

## FDA Route

When discussing the overall safety of consumer products that contain synthetic cannabinoids, a thorough and well-rounded approach is paramount. One that focuses both on the manufacturing process and the final product. The process and product must meet or exceed minimum safety thresholds to ensure employee and consumer safety. It is important to recognize that HB948 asks the advisory council to “recommend potential guidelines for safe methods of manufacturing, extracting, and synthesizing cannabinoids, including the sale of synthetic marijuana products”. Yet, it does not specifically ask the council to also investigate or evaluate the safety of the final product. The advisory council has chosen to provide information regarding not only potential safe methods of synthesizing cannabinoids, but also and just as importantly, an evaluation on the safety of synthetic cannabinoids in consumer products.

It is critical to recognize that the mere existence of a safe method of manufacturing, for any given compound, does not inherently mean that the compound itself is safe for human consumption. Consider methamphetamine. This compound can be manufactured or synthesized in a safe manner from readily available and legal starting materials. However, the product is not safe for use in the general consumer space and has resulted in considerable harm to public health. Therefore, allowing for the production and sale of any compound, including synthetic cannabinoids, based solely on if the manufacturing method is safe, is an extremely poor determining factor to use when considering if these products are safe for Montana consumers. The latest available research indicates that synthetic cannabinoids, many of which are nascent and unstudied, have high potential to harm public health. This is evident by the drastic increase in synthetic cannabinoid adverse event reporting, including fatalities, since 2018, as seen in the FDA’s Adverse Events Reporting System (FAERS).

Given the isomeric chemistry of cannabinoids, they can easily be manipulated and modified into an almost unlimited number of analogs, all of which have the potential to interact with the human body in ways that are unstudied and unknown. The scientific literature in this regard is sorely inadequate and will likely remain so as new synthetic cannabinoids are being created at a pace faster than researchers can study. What literature is available on the more established synthetic cannabinoids clearly indicates that some are over 30 times more pharmacologically active than naturally occurring delta-9-THC. Additionally, the synthetic manufacturing process uses toxic chemicals and reagents which can remain in the final product. Finally, as no chemical synthesis is 100% efficient, the process also creates unintended by-products which may include non-target novel synthetic cannabinoids along with a host of other unidentified compounds. All of which have unknown human health effects. Even if regulations existed to ensure the synthetic manufacturing process was safe, including the removal of by-products and reagents, the scientific literature does not support safe human consumption of these compounds at this time.

Should the State wish to entertain the idea of allowing for the manufacture and sale of synthetic cannabinoids, a logical approach would be to utilize the long-standing FDA pathways to ensure that both the process, and just as importantly, the product is safe. These pathways include the drug development pathway, along with the Generally Recognized as Safe (GRAS) and the New Dietary Ingredient (NDI) pathways. The drug development pathway involves a review process ensuring the drug is safe and effective for its intended use, the benefits outweigh the risks, and a risk management strategy is in place. A few natural and synthetically derived prescription cannabinoid drugs have been approved through this process and are available through the prescriptive power of a licensed physician. The FDA’s GRAS and

NDI programs ensure that the ingredients to be included in food or dietary supplements must meet certain assumed minimum safety thresholds for the conditions of its intended use prior to formulation in food or dietary supplements. This recognition of safety through scientific procedures is based upon generally available, accepted, and published scientific data. At this time, a successful application for a synthetic cannabinoid has yet to achieve a GRAS or NDI designation.