



FOCUS
Foundation Of
Cannabis Unified Standards



Cannabis Synthetics 101: An Introductory Webinar for Regulators

AFDO and FOCUS appreciate your interest in the Cannabis Synthetics 101 Introductory Webinar for Regulators. With over 800 individual registrations, and close to 400 attendees, it is clear that the proliferation of synthetic cannabinoids is a shared concern across the nation. We are thrilled we were able to provide such a valuable resource so broadly. Our intent is to develop and share valuable information related to cannabis with regulators and legislators that lead to improved protections for health and safety in the cannabis industry.

With so much material to cover on this ever-evolving topic, time did not allow for a formal Q&A during the live webinar. Instead, attendees were asked to submit questions through the chat that would be answered in a public forum to encourage greater understanding for everyone interested. Answers presented here were developed by the two knowledgeable presenters, Lezli Engelking, Founder of FOCUS and Chris Hudalla, PhD. President/Chief Scientific Officer, ProVerde Labs. They also addressed a few questions that were submitted by email. The resource will be sent to all attendees, along with the slides and recording. It will also be posted on the AFDO website under [Cannabis Resources](#).

Please send any additional questions, suggestions on future webinar topics, or alternate ways we can provide value to the cannabis regulatory community to AFDO@AFDO.org. Given the size and speed of this issue, it will be important for everyone to stay updated on new developments. Thank you for all that you do.

Webinar Q&A

What products or matrices are of most concern for uneven distribution of cannabinoids within products? For example, BFG (or extremely large gummies), large total package cannabinoid with 1,000+ mg with monolithic structure to the product and a high number of servings such as a 3,000 mg chocolate bar.

For most matrices, for which the cannabinoids are infused into the batch of batter or liquid, we do not see a huge problem with homogeneity. However, what we do see, which is a huge homogeneity problem, is the less sophisticated producer may “spray” a cannabinoid (in ethanol) solution on their gummies or other matrix. This type of application never works out well, results in large variance in homogeneity, and oftentimes, the cannabinoid mixture gets transferred to the inside of the packaging material — another reason it is so incredibly important for regulators to understand the processes being used by each company. State cannabis regulations overlooked this aspect, which allows unsafe ingredients and other practices that lead to the testing fraud and laboratory shopping we see today.

I reviewed a label this morning that said "Delta-9P THC." I assume they meant THCP, but who knows!

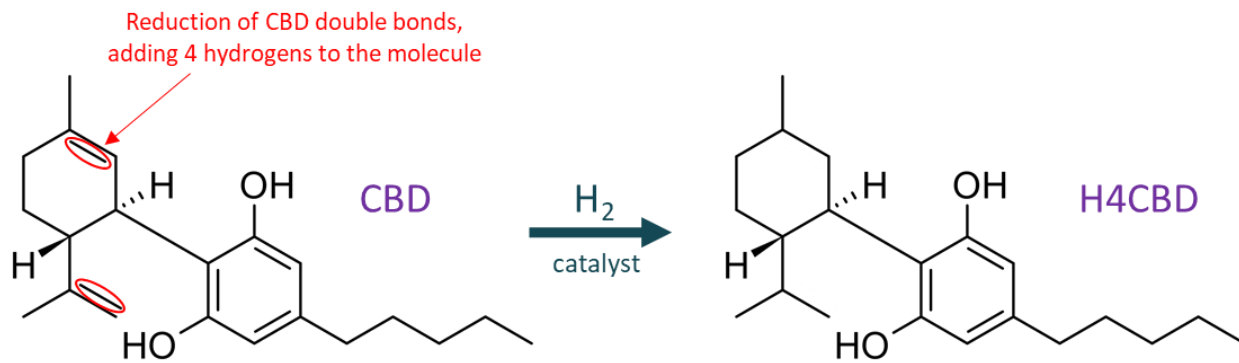
Big problem, and they probably did mean THCP. *Most of these producers are not chemists.* They mix up names, make up acronyms, mislabel packaging. It is a growing trend to just slap every imaginable acronym on the label, regardless of what is in the product.

The truth is, the producers know there are multiple “things” in their samples, they just don’t know what those “things” are. They put as many labels on the package that they can think of, sometimes even making them up as they go.

Nomenclature is a challenge across the board in both state legal cannabis as well as hemp. It is one of the charges AFDO’s Cannabis Committee is attempting to address this year. If you are interested in getting involved, or have suggestions on helpful references to consider, please email Tressa McGill at tmcgill@afdo.org.

H4CBD, haven’t seen that one before

Similar to the conversion of Δ 9-THC to Hexahydrocannabinol (HHC), created by removing the THC double bond, CBD is transformed into H4CBD by the removal of two double bonds. This compound has not been studied for efficacy, but is reported to have a slight amount of psychoactivity.



Do all of the synthetics of concern get you high?

It is a complicated question, and even harder to document. There has been one study on Δ 6a10a-THC, which exists as two different stereo isomers. One of the isomers is intoxicating, the other is not.

Most of these compounds have not been tested on rats yet, much less human subjects, other than the widespread distribution of consumer products which contain these. So, all information on intoxication is based on anecdotal, social media reporting, which tends to be inaccurate, due to being based upon incorrect product labeling.

However, intoxication is only one of the concerns with synthetic cannabis products. Even a product with low levels of THC could be extremely dangerous from a safety standpoint because of the additional unknown degradant by-products. Without understanding the process and chemicals used to create these synthetic products, we do not know which chemical byproducts should be tested for.

Manufacturers should be required to demonstrate full traceability back the USDA licensed farm as well as the specific harvest batch numbers that were used in their products. They should also be able to

demonstrate documented procedures and the overall process that material, and all other ingredients take before they reach the customer. However, we are unaware of any company in any part of the cannabis or hemp supply chain following these basic Good Manufacturing Processes (GMP).

Our regulators are really not well educated and they get their education from industry who has a motivation to be deceitful. It's incredibly frustrating.

Agreed. A national economist recently estimated the U.S. hemp-derived cannabinoid market to have estimated revenues of \$28 billion (see below). This has rapidly become a major industry with a nationally integrated supply chain. The hemp-derived cannabinoid market is currently larger than the entire legal U.S. adult-use and medical markets combined.

These companies also have incredible lobbying power. One of the larger synthetics producers spent \$5.5 million over the last two years on a NASCAR sponsorship. Just imagine how much they spend to lobby to keep their products flowing to consumers.

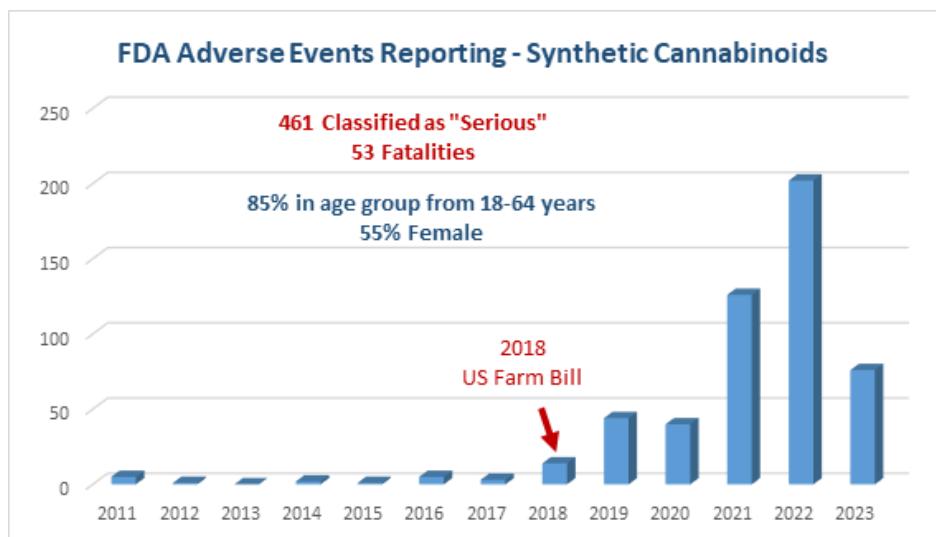
[Whitney Wire October 2023](https://mailchi.mp/78ea28987242/whitney-wire-vol-3-hemp-cannabis-data-statistics-insights?e=92535e8b5c)

<https://mailchi.mp/78ea28987242/whitney-wire-vol-3-hemp-cannabis-data-statistics-insights?e=92535e8b5c>

How many deaths do you see?

A 2023 paper reviewed data from the FDA's Adverse Events Reporting System (FAERS) which highlighted that as of June 30, 2021, there were 183 adverse reports noted to FDA via FAERS (the reporting system for non-approved products), especially for dyspnea, other respiratory disorders, and seizures: 33 cases were fatal, 109 serious, 41 non-serious, with 49 hospitalizations. The reports for delta-8 incidents was almost 3x those for delta-9 incidents. More respiratory issues were noted for delta-8 products than for any other cannabis or hemp product. This information is more than two years old.

For an industry that has grown from \$2 billion in 2021 to an estimate of over \$28 billion in 2023, a current review of the FAERS database indicates a concerning, but not unexpected trend in adverse events, including fatalities associated with synthetic cannabinoids:



[Review Paper: https://pubmed.ncbi.nlm.nih.gov/36742440/](https://pubmed.ncbi.nlm.nih.gov/36742440/)

What are the causes of death?

There is little information available which assigns a cause to the serious adverse event or fatality. The products that are being consumed can have so many contaminants, unnatural chemicals, residual toxic solvents, and acids, it is most likely difficult to assign an exact cause to each event. Unfortunately, these events are being tied to Delta-8-THC, which itself is most likely not the cause.

Below are links to some publications by the CDC and National Poison Control Center related to cannabis synthetics and toxicity. Note the data in last link from Poison Control was just published in September 2023, so it is very recent. We've also included two graphical illustrations of the September 2023 Poison Control data below the links.

[CDC Notes from the Field: Death Following Ingestion of an Edible Marijuana Product — Colorado, March 2014](#)

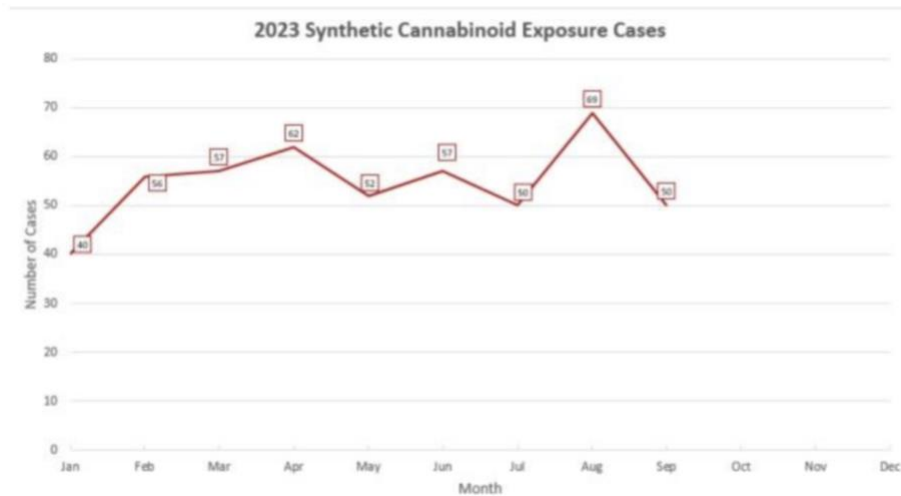
[CDC Acute Poisonings from Synthetic Cannabinoids — 50 U.S. Toxicology Investigators Consortium Registry Sites, 2010–2015](#)

[CDC: Notes from the Field: Acute Poisonings from a Synthetic Cannabinoid Sold as Cannabidiol — Utah, 2017–2018](#)

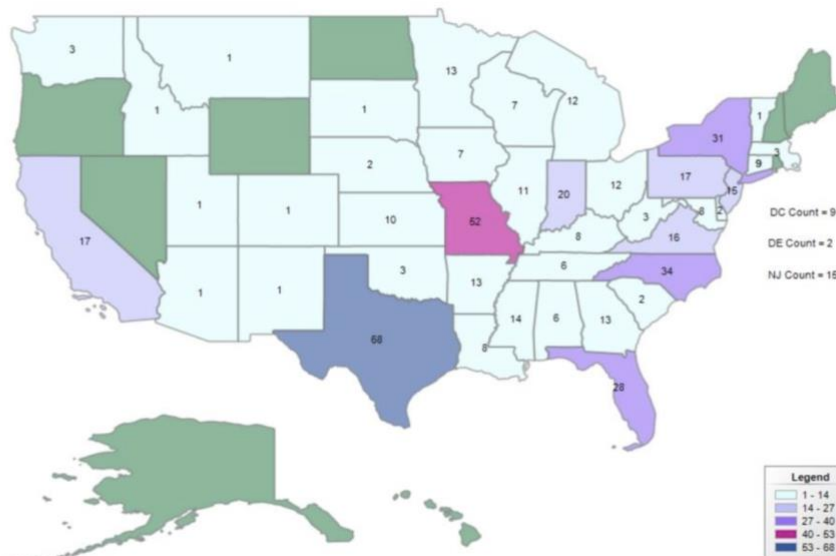
[CDC: Outbreak Association with Synthetic Cannabinoids Spreads to 9 states May 2018](#)

[CDC Health Action Alert: Increases in Availability of Cannabis Products Containing Delta-8 THC and Reported Cases of Adverse Events September 2021](#)

[National Poison Control Center Data on Synthetic Cannabinoids – September 2023](#)



Synthetic Cannabinoid Calls to U.S. Poison Centers (1/1/2023 - 9/30/2023)



PLEASE NOTE:
• These data are only representative of cases received by the poison centers and may not reflect the actual severity of the problem in the U.S. or any specific geographic location.
• As there is no mandatory reporting, there may be emergency room presentations and hospital admissions of which poison centers are unaware.
• Subject to the above bullets, these numbers are largely reflective of those users/abusers who have experienced adverse effects from the use of these products significant enough to warrant poison center or other health professional intervention, not all individuals who use/abuse such products contact poison centers or visit emergency rooms.
• Nevertheless, the data are a good surrogate marker for rising use/abuse patterns and patterns of adverse medical outcomes associated with their use.
• For more information about the National Poison Data System data, please visit <https://poisoncenters.org/national-poison-data-system>

Recognizing Products of Concern, is there a reason why DELTA 10 was not listed? I thought Delta 10 is a product of concern along with the other items you listed.

Synthetic cannabinoids will continue to be developed and expanded upon. A list today, does not effectively cover activities of tomorrow. Federal oversight and pharmaceutical standards (21 CFR 210, 211, 820, etc.) are required to assure safety and accurate labeling of these products.

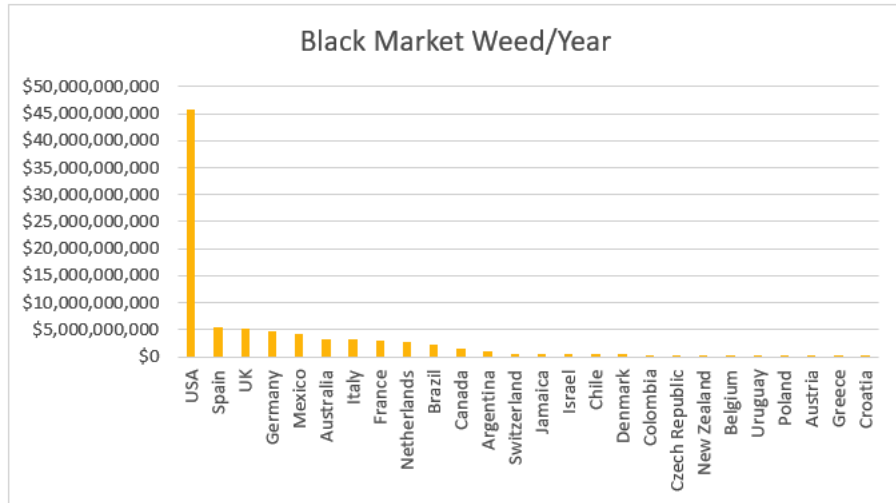
States might consider adding the CFR requirements above for hemp manufacturers in the wait for federal oversight. While the industry might push back, this prevents having to create an extensive licensing process like state cannabis programs use, which more often than not, wind up in multiple lawsuits. Current manufacturers would have a specific amount of time to either become compliant or pay to conduct a safety study with an analytical testing laboratory to validate the safety of the retail products and what testing is appropriate.

There are too many synthetics to name, but yes, Delta-10, Delta-7, Delta-6a7-THC would all be concerning. These chemical compounds *probably* will not kill you. But they have not been studied yet for toxicity or long-term safety and have not ever been widely consumed until the recent boom in U.S. products.

Do states that have recreational and medical use tend to have less hemp-derived synthetics?

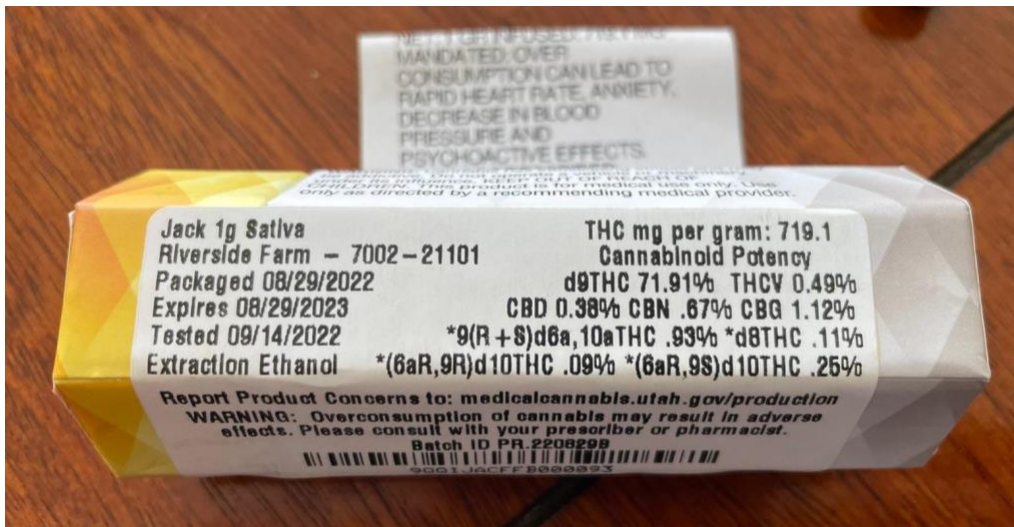
That seems to be a trend we see. There are legitimate medicinal applications for delta-8-THC, because it has some of the same therapeutic benefits as delta-9-THC, but with less psychoactivity. So people who could benefit from the use of medical marijuana, but who live in a state where it is not available, can rely heavily on these synthetic compounds. The problem is, it is a bit like Russian roulette on what product quality you might get.

According to a recent report by BDS Analytics, a cannabis data company, the illicit cannabis market in the United States is significantly higher than any other country.



source: BDSA, 2023

Initially, hemp-derived synthetic products began showing up in the South and other markets without state legal cannabis programs. However, marijuana operators have now discovered that they can add these synthetics into products as ingredients and significantly reduce their costs. Today, we see them showing up in all states, both in and out of state cannabis programs. The example below is a legal product sold through Utah’s Medical Cannabis Program. Imagine trying to discern what that means.



Is there any hope that the FDA may make a ruling concerning hemp derivatives for labeling ingredients and dosage of hemp derivatives?

There is always hope. But I do not think the FDA will address this any time soon. In the meantime, for consumers, it is “buyer beware!”

There is some talk that with the next revision of the US Farm Bill, expected sometime early next year, that there will be some verbiage to address the synthetic conversion of phyto cannabinoids into other compounds. Ironically, most experts agree that a legislative solution could be much quicker than the federal regulatory evolution that is our present quagmire. Those charged with protecting the health and safety of US citizens do not have the tools necessary to combat this onslaught.

One major area of concern is hemp-derived infused food products that FDA says don't meet the federal Food, Drug and Cosmetic Act.

Absolutely agree! Except for the GRAS-qualified hempseed oil and hulled hemp nuts, none of the hemp-derived products, including all products from the natural CBD, meet federal FDA&C regulations for use in food.

Not only are these products concerning due to the safety of the cannabinoid ingredients being used but most companies making food products with synthetic cannabinoids do not follow basic food safety standards.

FDA is needed in the regulation of these synthetic cannabinoid products. They are no different than pharmaceuticals. There is a world of difference between what is taking place where these products are currently being made and the inside of a pharmaceutical manufacturer. State agencies and testing labs simply do not possess the sophistication to effectively ensure the safety of these products or the folks making them.

Is this similar to the supplement industry in that it is only loosely regulated if at all?

It is similar in many respects. There are greater concerns with the synthetics market as many of these products are being created by “garage chemists” with little to no training in synthetic organic chemistry. Most of the contaminants in these products DO NOT EXIST IN NATURE and have never been seen or studied before. They don’t even have a name yet. These producers have NO IDEA what they are providing to consumers for ingestion and/or inhalation.

This is an interesting question, especially when state cannabis programs are also considered. State programs are based around plant material. The extractions taking place don’t involve chemical conversions like these products. Which is one of the reasons state legal cannabis products raise different safety concerns than these synthetic cousins.

There are states like Utah and Missouri that have allowed synthetic products into their medical cannabis programs. Reading these labels requires an advanced degree and so once this occurs, the labels do little to help consumers actually understand what they are purchasing.

Are there concerns about the restaurant industry trying to incorporate these derivatives into their food?

Yes, there are definitely food establishments adding D8 and other synthetic cannabinoids to food products. The company below, [Wake-n-Bakery](https://wakenbakery.net/), adds D8 and other synthetic cannabinoids to people’s coffee on their commute to work. In 2022 they were only in Illinois, but it appears from the website image below, they have expanded to multiple states. There are also restaurants starting to dabble in “cannabis dinners” which are special events with prepared food that includes cannabis, including delta-9-THC.

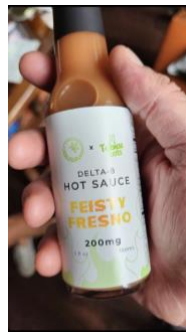
<https://wakenbakery.net/>

CHICAGO'S ORIGINAL FEDERALLY LEGAL CANNABIS INFUSED BAKERY & COFFEE SHOP



TikTok Famous Cannabis Cafe & Bakery Lakeview, Wicker Park, Homewood, Downtown Chicago, Oak Park, Tempe, AZ, Raleigh, NC,

There are also retail food products containing synthetic cannabinoids.



What is the common acetate used in the process?

Most often, producers used acetic anhydride for the acetylation of these cannabinoids. Acetyl chloride is another option, but less commonly used.

Do you think heavy metal residue from pesticides are carried over through extensive processing?

If these products are made from highly purified CBD isolate, the CBD is so heavily processed, that most contaminants do not make it through to final CBD isolate products. So we would not expect to see any heavy metal or pesticide residues left over from the raw biomass. However, some of these synthetic processes use heavy metal catalysts, so heavy metals are being reintroduced during the process.

However, CBD distillate, as opposed to CBD isolate, is not nearly as pure: it's usually about 80% purity. Which begs the question, what is the other 20% made of and what happens to that material through the chemical conversion process?

Neither the processes used to make these products, nor the products themselves, are understood or standardized, meaning that even well-intentioned regulations are unlikely to have much of an effect on the actual production without a basic understanding of how the products are being made and some sort of enforcement around process.

We do see evidence of heavy metals remaining in these products, so it is definitely a concern. Just as big of a concern, though, is the fact that NOBODY is checking these products for these contaminants.

What exactly can we do as Regulators whenever we find these products at the stores?

It is important to understand which products are being sold in your jurisdiction. Start putting together a list of what products are found and in what stores to understand the magnitude of the problem.

After that, it depends on your state. Does your state have a drug code that exists separately from the Federal Code? In many states, regulators and/or law enforcement have tried to intervene in these commercial activities, pulling product off the market. This has resulted in multiple lawsuits against the states from the retail operators and/or producers. As this plays out in the courts, we see the producers winning most cases. This is because these cases focus on the legality of synthetic cannabinoids, as hemp derivatives carved out by the U.S. Farm Bill. From a technical perspective, the chemistry/analysis of these synthetics is very complicated, and it is hard to explain to the courts. A simple violation of label claims may be a better approach to consider as an avenue to get these products off the market. An estimated 5% of these products would meet label claims.

Understanding the source material and supply chain for these products is crucial to protecting public health and safety. The only federally legal cannabinoid products in the US are those derived from hemp crops harvested from American farms that are participating in state sanctioned or USDA approved hemp programs. This means that the supply chain back to the actual production farm should be visible and auditable for all legitimate producers. Therefore, regulators can ask for supply chain verification from the retailer, distributor, manufacturer, etc. just as they would expect to see in food/supplement/pharma supply chains to determine legality.

Some states, like Alaska, have taken the approach to include these synthetic psychotropic substances in their existing programs, but as previously discussed, this creates challenges around legality as well as ensuring safety.

Another avenue to explore is the citation of the federal Controlled Substances Act (CSA) in the state constitution. Synthetic derivatives and analogs are expressly prohibited, so if a state has incorporated the CSA this into state code, there may be a legal avenue to get rid of the products that way.

Does the packaging tell you if the product has been acylated?

Typically, yes. Producers want you to know it is acetylated because it tends to magnify the intoxicating effects by about 3x, relative to an unacetylated product. You will typically see an 'O' appended to the base cannabinoid acronym: THCO, HHCO, CBNO. THCPO. Sometimes you may also see it spelled out: THC-O Acetate, or THC Acetate



Do they use any synonyms for THC products on the label.

Typically, no. These products are being marketed to folks outside of state legal cannabis programs so including THC is the greatest selling point, followed by lower cost/taxes.

How could CBD be made into heroin? That's actually possible?

A good synthetic organic chemist could most likely find a synthetic pathway. It would certainly NOT be economically feasible. The concept is included to show that, simply because it is a derivative product, does not automatically make it legal. It would be like saying, methamphetamine should be legal because it is a derivative of legal cold medicine...

I can't tell you how priceless this information is for regulators here in New Mexico. We're just now uncovering these chemicals and it's almost overwhelming at times. It would be so great to be able to do more of these whether in-person or through Zoom.

We often speak to state regulators and health professionals who are totally caught off guard as to the permeation of this synthetic industry that grew so rapidly, almost overnight. These products are everywhere, available to everyone, even children. They can be purchased on Amazon, even though we have reported them to Amazon dozens of times over the last few years. Both Lezli and Chris are available to answer questions and consult on these topics. It is only through collaboration, education, and consumer awareness that we can begin to challenge the existence of these harmful products.

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