very potent, at least at this point.
Jessica Tonani	So, really from the impairment or psychoactivity, we're really looking at the THCs. Fair assessment?
David Gang	Yeah, I think so. And it's also important to point out sometimes some definitions for cannabinoids have been compounds extracted from the cannabis sativa plant. The problem with that is that there's thousands of compounds that this plant makes. And most of those compounds are the same compounds that make up our bodies, like amino acids, sugars, lipids, fats, all those things that make up ourselves, they make up the plant cell as well. And none of those things have anything to do at all with the signaling pathway that affects how and why people use cannabis sativa for medicinal or recreational or other purposes.

	So, you can't just say that, because it comes from this plant, it should be called a cannabinoid, that actually doesn't make any sense at all from a biological biochemical perspective. Example, terpenes are important compounds we know about. It makes a lot of flavonoids, which are common to lots and lots of all plants as well.
Jessica Tonani	I was going to say inversely I've also heard people say interaction with the CD1 receptor knocks a molecule into the phytocannabinoids, and I think we had a little bit of discussion about how actually proving that would make it near impossible to kind of classify molecules within that space. But that had been used as a classification for…
David Gang	Yeah, and I think the artificial cannabinoids class kind of defines that. Right? These are compounds that are completely unrelated structurally. (unintelligible) They don't have the same backbone structure as the, what we call the phytocannabinoids here, but they bind to that receptor because they have a three dimensional shape. The final three dimensional shape is similar, even though chemical structure is a little bit, or a lot of it different. Right? So they bind to that receptor and have the same function. But they belong to completely different chemical classes. So really, you've got to think about both of those things.
Brad Douglass	Some terminology that we introduced in the first deliberate dialogue was psychotropic versus psychoactive, and I think what we're talking about here is anything THC related that has some CD1 activity is psychotropic. Whereas things may have an impact on the body, that may even have some other type of impact in the brain is psychoactive, but that class of psychotropic cannabinoids is very small as both of you are saying, David and Jessica.
Nephi Stella	I'm going to build on this on a couple of things that we talked about. I think the comparison with the key lock is a really good one. I think there's one lock that we can think about, which is the receptor, the cannabinoids CB1 receptors and the most famous key for the CB1 receptor lock is Delta 9 THC. Now, we're starting to actually talk about other phytocannabinoids like Delta 8 THC, and that's also a key that will open the same lock, the CB1 receptor. The second lock that the field has discovered is the receptor that is activated by cannabidiol. And cannabidiol is a very different system and therefore the lock

	is very different. The molecule is somewhat similar to THC, but it will open a completely different door. And therefore it will have a very different bioactivity. And then the 3rd way to think about it is that there might be some receptors or lock that we have not discovered, probably the one we will hear about in the near future is the receptor for cannabigerol. Because cannabigerol seems to have what I call bioactivity, it's changing the biological system, but we don't understand what the receptor is or what the lock is. And then the final category is what David was referring to as phytocannabinoids that don't do anything, even though you absorb them into your body, there are no lock or no receptor that it can engage and therefore it will not produce any bioactivity. So that's kind of how I think about it, I think about bioactivity as molecule that affect the biological system, and I think about psychoactive and psychotropic as a molecule that affects the brain and the mind function.
Jessica Tonani	I completely agree. And to add a little bit of complexity to it, a lot of people utilize CBD and THC at the same time. And one of the things that I tell people is CBD doesn't necessarily like the CB1 receptor, but it likes to interfere with it. So, I say imagine you have a whole set of keys and you have to find the right key. Sometimes it takes time and what the CBD does is kind of blocks that receptor. It slows things down some. And so there's even this interaction that goes on within the molecules, even if they don't like the receptor, kind of interfering with the molecules that do like receptors.
Nephi Stella	Yeah, the CB1 receptor is a fascinating protein. We could actually push it to the next level. It's a lock that has two slots for keys, one for THC that will open it and one for CBD that will slow it down. That's what you're talking about.
Kathy Hoffman	I appreciate all of the conversation. I wanted to go back. Brad, you gave kind of a definition. Let me find it on my note here. It was rather than saying synthetic cannabinoids, you could say products that are produced by chemical synthesis. I see lots of heads nodding. Is that everybody kind of agree with that?
Nephi Stella	I think it's an easier way to understand the process.

Kathy Hoffman	Okay. All right I want to circle back to that. The other thing I wanted to circle back to was Brad, if you had to define artificial, in this space, how would you define it?
Brad Douglass	To reiterate, I suppose what David had touched on, artificial is something that's not found in nature. So, were the endocannabinoids produced by animals or humans, phytocannabinoids produced by plants. Artificial cannabinoids are chemical cannabinoids that are not found in nature.
David Gang	In our last meeting we used the color example right? Food coloring? So there are, for example, red coloring. There are red agents that are made by insects or plants, or whatever, beets make them, many different examples that are red, that make your food red. And then there are these artificial compounds that are red, and those can be used in food to make your food red. But some of them are natural compounds, and some of them are not, some of them are artificial.
Brad Douglass	And I'd say we have a good example. I mean, we have a number of examples here of artificial cannabinoids, some are letter a number of combinations that most people aren't familiar with. But I'll direct everyone's attention to the last one on the list. And I'm going to draw attention to it as a sort of public service announcement, too. THC acetates. THC acetates are similar structurally. So, their analogs THC of which are phytocannabinoids. But they are not found in nature, so they're a product of chemical synthesis and they're artificial. I particularly draw everybody's attention to them now because THC acetates have a similar reaction, a similar degradation reaction when introduced to heat as vitamin E acetate. So if you're on the web, you may have noticed that Delta 8 THC acetate has become a popular thing. There's people out there that are considering putting THC acetate in pens or considering vaping them themselves, don't. So it could end up with the same sort of situation as with the EVALI. And the key team degradation potentially with THC acetates. So that's an aside, but figure it's worth everybody being aware of that at this point in time.
Nick Poolman	I just kind of had a quick question towards Nephi, the two lock situation on CB1 as you know, we've talked

	about, there's at least some different molecules that will interact with the active side on CB1, and you said that CBD is a competitive inhibitor, or an agonist. I don't know which term is better to use there. But is it possible or is there any research looking into other antagonists to that site as well like, that would also take that CBD spot.
Nephi Stella	Absolutely, so we in recent years, the field has been able to get the crystal structure of the cannabinoid CB1 receptor. So now we have a three dimensional view at the atomic level of how the receptor is organized. And what we saw was that the lock, the binding site where these compounds are coming in is actually a pretty big pocket. So that's probably why both the phytocannabinoids and synthetic artificial cannabinoids can bind to the same receptor because the lock is actually pretty big. So you can hijack it pretty easily. Now that we have this crystal structure, we can see that there's not only one big pocket where THC binds and endocannabinoids, but there's another pocket where CBD can actually bind so that's the second lock. The pharmacological term is a negative allosteric modulator, so it modulates in the negative way, the effect of THC, so that's why it reduces the effect of THC. And to your question, can we actually find new molecules? I am there, I think so, very much so. One of the most recent Nobel Prizes in chemistry is called evolutionary chemistry and they're able to synthesize millions, almost billions of different types of synthetic molecules. So, in those big libraries of molecules that people are designing in the lab, there is a very high likelihood that there will be some of those molecules that will be excellent keys for this second lock where CBD acts on the CB1 receptor. It's actually a very exciting field of research because you can think about a lot of medical properties in modulating the 1 receptor. Great question.
Jessica Tonani	I think when you asked what takeaway did you want for this questions, I think one of the takeaways is that a molecule can be both natural and synthetic. I think that's a really important takeaway from this. They are not mutually exclusive. And they can be the same molecule that is either made in nature or synthesized. The quality of synthesis means, oftentimes you're not just left with the molecule you're looking for, but if you have a pure Delta 9 it's the same molecule, whether it's natural or synthesized. it's a question of what else is in that solution of molecules.

Question 2: Is there a way to determine which cannabinoids are impairing and to make relative comparisons between different cannabinoids (both exogenous and endogenous)?	
Nephi Stella	Okay, I'm happy to. My goal is for everyone to become an expert in cannabinoid pharmacology, so I'm going to give some basic fundamentals, most of the terms that we'll be using are actually quite difficult to define and the first one that comes to mind right here is the word impairment. So as we started our discussion on cannabinoids, we started by the fact that there are some cannabinoids that are going to be bio active, which means that they are going to affect the biological system. They are going to affect our body and they can affect the body in in very different ways. The, the first terms that we talked about in terms of activity is affecting the mind, the brain functions. So whether it's psychotropic or psychoactive, those are the result of this bioactivity on the brain. The effect of cannabinoids, and I'm going to start focusing on Delta 9, and very similar with Delta 8. The psychoactivity of this compound is actually quite complicated. The first thing that people talk about when they say this is a psychoactive molecule is that it will change our sensory awareness. So, for example, music is much more salient and that's how people think about the cannabinoids producing the high. So that that would be one way to think about the bioactivity of THC on the brain. The other way of thinking about the bioactivity of THC on the brain is that it's going to be impairing and the way we think about that the most, easiest readout of impairment that we can see in animals and humans is impairment of locomotor activity. People have a tendency to actually not function correctly at very high doses so that would be an impairment, which is why there's actually concerned about driving under the influence of THC, if your locomotor activity is impaired you might actually increase the risk of accidents. So, already we have, we started with bioactivity on the brain. We have changes in sensory awareness. That's the high. We have impairment on motor activity, but actually the bioactivity on the brain could be medical. And that's a very different way of thinking about the bioactivity. It can produce analgesia. So, that means reducing pain. It can stimulate appetite, hunger, or it can actually even have an effect on the biology of our immune system. So the bioactivity of compounds is actually really complicated to define. It can be a high. It can be an impairment, or it can be a medical property. So I just wanted to kind

	of set the stage with those definitions. Because how can we determine, this question might be more precise if we could say, how can we determine which cannabinoid is bioactive and then think about what type of bioactivity it is it is producing. So what we need to do these determination of bioactivity or impairments is we need reliable readouts, we need measurements we need to be able to measure how are these compounds producing this bioactivity or impairment. And most likely one way that we need to think about that for the future, is that this read that more probably needs to have multiple results because the cannabinoids produce such a diversity in the bioactivity. That's to start thinking about the bioactivity of the compounds. So how being a Pharmacologist, how do we measure bio activity of a compound? And here there's more words, more terms that are difficult to actually understand and define, the first one is potency. So a compound what is a very potent compound? So the way to think about that in pharmacology is a potent compound is a compound that will act at low dose. So THC is a very potent compound at the cannabinoid CB1 receptor. It acts on this receptor at very low doses. So, that will be one of the readouts by bioactivity of potency the other way to think about the bioactivity is not the concentration, but the biological response is it producing a full biological response? Or is it producing a partial biological response, and here's an easy example to think about the effect is to compare the effect of THC versus some of the synthetic cannabinoids that act on the CB1 receptor, K2 has been mentioned, the synthetic compound. The synthetic compounds are what we call full agonists, they fully activate the receptor so they produce very strong responses. Whereas THC, actually, is what we call a partial agonist, which it activates the CB1 receptor but it produces a partial response. So, when we get into the discussion of how can we characterize different types of cannabinoids. And that's actually how it's done for the schedule one license. The route to define a cannabinoid in terms of functionality is there's several steps that one needs to address. The first one is a biochemical step. So, the first question, if we discover a new compound, synthetic, and the question is, is this going to be a cannabinoid agonist at the CB1 receptor? Is it going to be impairing? The first thing that people will do is test whether the compound is interacting directly with CB1 receptor. That's a biochemical assay. You do that in the lab, you have your little tubes, you add, and you see that THC binds to the CB1 receptor. You have an unknown compound, you put it into your little tube and you look at if the compound binds and activates the CB1 receptor, and it does. According to that first criteria, this new compound is going to be a cannabinoid CB1 agonist. The second criteria is we're going to move into a more complicated system from the tube where we do a biochemical assay. We're going to test whether the cannabinoid is producing a

	behavior in mice. So the field has studied for decades how mice respond to cannabinoid compounds and therefore we understand the bioactivity of cannabinoids in mice. There's typical behaviors, including for example, impairment of locomotor activity, mice stop moving, they stop walking around. So that's impairment of locomotion. So that's our second level of investigation in a more complex system, which is the mouse. And then the third level is to try the compound in humans. Of course, this is not commonly done, this is done only in terms of research. And in this case, there's been quite a bit of papers that have been published at NIH where you had subjects that would arrive in the laboratory, you would provide them with the cannabinoid compound. They did it mainly with THC, the individual takes THC and there are actually individuals that have used cannabinoids before. So they actually know the sensation and they rate, they rank the biological activity of this compounds in human and this is what we call the subjective high. So there's a scale and people can actually take this compound, THC, and then they rate how the bioactivity of this compound, how high is it? And so THC will reach a certain level and if the individual were to take a synthetic cannabinoid, Spice, the activity would actually be much, much, much bigger. All of these assays, the biochemical in the tube, the mice in lab and the humans in NIH, all these bioassays have been actually validated and the way you validate that is, you give the compound THC. And then you add a blocker, an antagonist to block the receptor, and you showed that THC doesn't work anymore. So, if you do that in the biochemical assay, you do a block, you add a blocker, and it won't bind anymore. You add it to a mouse, you have the activity of the mouse you had the blocker it doesn't work anymore and even in humans they did it where the human subject takes THC, has the psychotropic effect, you add the antagonist, the blocker, and it doesn't work anymore. So the field has actually this process of defining what a cannabinoid is at the functional level by testing biochemically in rodents and mice and humans and therefore, is there a way to answer this question? Is there a way to determine which cannabinoids are impairing? Impairing his hard, but maybe bioactive and make a relative comparison between different types of cannabinoids, endogenous and exogenous, that would be the process. The easier one is you have a new cannabinoid you tested biochemically, next step in mice, and then it's very important, then we can also test in humans. So that would be the first way to think about that.
Brad Douglass	So, in our discussions, Nephi, you briefly step through the timeline for going through those three different approaches, biochemical, in mice, and humans and I thought that was helpful for us with a panel, and probably helpful for people to understand in this case related to cannabinoids.

Nephi Stella	Yes, I think so. These experiments are actually increasing in complexity, so it's actually quite easy to test compounds biochemically so the timeline could be very rapid. A lot of laboratories have these biochemical assays in place. You just give the compound and you can say yes or no, is it activating the cannabinoid receptor? Is it a full agonist? Is it very potent acting at small concentration? All these questions can be addressed quite quickly biochemically. The next level would probably take more like months where you would actually have, because these mice actually are trained to recognize cannabinoids. They're used to press that little lever. And they know that they're going to get THC and they recognize the sensation. So the way actually my understanding, the way the DEA goes to the process of classifying these drugs is first they do the biochemical assay, if it binds to the cannabinoid receptor, then they test it in mice and these mice are trained to recognize THC every day they press a little THC and they get the psychotropic effect and then one day, instead of giving THC you give this new compound that is unknown and if the mouse presses for the lever, it means that it has the same sensation as THC and that would take several months to actually figure it out and then my understanding that is the time where if the mouse recognizes that this new compound is acting just like THC, that new molecule will end up on the schedule one. So, at least several months. To test a compound in humans I imagine that would actually take years because then you need to you need to justify with the IRB, and it would probably have to be justified. You couldn't test every compound. They would have to have a very strong justification just because we're not allowed to give everything to humans. We need to go through the IRB. Does that help?
Brad Douglass	That was great.
Jessica Tonani	One of the things you talked about, Nephi was a blocker, and if we kind of go back to our lock and key, I think of a blocker, just to kind of put it in easy context it is like putting glue in the keyhole. So you can't use your key anymore. I don't know if there's a better analogy.

Nephi Stella	I like that. It's a key that gets into the lock, but doesn't open, or it breaks while the, the antagonist, the blocker can also come out.
Jessica Tonani	Yeah, I agree.
Nephi Stella	Absolutely. So, maybe I'll add one more thing because I see at the end of this question, there's a comparison between exogenous and I'm going to think about exogenous as phytocannabinoids or synthetic cannabinoids that act on the CB 1 receptor, compared to endogenous cannabinoids that are produced by ours cells. So, one of the questions that we get is THC is the exogenous drug, it will act on the CB1 receptor. And you're impaired. Why are we impaired if our body is producing also these endogenous cannabinoids? And the difference here is in how long the molecule, the key stays into the lock. Because they are produced by cells and they use that to communicate, you communicate much better if you send a message and then it stops. So, the communication, the activation of the CB1 receptor by the endogenous cannabinoids is very short lived, it's a message, go on. And this is the message. By comparison when an individual takes THC it goes into our body, floods our brain and stays there for minutes, and therefore the lock, the key stays in the lock for minutes or even hours. And that is why people think about changing the state of mind is because this lock has been engaged by that key for a long time, in minutes instead of seconds. And that continuous activation of the CB1 receptor. changes the mindset, and therefore could be either sensory awareness or impairment of locomotor activity. You're absolutely experts in the pharmacology of cannabinoids now, I've pretty much covered all the bases.
Nick Poolman	Nephi, you brought up something very interesting. So, I think this question kind of addresses, potentially, what is the, let's say, maxima of the curve or the inflection point binding, but you brought up, I'll say area under the curve or integration. Do you think that one may be more valuable to think about than the other, meaning that maybe it doesn't have the highest inflection point, but has a longer curve? Is that going to be as impairing or differently impairing as another cannabinoid?

Nephi Stella	So this is a good question, and this is actually what a lot of researchers are thinking about, especially medicinal chemists who are trying to create new synthetic artificial cannabinoid molecules. Because two parameters that we have to think about is how potent the molecule is, which means it will act that very low concentrations, and for how long. So we are able to actually design some molecules that will have different potency, work at very low concentration, or at very high concentration, and that will activate the receptor key lock for different amount of times and there are some thoughts that maybe by changing these parameters, we can actually optimize the medical properties of the cannabinoids versus the impairments. It's still a lot of work in progress. The field is extremely young. Our field of cannabinoid research is very young. It's been maybe ten or fifteen years behind the opioid field. When I started the research twenty years ago, there were a hundred or a hundred and twenty-five people at the international cannabis research society. So a very small field, and because of the legalization and the field starting to actually be interested in cannabinoids, now the field is much bigger so I'm hoping that the research will go faster just because there's more researchers that are interested.
Jessica Tonani	One thing, Nephi, that maybe you can bring up is around toxicology. I tell people all the time that Delta 9 is a relatively safe molecule as we know it. A small amount of it can make you feel like you're going to die, but it would actually take a very large amount to die. Do you think there's different toxicology points or LD fifties, or essentially the lethal those for fifty percent on these different molecules?
Nephi Stella	Yes, so there's going to be, the toxicity is usually associated, is linked. Each molecule will have its own toxicity profile. And it's true that the safety profile of cannabinoids is considered to be really good. They're very safe drugs, because you can absorb them at very high concentration and you will not have a heart attack or heart arrest, or problems with your blood pressure, or things like that. And that is due to the fact that the cannabinoid receptors are expressed in the brain, but they're not expressed in key parts of the brain that control these organs. And the easy way to compare it again is the cannabinoids and the opioids. So the opioids, which is the same idea. We have the endorphins, that's the

	endogenous that we produce and it acts on the opioid receptor, and we have the exogenous, the morphine, the heroin. While these locks, or the opiate receptors, are in the part of the brain that control heart rate and respiration. So, that's how you overdose from opioids because these opioids are acting on those receptors in those parts of the brains that are controlling. And because cannabinoid receptors are not expressed in those parts of the brains, their initial safety profile is much better than opioids just because you will not have a heart attack following cannabinoids. However, toxicity, there's always toxicity, it always depends on how much you take, and therefore there is toxicity that is associated with cannabinoids, but it's at very, very, high concentrations and for very, very, long amount of times. And the last thing I want to say also about toxicity is that toxicity depends on how vulnerable you are. If you're a very strong individual, the toxicity will not be too bad, but if you're a vulnerable person and what I'm thinking about is the adolescent and population with their developing brain there will be a toxicity profile that'll be different just because they're more they're more vulnerable to these compounds, so toxicity can also change with age.
David Gang	Nephi, if you could you also comment on acute versus chronic perspectives for toxicity in that regard?
Nephi Stella	For toxicity. So, maybe commenting on this, for a molecule to be toxic and acute, it will have to be either that the lock, the receptor is an area of the body that is fundamental for our life, like, for opioids if you were to go very, very high. And so that would be the first thing to think about for acute toxicity, and for chronic toxicity, then it's different because sometimes chronic toxicity is not only associated with the molecule acting on the receptor, but the molecule being processed by our body and then by our liver, for example, and starting to produce metabolites, and if you use it chronically, maybe those, some of those metabolites cannot be eliminated fast enough. And there's different types of toxicity that can that can appear. So, that's the first thing that comes to mind. Is that what you were thinking, David?
David Gang	Oh, yeah, I think so. And I guess my question then is, is there any evidence for any chronic toxicity with these compounds.
Nephi Stella	Well, the 2 that actually my lab is really interested in is chronic toxicity associated with chronic use of THC in adolescents. And that toxicity is a toxicity associated with changes in neural function, because this

	cannabinoid system, so the receptor, the lock, and the endogenous cannabinoids that are simulinked between cells. Our brain is using this simulinked system to actually being built during development, and because an adolescent brain is not fully developed, and it can go all the way to after 20 years old of age where the brain is still developing. As the brain is developing, the endogenous cannabinoids are using the cannabinoid receptors to form this brain, but if the brain is full of THC, all the time, that simulinked system is going to be impaired, it's going to be hijacked, and therefore the development is going to be affected so that's why the toxicity in that term is for the vulnerable population of the adolescents.
Brad Douglass	So, it might be a good point for me to interject this. And I know we're only on question two. We got a little way to go, but Nephi elucidated how the DEA goes to the process of evaluating, whether something has similar activity to a controlled substance. First, you have the biochemical step, then you have an animal step. This is essentially what undergirds the federal analog act. So how you judge a new molecule is similar to something that's already been placed on the controlled substances schedule. And I want to read from the analog act and it's a two pronged test, because I think it ties our first two questions together. And it's important because it shows how you interpret science into policy. So, in the federal analogue act, the controlled substance analogue is defined as something that has the chemical structure of which is substantially similar to the chemical structure of a controlled substance, and which has a stimulant, depressing, or hallucinogenic effect on the central nervous system that is substantially similar to a controlled substance, so that two pronged test essentially details the two different approaches to categorizing cannabinoids that we've been talking about. First, structurally chemical similarity and then with this question, functional similarity. And I think that this is important, because when this definition was first put down in statute, the DEA asserted that one of these was sufficient to bring a molecule under the analogue act. But the courts then decided that you need both of these things, both chemical similarities, so, structural similarity and functional similarity, to avoid sort of inane results like caffeine, for example, having stimulant activity and being judged a controlled substance. So, I'd throw that out there just as some precedent in a way that the complexities of science are interpreted in, I guess, solving a similar problem.
Jessica Tonani	Brad, if caffeine ended up on the CSA, I think a lot of us would be at a big trouble.

Brad Douglass	Yeah, big problem. Pitchforks and torches.
Nephi Stella	And maybe I'll add to what Brad was just saying. That's really interesting. The federal analogue act. We think about the functionality, you mentioned a stimulant, a hallucinogen, and depressant. One of the challenges with cannabinoids, they're not actually in that category of psychotropic molecules, they're in the category, which is very obscure, which is called mind altering drugs because they're not stimulants. They're not depressing. So, even the definition of that definition actually is probably, should be adjusted for cannabinoids.
Question 3: Do you think consumers should be informed whether a product has undergone a chemical synthesis?	
Brad Douglass	Absolutely, so I'll offer again. I like to speak to precedent and what's been done and other regulated areas. So, the offer is in food. Ingredients aren't typically labeled, though, whether they're natural or synthesized for food ingredients, as far as the FDA is concerned that meets the purity and other requirements of the substance. It's immaterial whether it's national or synthetic. Now, the opposite is true when it comes to flavor compounds in food. So you are required to declare on your label, whether you're using an artificial flavor compound or a natural flavor compound. In this case artificial refers to both natural compounds that are chemically synthesized and actual artificial flavors. So there is precedent for both ways. Now, in my opinion, it hinges on whether the consumer thinks it's important and this is something that consumers should be polled about, but also the industry and regulators should discuss. Is it important enough to put on the label? Does it have an impact and do most consumers want to know? And is it important enough to take up label real estate that other important information could occupy. So, I think that's the test. How important is it? And it really is important to consumers, and it should probably be declared on the label.
David Gang	I thought Brad answered it really well, actually.

Jessica Tonani	And Brad, we did have a little bit of discussion around, what may need to be on that label and things like decarboxylation, and things you had mentioned Oregon had decided not to put that on. Can you speak to that at all?
Brad Douglass	Yeah, that's a good point. That's good. So the recent legislation in Oregon around this similar topic, they carved decarboxylation out as a chemical step, the chemical alteration that wouldn't necessarily put it in the same category as something that's the product of chemical synthesis, and therefore wouldn't be subject to the same sort of disclosure requirements. So there's some deep decisions that would probably have to be made and categorizing what it is something that's a product of chemical synthesis, and what's natural. And I'll also add too because I think we brought it up in our, our panelists discussion, a useful example. So tangible examples are helpful here. Citric acid. Citric acid is something that's pervasive in food, beverages, it's an acidifying agent. It was, or it's found, naturally occurring in citrus fruits, hence the name citric acid. But essentially all citric acid that's used in commerce, in food and beverage products is synthetic. So, you would know that from a product label, because it's not declared, but it is the case that almost all citric acid that's currently used is the product of chemical synthesis. Same goes for caffeine.
Nicholas Poolman	I know we talked about this pre panel, so this is a little bit of me cheating, but you said that for food, the molecule is a molecule, but for flavoring chirality seems like a bigger deal and I'll tie this back to our first point with the handedness. At least in my view it seems like cannabinoids have a lot of chirality and have a lot of stereo importance to them. So, do you think it kind of leans one way or another? And I know you said that it should definitely come down to the consumer, and the producer processors to have that conversation with policy. But would you say it leans one way or another in your view?
Brad Douglass	Yeah, I think that’s a good point Nick, that when you're talking about molecules like caffeine or even citric acid, they're mostly achiral, pretty simple molecules, but a lot of your cannabinoids do have stereogenic centers and have chirality, which adds the multiple, additional level of complexity that makes this conversation about what disclosures should really be provided to consumers more challenging.

Jessica Tonani	One thing I think we talked about, Brad, a little bit and I talked to about that with David a little bit in different discussions is the potential of testing for chirality and it's not necessarily available in I502 testing now, but can you kind of circle up on the fact that there is some potential for testing that.
Brad Douglass	That yeah, absolutely. So there's four different stereo isomers of Delta 9 THC. You have the trans plus, the trans minus, the cis minus, the cis plus. The cis aren't very common, and there's not much data about their synthesis. They can be synthesized, but they're not common. The trans minus is naturally occurring, the trans plus is commercially available as an analytical standard. And there are some instrumentation companies who have developed methods that allow you, and they're chiral separation methods, that allow you to test and tell whether you have the trans minus or the trans plus. Kind of chromatography, it's a pretty well-known form of chromatography, but it allows you to discriminate between stereoisomers. So, can it be done? There's some methods for some of them and there's analytical standards for at least the non-naturally occurring plus trans plus. But some of the other stereoisomers are, although they've been characterized, aren't easily testing for. Yet.
David Gang	Yeah, and one thing to add, Brad mentioned this a little bit his comments, but I want to emphasize is that to be able to do that kind of analysis, to tell the chirality, that's a left and right hand again, to tell the left hand from the right hand you have to have standards for those types of chiral separations, to be able to know what you're really looking at. So, if there isn't a good standard available. It's very, very difficult to do that kind of analysis. So, availability of standards is really critical for that.
Kathy Hoffman	David just how long does it take to create standards? For the audience, I think this is something that we've talked about a little bit before, but it takes a while, doesn't it?
Brad Douglass	It's time and resources it's a question, right? So, for a cis isomer of Delta, 9 THC, you would first likely have to synthesize it. So, to do that, you'd have to come up with the synthetic route. There's some routes in the literature. So, you'd have to find the resources to produce that. Then you'd need a certified standard provider, at least if the standard is going to be providing commercially, to actually synthesize that, get the

	concentration exactly right, to be able to sell those to labs that can then use it to run the test. So, it's relatively involved
Jessica Tonani	And Brad, one of the things around that is depending on commercial lead, the companies that are producing these standards are commercial companies. And so if there's a commercial need, they may have a little bit more emphasis to do it quicker. If there's no commercial need, if they're only going to sell a couple of these a year, it may take a substantially longer wait time. Some of it is dependent on the commercial viability of creating the standard.
Brad Douglass	That's very true. There have been instances in the past where companies that were looking to develop a new molecule, solve a need, having the standards available, and they helped some of these standard creation companies with the material to help make sure that those standards are available. So, you could test the quality of the products. So, there's an opportunity and perhaps a responsibility from industry perhaps just as much as there is, maybe from a regulatory standpoint, saying okay, we need these, to provide that impetus to create them.
Question 4: What is the safety of the chemicals being used? Literature describes the use of sulfuric acid, hydrochloric acid, methylene chloride, benzene, toluene, toluenesulfonic acid (p-TSA), and other chemicals.	
Brad Douglass	Absolutely. So, in my mind, this is two separate questions. First, you have the safety of some of these compounds when they're in the finished product. And at what level they show toxicity, or are safe or not. And the second question is the safety of the processes, and the people that are running these processes in facilities that are doing some of this stuff. I think these are two very different questions and if you look at the first one, the safety of some of these components in the finished product. If the finished product doesn't have these components, then it's immaterial whether they are used in the process. So if you can demonstrate that your products do not contain these, then great, it represents no safety hazard for consumers of those products. But very importantly is how these compounds are used. Facilities that use these compounds. You have to have safeguards for employees, personnel that use some of these compounds. You have to have the right facility and equipment make sure you're not having exposure

	events. And there's a way to handle all these compounds that are listed here safely. But you do have to have some expertise. You do have to have very, in some cases, very buttoned-up procedures to do so.
Jessica Tonani	So, we're essentially looking at consumer safety and employee safety. Is that right, Brad?
Brad Douglass	I think that's how you tease apart this question, absolutely. And there are, again, I sound like a broken record, excuse me, but I think there's precedence for answering both questions. For the levels that are permitted in finished products, you have ICH levels for residual solvents, acids, things like that that can be looked at. We've used those in the past in regulating cannabis for residual solvent levels. And in terms of safety of chemicals, being used, you have OSHA and other requirements about what constitutes a safe working environment, if using some of these compounds.
Participant Question and Answer Session	
Participant Question 1: **Hemp-derived THC is analytically identical (when tested in a state certified testing lab) as THC from other extraction methods because it is the same molecule. Correct? It is simply the same thing created with a new method.** **In Washington for a licensed Producer to compliantly enhance an existing marijuana product with CBD the CBD isolate is required to be tested for pesticides and heavy metals twice. By contrast all other marijuana products in Washington are NOT required to pass a mandatory pesticide and heavy metals test. Wouldn't that make enhanced products the safest products in i502?**	
Kent Haehl	Yeah, I've got I've got a couple of questions you can see right here. I mean, some of these things came up a little bit earlier and specifically around hemp-derived THC being analytically identical, so you can see here. My question is really if we're talking about something that is the same, because it's a molecule. I mean, we're really talking about something that was created with a different method, but it's the same. So I guess this kind of tails off into discussions about whether something like this should have a distinction

	attached to it that it was made in a different way or synthesized, if we want to use that term. It doesn't seem to make a whole lot of sense to me when we're talking about cannabis made from hemp.
Brad Douglass	I'd be happy to address that. I think that's a good question, Kent. And I think that is the question at issue, whether THC from other sources is identical to THC found in cannabis. And I think for us on the panel here, least I'll speak for myself, that is what is unclear, but it's unclear whether THC produced from other sources is, in fact, minus trans Delta 9 THC. Or are there other stereoisomers in there? And I think really that is the key issue, but from a safety and science standpoint, if two sources of THC, and I'm talking, being chemically specific here, Delta, or minus trans Delta 9 THC, it's the same molecule. It shouldn't matter where they come from, again from a safety and science perspective.
Kent Haehl	Thank you and my second, question was really focused on -
David Gang	Actually, before it before you go with your second question, I'd like to add something to what Brad said and that is from hemp there's actually two ways you could get THC from hemp. Right? One of those is THC is present in hemp. In the acid form at low level, right? Just like it is in recreational or medicinal cannabis, it's the same species. It's just been differentiated artificially by regulation to say, this is one type that we're going to call cannabis, recreational and medicinal and this is the other type which we're going to call hemp. It's the same exact molecule produced in that species and those different types. In hemp, it has to be less than .3% so you can extract it directly from hemp the same way you can extract it from other types of cannabis. The other way is you can take CBD that you extract from hemp, and then you can go through a synthetic process in the lab and convert that CBD into Delta 9 THC. And then, at that point, the question goes back to what Brad said, what form did you actually produce? Did you produce one hundred percent minus Delta 9, minus trans Delta 9 THC, or, in that chemical synthesis process that you ran that CBD through, did you convert some of it into either the cis form, one of the two cis forms, or the plus form of the trans, and that's still an open question. It's going to depend on the chemical method, chemical synthesis method that was used. As well, as purification and other things like that, so it's going to depend on how you get it from hemp, whether or not it's the same molecule or not. Or, if it has a possibility be to be converted into something else in that process. I just want to make sure that was really clear.

Kent Haehl	All right Thank you David. My next question is, in order for this to be done currently in a compliant manner following both the state law and the WAC using CBD isolate, both of those processes would require that the CBD isolate be tested for pesticides and heavy metals. Not once, but twice. By contrast all other marijuana products in Washington state are not required to pass mandatory pesticide tests for heavy metals, for pesticides and heavy metals. I guess it's almost a rhetorical question, but I would take the position and would ask the group here, wouldn't this make a product made from a (unintelligible) like this be not the safest products inside of i502, given that it's required to pass those tests. And others are not appointed to be sold in i502.
Brad Douglass	I was going to say, unless you wanted to go, David, that there's different metrics of hazard. I like to talk about hazard rather than safety, and pesticide and heavy metal content is one metric of just determine the amount of hazard or lack thereof. I think the type of testing that you might need to do for evaluating stereo isomers, like we've been discussing a lot, is different from heavy metal and pesticides. How that all wraps together is sort of unknown, but I think it's tough to categorize saying that the safest products in i502, just because they're tested for these two different metrics, but there's other things that could have an impact on the safety or hazard.
David Gang	That's pretty much what I was going to say. Yep.
Kent Haehl	Thank you very much for your comments. I appreciate it.

Participant Question 2:

1. When considering Hemp Sourced THC my understanding is that there are two major concerns.

- **Safety of the product**
- **Competitive nature to marijuana derived THC.**

2. If there was no safety concern, then would new innovations such as the Hemp Sourced THC be allowed?

While (-) trans Delta 9 THC is the predominant THC stereoisomer found in cannabis, there are also other Delta 9 THC stereo isomers that can be found in cannabis. It has been studied that the stereoisomers are 100 times less potent than the predominant (-) trans Delta 9 THC. Will both Marijuana and Hemp sourced THC need to be stereoisomer tested even though the other stereoisomers are 100 times less potent? **3. Dronabinol which is a pharma grade THC product is not a "synthetic" THC such as the designer drugs like Spice and K2 but a true THC molecule made from an organic synthesis process. –However, it is not Hemp or plant derived. The pharmaceutical drug Dronabinol contains the same stereo isomers that have been previously discussed as points of concern. Does anyone know what is the concentration of the stereo isomers in Dronabinol?**	
Rusty Sutterland	I appreciate you guys taking time out of your busy schedules for this. So a couple of questions here at first, listening to the term synthetic or synthesized. It does sort of get confusing. Actually, I can definitely see where some of the chaos comes from there, and I was wondering, could, would a better name for this be like a hemp sourced, because as we know the Delta 8 material, it does come from hemp. I do know, we just talked about the stuff that's below the point .3% and some of the stuff that was derived from CBD. I didn't know if that might make it a little bit simpler to coin a phrase that says, CBD derived or hemp sourced THC, and what's your thoughts on that?
Jessica Tonani	I think to some degree that's a marketing call for lack of a better way to put it. I think that the reality is that CBD is being converted into Delta 9. So, I don't know the best terms, but I think what we've been trying to do is bracket that so people know natural versus synthesized versus artificial, and kind of try to give a pretty clean definition. I'm not sure, it sounds like we might not have been extremely successful, but I don't know if anybody else in the panel has anything to say around that.
Brad Douglass	Yeah, I'd say, in my opinion hemp sourced doesn't add anything to making the terminology more precise. So, we're chemically precise. We would say trans minus Delta 9 THC. If it's the same molecule it's the same molecule, it doesn't matter where it comes from, hemp, the moon, yeast, it shouldn't matter, and I think that's the key - being precise in our terminology for chemically what these things are.

Nephi Stella	And maybe I'll add that it's the same way to think about this in terms of pharmacology - the molecule, wherever it comes from, if it's exactly the same molecule, will have the same bioactivity, will produce the same biological effects. So, we don't really, it's not very important in terms of the bioactivity, the pharmacology, where the molecule comes from. It will produce the same effect. If they're exactly the same.
David Gang	Yes, that's another point though. And that is, are they exactly the same? So Brad mentioned if you get the purified compounds. The question is, is the process that you're using to generate that compound, not extracting it from the plant but generating it from another compound, is that going to, and there could be different people to use different processes, that along the way, they may use different solvents that were mentioned on previous slides and earlier, et cetera, different things could go on to produce that compound. And, the compound itself will be the same, but there may be other things that are carried along with it. The question is, what are those things? What are the contaminants? What are the byproducts of that process? How critical are they in terms of hazards or other things, and that's something that's, I think, very difficult to understand, except for looking at it on a case by case basis to be honest.
Rusty Sutterland	Okay, and in regards to some of those, those other by products that were discussed on the different stereo isomers that has come up several times also. And I was trying to Google. You guys are probably familiar with the pharmaceutical grade compound called dronabinol. That is made, that's a true synthetic molecule not made from a plant or anything. And I believe it does have some of those same stereo isomers that we've discussed before and that, but I haven't run across any references that actually say how much of those stereo isomers are there, are there any effects, because I know there's been, even though I think there's probably some evidence out there showing that these, these other stereo isomers are not toxic. I haven't seen anything necessarily conclusive yet, of that, but some of these stereo isomers are produced in that pharmaceutical drug. Have you guys come across what those concentrations are and is that, whatever those limits are, those concentrations, would that be deemed an acceptable limit of those stereo isomers in these compounds?

Brad Douglass	It's an interesting question, Rusty, and what I can tell you is that the United States Pharmacopeia monograph for dronabinol, right, the generic of Marinol, branded dronabinol, synthetic THC is achiral, so you're are permitted via the USP monograph that have both the minus trans and plus trans Delta 9 THC in that product. Now that's, well, one of the methods by which dronabinol, is produced is, it sort of bakes in some of your stereo chemistry, so it's, it's less, perhaps less of an issue, but via the monograph, you are permitted to have both of those stereoisomers and if you look at the monograph, it's instructive for other reasons, right? Other than being achiral and dealing with the stereo isomers we're discussing here, it also gives you limits or tolerances on other impurities. So, for example, in dronabinol, you can have up to 1.5% CBN, you can have up a 2% Delta 8 tetrahydrocannabinol can have at all and up to half a percent of exo THC so, I think that's a very useful resource in our discussion here. What has been done with respect to dronabinol, which you identified as THC, produced via chemical synthesis.
David Gang	And I think another comment on that is that dronabinol, in the form of Marinol was approved by the FDA, the Food and Drug Administration as a pharmaceutical drug. And in order for that to happen, it had to go through pretty significant safety and other evaluation trials, right? So it has been deemed by the FDA to be safe. And as long as it is being administered, according to the prescription protocols that are supposed to be followed. So, I don't know that we can question the FDA's conclusions about safety with that regards. So that's I think that's what we can say about it.
Rusty Sutterland	Okay. So, yeah, I definitely agree with you on that respect. So, but with that being said, then, is there really a topic that needs to be discussed on these other stereo isomers? If the FDA has already said that they are not toxic or if they're safe.
David Gang	Well, I don't know that it's actually said that they're not toxic or safe. I think it's said that dronabinol, as prescription drug, can be used in a manner that they would deem as safe as long as it's used in that manner. Now, if you then take that compound and put it into a, many different, I don't know, I mean, you've got vaping, it could be added to the edibles. There's lots of different ways that it could then be put into the human body. And then your dosage becomes completely unregulated. And then the question about safety

	becomes a completely different issue, because it's no longer being monitored by a physician at specific doses.
Rusty Sutterland	Okay, I guess that's sort of like a Delta 9 THC also, it's definitely being used. I'm sure the FDA doesn't necessarily approve it for all the all the current ways that it's used now, but it is, they do not seem to draw a concern around the, some of the other isomers though so, I was just wondering if they do not draw a concern, should we also draw a concern around it?
Brad Douglass	I can respond to that in two ways, Rusty, one is that they're only speaking of, in terms of achiral, the minus or plus trans isomers. Isn't speaking to cis at all, and the other way I can speak to that, and this is a bit of a corollary to what David was saying, that in the process of getting a process approved to produce an active pharmaceutical ingredient, you're characterizing all of your individual impurities that are produced by that process. So, in the process of synthesizing THC, the sponsor was required to tests trans THC by itself and understand some of the toxicology and those, the responsibility of the sponsor that is bringing that product produced via that process to market. No, I think that's a (unintelligible) point here.
Rusty Sutterland	Yeah, so it does sound like it has been studied then from what you're saying, Brad.
Brad Douglass	Again, at least the one isomer, so the plus trans Delta 9 THC but not necessarily a cis.
Rusty Sutterland	Okay, (unintelligible) okay then from my understanding.
David Gang	We can't say that. There's no data to say that. Also it's important to recognize that whole process for approval followed the dosage regime that was going to be used for the final pharmaceutical drug, right? It

	isn't what you're going to be getting in some extract that you get a vape shop, or in some edible that you buy at some store or something like that. Right? It's going to be different. So, it's those, could easily be different and could fall outside the realm of the levels that were tested in that process for FDA approval. So, it's really hard to say at this point that something that could come on the market would fit within that range or not. Is that reasonable to say, Brad?
Brad Douglass	That certainly is. I'll add one other component there is that when you are approving a drug or a substance for an indication, you're doing a risk benefit analysis. So sometimes something will be approved for a specific condition and that risk will be deemed acceptable. So that risk calculation can be different, whether it's a different disease or it's the difference between somebody using it to treat a medical condition versus somebody perhaps using it for just any old adult use.
Rusty Sutterland	Yeah, thank you. Yeah, hopefully, we can work to determine what some of the compounds are in this and see, hey, is that cis even made and some of the process steps. Thank you.
Jessica Tonani	Rusty, have you requested whether or not you can get any of that data from the FDA?
Rusty Sutterland	I have not made that request yet, so that's on my agenda.
Jessica Tonani	I think the panel would love to see any data that you potentially get, I don't want to speak for the whole panel, but my guess is they would.
Rusty Sutterland	Yeah, we have actually sent an email in to request that information, but have not heard anything yet. We'll definitely keep you guys informed what we find out. Yeah, one of the many things I was, I was thinking of, hey, this is not necessarily a new, anything new or s new concern but it has been looked at

	before though. And so, let's take a look at what the, what the findings were and go from there and let the science decide.
Brad Douglass	I think that's a great starting point, Rusty.
Rusty Sutterland	Yeah, absolutely. It is hard. Sometimes, you know, talking to the FDA they're definitely not going to say, oh, yeah smoke all the native trans Delta 9 that you want. So, it's sort of a little tricky slope that you tread on. Thank you guys.
Participant Question 3: **1. Several states are in the process of approving or have already created a regulatory framework for hemp-derived THC. With national legalization on the horizon and interstate commerce soon to be a reality what should Washington be doing to embrace this innovation and regulate it?** **2. If the argument is being made that there are potential "unknowns" in Hemp-derived THC products, the same argument can also be made that there are potential "unknowns" within other more commonly known extractions to produce THC products. How does one effectively regulate one version of the same compound (delta-9 THC) to a greater degree than traditional extraction methods with a greater percentage of "unknowns" relative to total cannabinoids?**	
Kathy Hoffman	So, I don't know if that's necessarily a question for the panel. You're welcome to answer and I know LCB isn't going in on this at the time, just in my opinion, this is more of a policy question at this point, but I'll turn it over to the panel if you have ideas or opinions on that.
Jessica Tonani	I agree on that. It's a policy question, Kathy. I don't know how other people feel.

Brad Douglass	I agree, it's certainly a policy question and has certain components of policy. I think there is a science component to it for a safety component. And I think that deals just potential innovation in general. I think there's a danger when there's a new innovation or potential for innovation to clamp down on it. On one side, and on the other side, there is a potential for underestimating the hazards. I think there's a dynamic tension that is involved here for demonstrating the safety or ensuring the safety of a new process or product produced by a new process. So, from a science and safety standpoint, that's all you're looking for, you're looking for a safe product that can be produced safely and is safe for consumers to use. And I think that involves multiple people, multiple stakeholders to do that successfully.
Blade Boden	Wonderful, my apologies on the audio complication there. Yeah. To clarify a little bit it was more on the safety and efficacy side of it like Brad stated. So, I appreciate his answer to that the best that he could. Does anybody else have anything to add for question one? Okay, so my next question is, if the argument is being made that there are potential unknowns in hemp derived THC products, the same argument can also be made that there are potential unknowns within other more commonly known extractions to produce THC products. How does one effectively regulate one version of the same compound Delta 9 THC to a greater degree than traditional extraction methods with a greater percentage of unknowns relative to total cannabinoids? And I guess it's basically, it just seems like this, the unknown and byproduct argument is being made without acknowledging the fact that there are also unknowns in traditional extraction methods.
David Gang	I think I agree with you 100% that you should acknowledge that there are lots of unknowns in extracts that are derived from cannabis plants. There's a lot of, if you look at detailed analysis of those extracts, you can find (unintelligible) analysis, for example, see lots of little small peaks, little small levels of compounds in most of those, we don't know what they are. That's true. But an extraction and a chemical conversion are two different things. And I think we need to, in both cases, you're having an extraction from hemp, or from recreational cannabis. For example, in both cases, you're extracting. And then one of them is run through a process that causes chemical conversions to happen. Right? Where you're converting the CBD into THC, and we talked about that stereo isomers of THC that can be formed. And what we haven't talked about is what happens to all of those unknown compounds that are there when that chemical transformation occurs. So now you've got that compounding the whole system as well. It gets really

	complex really quick. Most of them are found at very low levels. Most of those compounds are probably not going to be hazardous. Probably not a concern, but the reality is, we don't really know about most of what those are, and what could happen to them and what their safety levels would be. We really don't know. There's a lot we don't know. I think it's really important that we emphasize that, there's really a lot we don't know.
Brad Douglass	I would just further underline what David said that they're different unknowns. The unknowns that are found in processed cannabis material are one set, those potential unknowns in those and THC generated from hemp or from product of synthesis are another set of unknowns. We just don't know enough to know which are potentially more hazardous or not. I think that's the question.
David Gang	And I think the comments that he made earlier about potency are really important to consider here. Right? We, if we don't know how potent these compounds are, it's hard to make that judgment. It may be that they have very low potency and therefore, because they're found at low levels, the threshold for any kind of hazard or toxicity is such that it won't be a concern. But it's also possible, I don't know that it will be the case, but it's possible that any one of those compounds or derivative compounds could have a higher potency. In which case it could become a concern. But we don't know that right now.
Nephi Stella	Yeah. That's correct. If, if there's low traces, low amount of a compound that is very highly potent, then it actually might produce a bioactivity that we don't know yet. In an ideal world, both would result into exactly the same molecule. The independent of the procedure if we were able to analyze the product and the final product or one hundred percent equal, then there's no concern. But because maybe of the differences in either synthesis or extraction procedures, there might be some byproducts even at low levels that might differ between the two routes of synthesis or extraction then it's true that there might be different unknowns. Coming from one versus the other. Every, one way to think about it in pharmacology is every compound is safe and every compound is toxic. The same compound at very low doses very rarely is going to be safe.

	But that compound at very high dose very commonly is going to be toxic. And what we need to understand is, what is the window where somebody can actually use this compound safely. And have a biological effect, if there's a biological effect.
Jessica Tonani	One of the things as well as the panelists, as Nephi pointed out, we've been talking about what's hypothetically produced. I don't think any of us have actually seen what's really produced, and at some point looking at analysis of different extracts may be a valuable component to figure out what's there, there may not be cis components. There may be cis components. We're talking about what we believe could be a risk in the product, but we don't actually know what are in the products that are being produced.
Nephi Stella	That's right, that's right. Jessica. That was the chromatogram that David was referring to. As you analyze your compound, you inject it into your HPLCMS, for example, if your peak that comes out this is the compound that you know and you're looking for. And if your product is not 100% pure, there might be other peaks that are coming out. And now it depends on again, as Brad was saying, resources, do we have the resources to go and find out what this compound is isolated and study its safety profile or bioactivity profile. It depends.
Brad Douglass	Yeah another thing to think about is, is that how uniform and consistent is the conversion process. Right? So one company may come up with a process that's extremely reproducible in their hands. They always do it the same. They always get the same products. You put that into somebody else's hands, it may be slightly different. Or another company may come up with another process that's similar, but not the same. And you could end up with different compounds, different by products. It could happen. The other thing is the source material, so different hemp varieties have very different chemical profiles, and I know from personal experience. And so, depending on what you're looking at what you have as have as a starting material, you could end up with different unknowns that end up being generated. You just don't know. Right? So, none of this stuff is 100% consistent at this point. It's hard to know what we're going to be seeing, doesn't mean that, yeah, I'll leave it there for now

Jessica Tonani	One of the things the FDA does, and I realize that we are not a FDA regulated system, but one of the things they do with biosimilars is essentially if you want a biosimilar, which is about therapeutic and generic to be released, you have to prove that it's similar. And it's been a fairly good method for them is the manufacturer is required to prove that their material is similar with any certain profile.
David Gang	Right, and botanical drugs fit under that category, for example. They're very difficult to get approved because it's very difficult to demonstrate that you're going to end up with the same exact biosimilar product at the end of the day when you have different starting materials. So you have to be able to demonstrate that your source is very, very consistent. There are very few botanical drugs on the market right now. I don't actually know of any. But there may be some that exist, but they're difficult. There's not very many. They're very difficult to get approved.
Jessica Tonani	Yeah, I think Epidiolex the is the only one I know
David Gang	Yeah, oh, yeah, that's right.
Blade Boden	No, so in summation I guess it would it be safe to say that there are unknowns whether it's hemp derived THC or I guess you can say a traditional THC extract, it just ultimately comes down to what those unknowns are and what their potential potencies or effects may be.
Nephi Stella	Yes, I think that's a good summary. And the unknowns can vary, depending on the procedure to extract or to synthesize.
David Gang	And that was a very good question, Blade, by the way. It was.

Participant Question 4: **1. A lot of people get confused or do not understand the difference between "Hemp Sourced" THC and "Synthetic" THC. "Synthetic THC" is the historical term that was originally meant to describe designer drugs that mimic cannabinoids but that are not THC. This includes K2 and spice and other designer drugs. To avoid confusion can the term "Hemp Sourced" be used when referencing the conversion of hemp or CBD to THC instead of "synthetic THC"?** **2. Analytical laboratories always have a standard deviation in their measurements. From numerous conversations I have had it seems that a typical cannabis laboratory will have a potency standard deviation of plus or minus 5%. Therefore, if a pure oil that was truly 100% cannabinoids was analyzed then it would be reasonable to expect results that range from 95-105% total cannabinoids. If a hemp sourced THC was analyzed and the total cannabinoid concentration was also between 95-105% THC then would this be considered an acceptable value to bring to market? If not, then what would be an acceptable value?** **3. The analysis of cannabis oil derived THC from Marijuana plants typically does not add up to >95% quantifiable material. Is there a goal to identify and quantitate these other unknown components?**	
David Gang	Well, one thing real quick, I think we, we use the term artificial. I know synthetic is used a lot of, I think. I think we like the term artificial, instead of synthetic, because of the, as you described before, it's just clearer what it means, and I agree with Brad's comment about calling it, what did you call it again Brad? Produced via synthesis, chemical synthesis means.
Brad Douglass	Correct, it's less loaded with baggage I'd say, yeah. Now, just reiterate the other point, we did answer this question already, but it just bears repeating that hemp source was ambiguous as David mentioned, hemp source can be natural THC extracted from hemp or THC and potential stereo isomers produced by the conversion of CBD. So, we aim for from a scientific standpoint, precise chemical terminology, speak to trans, minus Delta 9 THC or other very specific chemical names.

David Gang	Yeah, the other is, I think it's Jessica mentioned the other hemp source sounds more like a marketing terminology.
Nephi Stella	Maybe to add the word designer drug is interesting, because that really makes us think about artificial synthetic drugs, things that have been designed in the lab and do not actually occur in nature. That's another word to actually probably define.
Jessica Tonani	And the reality is that if the samples were getting pure enough, the molecule is what the molecule is. We're just talking about this because they're complex mixtures I guess in my mind.
Kathy Hoffman	I think in some of the discussions around this topic at LCB, we've seen all these terms used. And several more to describe, I think the same thing, but this is one of the challenges that we have moving forward with respect to creating a regulatory structure, and that is making sure we're using terms that are scientifically accurate and get away from the kind of multiplicity I'm seeing in terminology and inaccurate terminology, I think that's what I'm kind of hearing the panels say. Anything else on question one before we move on? Okay second question. Analytical laboratories always have a standard deviation in their measurements. From numerous conversations I have had it seems that a typical cannabis laboratory will have a potency standard deviation of plus or minus 5%. Therefore, if a pure oil that was truly 100% cannabinoids was analyzed then it would be reasonable to expect results that range from 95-105% total cannabinoids. If a hemp sourced THC was analyzed and the total cannabinoid concentration was also between 95-105% THC, then would this be considered an acceptable value to bring to market? If not, then what would be an acceptable value?
Nephi Stella	Well, maybe I'll add one comment. In with the view of a pharmacologist, when we look at a dose response. Increasing concentration of a drug, it usually from no biological activity, to full biological activity, if it's a simple response, it goes over two orders of magnitude. So if you have one milligram, it doesn't do anything, ten milligrams you're about halfway, and a one hundred milligram, you're at one hundred percent of your response. So, two orders of magnitude. So pharmacologists also have the standard error five

	percent because five percent the difference between ten milligrams versus eleven milligrams, it is not going to do much difference in terms of bioactivities. So, in terms of a pharmacologist, this standard error is somewhat acceptable.
Brad Douglass	Yeah, two parts of this question, one it's true that all analytical measurements, all methods have standard deviation. Sometimes the plus minus standard deviation is acceptable and I can come from many different areas. People weighing out sample to the instrumentation and the method. But I will say that if you have a C of A and it has over 100% anything that you should question where you're getting that C of A from. So that's my first comment, my second comment is, it's a question of purity and impurities. So, if you have a one hundred percent and again, being chemically precise, minus trans Delta 9 THC, and that's equivalent to the naturally occurring THC, then great. But if there's one percent, five percent of something else, it's important to know what that is. And if that's something else to the stereo isomer, or whatever, you want to know, whether that's going to have an impact on the safety of hazard or the material. So it goes a bit deeper than just quantifying the purity of your total THC analogues.
Nephi Stella	I agree that I was commenting on the standard error of the actual active ingredient itself, but if it, the standard error includes five percent of other ingredients, I agree with you. We really need to find out what they are.
Brad Douglass	Absolutely, Nephi. I agree.
Kathy Hoffman	All right, and I'm not going to read the third question. Anybody want to tackle that? I kind of want to get to the audience questions, attendee questions.
Brad Douglass	I'll just say quickly with David, and I already said there's a lot that we don't know from the food we eat on a daily basis to perhaps the cannabis products we consume. Ninety-five percent known is pretty good when

	it comes to the universe of things we don't know and we put in our bodies. So, is it important that we know what else is in there? Probably, but I think how important is the question.
Participant Question 5: **What if customers care about the sustainability and what waste are generated by the various chemicals used in the process.**	
Crystal Oliver	Okay, yeah, and I was just speaking to the fact that we talked about it being immaterial if the residuals are removed from the product. But I do think there is a component of the sustainability of the chemicals that are utilized in these conversion processes and kind of wondered what your thoughts are on I guess the sustainability and the chemical waste that's generated in creating these synthetic cannabinoids.
Brad Douglass	I can answer that. I think that's a great question, Crystal, and I didn't mean to minimize the other impacts that some of these processes can have. And I think there's a consideration if you're a consumer, you want to know all the things that impact what you put in your body. The decisions you make, so, from a science perspective, you're making judgments on what impact perhaps a particular product can have on your environment or your society. I think that's valuable information for consumer to know.
David Gang	I think that's something that many people in our society are very concerned with. So, I think this is something, it doesn't, I think, go directly to the questions of policy that we were, sorry, the scientific, questions we were talking about today with regards to the specific definitions of what a cannabinoid is et cetera, but I think you're right that a lot of people care about these things and somebody that's working in this industry should definitely think about this seriously. I think it has an important role to play.
Participant Question 6: I have a safety question with the research from the Chernobyl disaster and the cannabis plant being able to uptake heavy metals. Also, knowing about the green run iodine 131 release from Hanford to 1949 with secret, ongoing, heavy metal releases happening until the 1960s. Could any of these processes that are being talked about today also bring in these toxic heavy metals into the products? Also since we don't test for any of this stuff could we be poisoning our consumers?	

Jeff Merryman	Perfect, so hopefully there's some research there and my question from FOIA requests that are out there on the Interwebs. But I know a lot of those heavy metals were found all the way up to Wenatchee by the US government. And with what we know from the Chernobyl project of the cannabis plant being the only plant known to man right now that can pick up some of the heaviest metals known to man. When we start stripping these things out, are we bringing along stuff that we should not be bringing with, and because we're concentrating could this be something that 20 years down the line we find out we're killing people because we have a product that we've designed or created, or made using a process and concentrated something that should never been concentrated?
Jessica Tonani	I can try attempt to answer some of that and I'm definitely not a heavy metal expert, so I defer to David or Brad for this one as well. But I think that that's one of the reasons that people have strongly advocated for both pesticide and heavy metal testing in the i502 supply chain. It's currently an opt in honor system and the reality is, is that there probably are a lot of products out there in the current regulated system that have heavy metal or pesticide contamination within them. And so I would advocate that products do get tested. And I do know that there are a couple of brands out there that routinely test their products. But a lot of people just don't. And the reality is, is there's that cost equation for people testing and since not everybody is required to test, it makes it easy for everyone not to test and run a sustainable business. I'll turn it over to Brad and David if there's anything else on that.
Brad Douglass	Yeah, that's an interesting question, Jeff, you know, because even hemp or cannabis that is tested for heavy metals isn't tested for something like iodine, or some of these heavy isotopes. You could run into a situation since hemp or cannabis is a heavy metal remediater, they do find if these isotopes are present in the soil, or the media that they're being grown in, you do find them in the, the natural products of those plants. Whereas you may not find them in something that's produced from, say, a purified starting material stream like CBD. So, it's kind of an interesting point. But I don't know how prevalent that contamination is, but we may be blind to its presence in some of our manufactured cannabis and hemp products.
David Gang	Now, I don't know that I have much more to add. And that I, I think those are all good comments. I think it's definitely something that is of concern and needs to be evaluated and looked out the questions how to do that that Jessica mentioned.

Jeff Merrimen	All right. Thank you. Very much. I just brought it up since we have Hanford in our backyard and a lot of our products are grown in fallout areas from Hanford.
Participant Question 7: **Just wanted to confirm my understanding that cannabis plants produce molecules of one chirality and so synthesize molecules of a different chirality would technically be artificial cannabinoids.**	
David Gang	I think that's safe to say. I've looked into this, there's some old literature that suggests that maybe like, that the other versions exist, this was all published back in the nineteen seventies. And I went and read some of those papers and the data's really not there to support the conclusions. So, the data that we have right now that I think we can rely on suggests that yes, it's the minus trans Delta 9 THC that exists. The others are really not present. Now if the material was collected and processed in a way that could lead to conversion into those other compounds, and that could definitely could be there in a product derived from it, but I think it's probably safe to say that the acid forms of these compounds, with that stereochemistry, there's no evidence that the other forms are there, not that I was able to find yet anyway. Unless somebody else here on the panel found a paper haven't found.
Nephi Stella	Maybe just to, also from my own knowledge, if I remember well, there's only one enantiomer, one stereoisomer that has been that is produced by the plant because it's an enzymatic pathway that produced this molecule and enzymes typically are stereo selective. That's why the plant does only this one enantiomer, whereas in the lab, when you do your synthetic, your chemical synthesis, you can actually have much more diversity in the enantiomers and it's not as stereo selective. Is that a good way to think about it?
David Gang	Yeah, I think so. I think that's a good way to describe it, in regards to other examples where you've got classes of compounds where one plant makes the left handed version, another plant right handed version, and a third plant makes both of those. I happened to work on a group of compounds when I was a grad student and that's exactly what we did. We looked at we were looking at this question in a totally different class of compounds, it's very fascinating stuff, but it was different enzymes. Each enzyme was pretty

	specific to what it did, some were very specific. And then you've also got some enzymes that are racemic, they just make a mixture of everything. Right? But we don't have any evidence that, in the case of the cannabinoids, that that's the case, cannabis sativa evolved, something happened and its evolution and developed this new synthase that leads to production of these compounds that exist only in this plant and it's pretty specific to what it does.
Gregory Foster	Thank you.
Participant Question 8: **I hope it's okay this question. It's the discussion of Canada, but cannabinoids in the potential inversion into the market, and the potential chemical conversion of the CBD coming in from hemp to THC that got me thinking about this a little bit and it's a question, but I think falls outside of the potential realm of i502 5052 regulation. However, it's pertinent to the industry and I think pertinent some of the issues of competition that have been raised and the question is this: if a CBD edible, the type that are available in in coffee shops now in the state, gas stations, convenience stores, not the regulated stores, the stuff that's kind of nonregulated. If one of those were to contain inadvertent THC, but still at a level less than point .3%, right, and, in my question was .2999% THC by weight, would that be considered still a hemp based product? And therefore, is it something that falls outside of the regulation of the LCB and I guess to an extent the DOH, aside from just the manufacturer of commercial food stuffs, that's my question is, is that outside of this regulatory scope, Am I right on that?**	
Jessica Tonani	I was going to say, Jim, honestly, I don't know, I'm not as familiar with the regulations around weight volume and hemp products, and the definition of that, I don't know if Brad, you have any additional information on that, but I'm not up to date on that regulations around that.
Jim McCrae	Thank you, Dr. Tonani. I just did to clarify, the reason I brought this up was because of the discussions that the normal concentrated juice, if you will, is in itself not a hundred percent pure. It's going to have a little, somebody said there's a little bit of CBN, there's little bit of CBG, all that sort of stuff. So it struck me as natural that if somebody were making a CBD infused edible having zero amounts of other minor cannabinoids in that product would be normal and expected, and then hence I wondered if that point three

	percent threshold that seems to define at least at the plant level the distinction, legal distinctions between cannabis and hemp applies to that hemp based product definition that was put into Washington law in 2018, so that I appreciate that Jessica. Thank you.
Brad Douglass	I can add a little bit of perhaps history there. The point three percent THC limit was meant to discriminate between THC containing cannabis, marijuana, and hemp. What it was meant to be just for the plant material itself, it was never, I believe, intended for manufactured cannabis products because, as you sort of identified here, Jim, you can have a situation where you have a hundred milligram brownie, sorry a hundred gram brownie. That has point three grams of that's three hundred milligrams of and by this definition of weight percent would be considered a hemp product right? Something (unintelligible) intended. And I can say that from a science standpoint that there's other regulatory groups that are grappling with this now, I think the best way you could define a manufactured hemp product is not only by weight percent, but by absolute concentration of the substance you want to limit. So, if it's THC not just by that weight percent, but say a certain number of milligrams, no matter how big the unit mass of that finished product is.
David Gang	The definition of hemp is that it's on a dry weight basis. Right? And so it's going to depend on, and that's a really good question of what the original source is. My understanding, I will have to go back and read the law again. I've read it many times, but I have to remind myself all the time about this because the language. You got to think about a different when you have a different question. I think the whole point of, you know, it's all based on the 2018 farm bill and our state put into its codes how we're going to deal with that and how we're going to manage within that framework. And our State Department of AG oversees that and I'm pretty sure, as Brad said, the intent there is that it's hemp derived products are really what fits within hemp. So, if you get something from the field that is hemp and it maintains those levels below .3% you can still call it hemp. If you start out, and I think this may be true, but we probably want to have somebody verify that, but if you start out with non-hemp cannabis, so high THC cannabis, you're already in the illicit market, according to the federal rules. And you can't get out of that. So if you're using THC derived from recreational cannabis and putting that in and then putting it at this level it's still considered, as far as the DEA is concerned, it still should be considered non hemp. It should be considered what they call marijuana. I'm pretty sure that's how it works. Not one hundred percent sure. I'm pretty sure that's how it works. But, yeah, does that make sense? I don't know. It's the way the regulations work, right?

Jim McCrae	It did. It did actually, David, thank you. And I appreciate your answer and your work by the way the way. Flipping it on the other side, if you don't mind, because it's, I'm getting to a point here that I think goes to how much of a competitive threat this potentially is to the industry because a lot of folks have been concerned about what it will do to the biomass producers and stuff like that but under my understanding to flip back into the 502 system now, my understanding is that under the current rules someone could bring in the hemp based flower, hemp based CBD oil, could do a chemical conversion arguably of the CBD to something that contains a significant amount of THC but a non-zero amount of CBD in the remaining goop. That goop then could be sprayed on the CBD hemp flower to enhance the CBD of it because there's non zero CBD. But in the meanwhile, they've converted it over to fifty-three percent THC. So, now you have a completely hemp based product, plus a little bit within 502 or some CBD hemp oil has been converted partially to THC that sprayed back on or infused back onto the flower. And suddenly you have something that hasn't touched a single grower or, or, there's no Washington regulated cannabis product in that thing that's now flying off the shelves that's an infused joint that's all basically hemp, but has a sufficient amount of THC in it because the CBD with which you are now juicing the flower happens to have been converted and I don't know what the conversion percentages are, the efficiency. But I've seen numbers as high as fifty-three percent. If you have a liter of CBD, you can make 530, .53 of that, of THC, I suspect it could be higher, but that's at least the, the biggest that I've seen in in writing. If you do that, that original intent of 2334, the legislation that's enabled this to come in, where you can only use it to juice the CBD or to increase the CBD, if a carrying agent now is within that now diluted CBD stuff, you're still juicing the CBD, you're, you're increasing the CBD. You just happened to be putting a lot of THC in as well, so, just, you know, thinking about that, basically everything in the market is potentially at risk. If you were trying to grow it as a regulated cannabis producer right now, just a thought.
David Gang	Yeah, that that raises an interesting question, because if you think about hemp, the definition of hemp at the federal level, and what's pretty much mimicked in our state law, is that as long as you stayed below .3% THC you can call it hemp. As soon as you get above it, it's no longer hemp, it then becomes the federally elicit substance right? Controlled substance. And so now it's not a hemp product any more at all, and somebody who is handling it is now working within the legal framework of the state separate from the federal framework, and this is something that we deal with the at the University, because we're not allowed to deal with anything that's non hemp because of issues with regards to the whole illicit substance

	act and stuff like that. But anyway, yeah, this is a really interesting question because, I have to think about this.
Jessica Tonani	I think one of the things that I believe the law states is that synthesis of Delta 9 is illegal outside of the 502 system, and so I think that the only caveat in that scenario, Jim, is that if you are intentionally synthesizing Delta 9 outside of the 502 system it is not legal, is my understanding, but don't know that for a fact.
David Gang	That was my understanding too, but again I'm not one hundred percent sure. But somebody that's within the 502 system and has a license to work with it, could they then proceed and generate products because they have a license to be a high THC producer? I think they would have to do, would have to be somebody that's got a license to do that within that framework.
Jim McCrae	Possibly, I was not in that in the instance of the coffee shop brownie, the non-regulated one. I was not really thinking about people synthesizing THC, Jessica. I was thinking about 200,000 hectares of hemp at .3% spewing out a lot of THC in and of itself that's available.
David Gang	Yeah, but as soon as you, as soon as you separate the THC and concentrate it so it's no longer point three percent of whatever you're handling, it's no longer hemp. Once it goes above that level. So if you keep it at your .2999%, the problem is you're not going to get a brownie like that because in order to get the brownie at that level, you're going to have to have an extract, somewhat higher than that to put into the brownie, right?
Jim McCrae	Well, you could call it an extract if you want. I could call it a homogenization, interim. I think someone could put together a process flow. You can't escape the fact that you have to bring it up above .3%, I agree with you that logically, but I think you could do something. Let's put it this way, you're pushing into a gray area that if the state allows this to happen within the regulated market, you're kind of almost setting a standard by which who's to stop me going down and buying a 12 ounce can of soda that has 106 standard doses of 10 milligram THC in it, which is by the way about what the amount would be if you are at .3% on

	a 12 ounce can of soda. And it, you know, it, it's obviously, it doesn't feel right, but it doesn't feel right. Frankly, as a consumer that I've got this market out here, there's a bunch of people that have been looked at very closely for years and their quality assurance cameras, everything. And suddenly, I can't go to the, I can't go to a store and buy something and not know it wasn't grown over the Chernobyl site or my preference is to say a landfill in outside lower Pakistan, and subsequently concentrated, brought into Washington, and done with whatever. So, just from a consumer perspective, I know if it's done right, even in that situation and that bad image, it can be done safely. Who's to say it's being done right? Thank you.
Brad Douglass	Honestly, Jim, I think there are two different issues here. One, you recognize is the definition and the farm bill of what hemp derived means, and whether you can have in process hemp materials that are above .3% THC and can those make it into hemp based products that are sold in coffee shops or convenience stores and that potentially have large quantities of THC in them. I think that's one question. I think that will be resolved at some point by FDA, they're likely to be the regulatory agency on the federal level that resolves that. And you have some state based regulators, like New York state, that have started to advocate for definitions of in-process hemp material that can have higher quantities of THC. But I think the other question here is what we can address in the state regulated markets, and I one hundred percent agree that these illicit markets represent a threat to the tested regulated marketplaces. But I think that our questions with respect to this discussion of where THC comes from are different in terms of the quantities you can find in the products and the regulated market, and those that you can find outside of it. And I think there there's different precedence there.
Jim McCrae	Thank you.