October 5th, 2022

To whom it may concern,

I am the Founder and Chief Scientific Officer of ProVerde Laboratories, established in 2013 as one of the first ISO 17025 accredited analytical laboratories specific to cannabis. For the last nine years, we have been focused on the required regulatory testing of marijuana products produced within our State's regulatory framework, but have also provided significant support to the hemp/CBD producers, with a global client base.

I am writing today to express my serious concern with the recent wide-scale commercialization and distribution of synthetic cannabinoids. Previously, the distribution of synthetic cannabinoids like spice and K2 were reserved for the black market. But under the guise of "US Farm Bill Compliance", we now see these synthetic products, often times transformed from hemp derived CBD, widely distributed to consumers in the regulatory and grey markets.

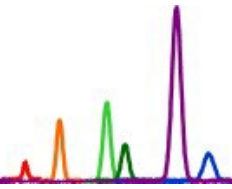
When referring to synthetic cannabinoids, the term "synthetic" refers to chemical compounds created through a chemical process by human agency, as opposed to those of natural origin. These compounds can be synthesized to imitate a natural product (e.g. Delta-9-THC), or they can be synthesized to create a compound not found naturally (e.g. Delta-9-THCPO).

These synthetic compounds are typically the result of intentional chemical processes, but can also result from the unintentional chemical processes active during normal manufacturing activities. Synthetic chemical processes, whether intentional or unintentional, are typically non-specific and it is common to have multiple parallel competing chemical reactions, resulting in a synthetic product that is comprised of multiple synthetic outcomes.

A good example of an unintentional synthetic outcome can be observed from the distillation of a cannabis extract, intended to concentrate and purify the Delta-9-THC component of cannabis. Normal distillation processes, when performed and optimized properly, are very effective at creating a highly concentrated Delta-9-THC product. We provide testing for dozens of these distillates each day, without issue. However, if distillation conditions are inappropriate, uncontrolled parameters can result in the unintended isomerization of the Delta-9-THC to other non-naturally occurring isomers like Delta-10-THC and Delta-6a10a-THC. As with many synthetic drugs on the black market, there is no known safety or toxicity profile for these other isomers of THC which are not found naturally.

Intentional synthetic processes have been used successfully to create a synthetic version of Delta-9-THC, also referred to as dronabinol, which is currently manufactured as a Schedule II drug under the trade name Marinol®. The synthetic production and distribution of this drug is under FDA regulation, which has at its foundation, a strong component of consumer safety. When synthetic impurities are observed in the development of these synthetic drugs under FDA regulation, producers have two options on how to address those:

420 Fortune Blvd. ◆ Milford, MA 01757
(617) 221 - 3356



1. Isolate the impurities to be studied for toxicity and biological relevance, so that inclusion in a final drug product will not present risk to consumers.
2. Remove these impurities from the post-synthetic mixture prior to distribution to consumers. This approach is common and often achieved by a chromatographic purification.

At what point do these synthetic byproducts or other contaminants need to be addressed? What level of impurity in a product would be considered acceptable? The FDA Advisory Committee recommends a threshold of 0.1% above which unidentified constituents should be identified and characterized for toxicity.

In view of that recommendation, please consider the semi-synthetic isomerization of CBD to THC (e.g. Delta-8- and/or Delta-9-THC) which is known to result in multiple synthetic byproducts. We have recorded in excess of 15 synthetic byproducts, some with total concentrations greater than 30% of the total cannabinoid concentration. Some of these byproducts are isomers of THC which do not occur naturally (e.g. Delta-10, Delta-6a10a). Some of the byproducts have unknown chemical structures, and without being identified previously, do not even have names yet by which we can identify them on our Certificates of Analysis (COAs). More concerning, is the fact that there is **no toxicity information** for any of these unnaturally occurring compounds.

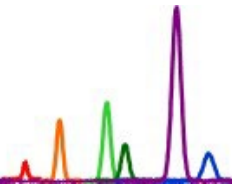
We have tested THOUSANDS of delta-8-THC based consumer products, and in all those thousands of samples, have not yet seen one that is NOT contaminated. Typical levels of contamination from synthetic byproducts can range from 3% to more than 30% of the total product. Please consider these levels compared to FDA advisory guidance of 0.1%. Because we do not know what to call these synthetic contaminants, our laboratory includes a note on each certificate of analysis that says:

> *In addition to compounds reported here, multiple cannabinoid isomers or byproducts, which do not occur naturally, were observed in this sample and cannot be identified. No toxicity data is available for these unknown compounds, and as such* ***would not be recommended for human consumption****.*

Most laboratories ignore the presence of these unknown chemical signals, producing COAs with no indication of any potential contamination or hazard for consumers. The public is consuming these products with no knowledge of their potential harm.

We have zero data that shows these chemical compounds are not toxic, that they do not cause birth defects, cancer, or other long-term health implications. They "probably" are not toxic. But who knows? Most of these have not even been studied yet in animal models, much less on human subjects…..except through the wide spread distribution of these products with no safety profiles. Essentially, we are using, in real-time, un-suspecting consumers as guinea pigs to see if there are any long-term negative health impacts associated with consumption of these synthetic products.

So far, I have only brought up the issue of synthetic byproducts. But there are other safety concerns. These synthetic processes require toxic organic solvents and strong acids. Some producers use heavy metal catalysts. While these reagents are not uncommon during production in a pharmaceutical



environment, the chemical technicians are trained in their use, and more importantly in their removal from a final drug product. In addition, final analytical testing of a drug product is required to ensure that removal of these toxic reagents has been successful. This does not happen today for these synthetic cannabinoids.

I have sat in on many regulatory discussions on the topic of synthetic cannabinoids, and frequently hear regulators suggest a legitimate pathway for production and distribution of synthetically derived cannabinoids, with the caveat that "*we will just ask laboratories to test for these synthetic contaminants*". As if it was just that easy. These contaminants are challenging to test for. We do not know their structure. We do not have certified reference standards that we can use to confirm their identity and provide quantitative information. The standard methodology for testing phytocannabinoids, HPLC, employed by the majority of cannabis testing labs, is inadequate in resolving these complex signals from each other. Analysis often times takes more sophisticated instrumentation that is prohibitively expensive and not available in most laboratory settings. Testing for the residual toxic reagents can be complicated as there is no common SOP for production. Each producer has their own recipe for synthesis, resulting in a very specific profile of potential contaminants which will vary from one producer to another.

It has been estimated that the US market for Delta-8-THC vapes this year is as high as $10B. It is a lucrative business, lots of money to be made, and as such there are many lobbyists pushing for a legitimate path forward. It is not uncommon for me to hear regulators and public health officials acquiescing to these industry lobbyist in favor of creating this path forward with the rationale that we do not know if these products or contaminants are harmful.

Lack of Evidence of Harm ≠ Safety

As regulators, public health officials, clinicians and researchers, we have the responsibility to protect public health and safety.

I am excited about the therapeutic (and even recreational) potential for synthetic cannabinoids, but only if can be regulated in a way which ensures consumer safety. Developing analytical methods to test for these contaminants, finding ways to remove these contaminants, and studies to understand the toxicity of the contaminants could take years. Cleary, the cart has been put before the horse. It is now in the hands of our regulators and public health officials who have the power to correct that. And I urge you to do just that.

Thank you for taking the time to consider my concerns. Please feel free to contact me if you have any additional questions.

All the best,

Christopher Hudalla

Christopher Hudalla, Ph. D.
Founder/CSO
ProVerde Laboratories