FDA U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR FOOD SAFETY & APPLIED NUTRITION

Memorandum

Date January 31, 2024

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Subject Updated literature search and GRAS evaluation on delta(8) tetrahydrocannabinol

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Keywords: delta(8) *trans*-tetrahydrocannabinol, delta(8) tetrahydrocannabinol, delta(8) THC

This is an addendum to the December 2, 2021 memorandum that discusses the regulatory status and review of available data and information pertaining to delta(8) trans-tetrahydrocannabinol (hereinafter referred to as delta(8) THC). That memorandum concluded that the use of delta(8) THC in food does not meet the criteria for GRAS due to inadequate data and information on the safety of its consumption, and the information that is available indicates that the use of delta(8) THC in food may be harmful as described in the memorandum. As such, the memorandum concluded that the use of delta(8) THC in food constitutes use of an unapproved food additive, rendering it an unsafe food additive within the meaning of Section 409(a) of the FD&C Act [21 U.S.C. § 348(a)], and therefore adulterating the food to which it is added within the meaning of Section 402(a)(2)(C)(i) of the FD&C Act [21 U.S.C. § 342(a)(2)(C)(i)]. This addendum summarizes the findings of an updated literature search of the publicly available data and information since the original review and determines whether the new information continues to corroborate the previous conclusion.

Following the methodology described in the original review, updated searches of the published literature were conducted from the last date of the original memorandum (December 1, 2021) through October 26, 2023. The results from PubMed and Web of Science Core Collection databases are summarized in Table 1.

Table 1: Summary of literature search terms and results.

Search Term	Database	Search Results (Number)
("delta(8) THC" or "delta(8) tetrahydrocannabinol") AND ("toxi*" or "oral" or "food" or "chronic" or "subchronic" or "acute")	PubMed	26
	Web of Science (Core Collection)	18
("delta8 THC" or "delta8 tetrahydrocannabinol") AND ("toxi*" or "oral" or "food" or "chronic" or "subchronic" or "acute")	PubMed	10
	Web of Science (Core Collection)	5

The majority of articles retrieved from these searches were not relevant to the potential for oral toxicity of delta(8) THC. Multiple articles discuss studies that were designed to investigate potential or purported therapeutic and/or beneficial pharmacological effects of delta(8) THC, particularly as an analgesic or anxiolytic. Nine articles were deemed relevant to the general recognition of safety of delta(8) THC for use in food. These articles are cited and discussed below. None these articles address concerns for safety or refute the conclusion of the prior memorandum.

Two *in vivo* toxicology studies reported adverse effects following oral delta(8) THC exposure in rats, and include dose-dependent decreases in body weight, and relative organ weights for the epididymis, heart, liver, lung, and spleen (Kulpa et al., 2023), and a decrease in food intake and an anxiogenic effect (only males tested; Jenkins et al., 2023). Additionally, a toxicokinetic study in rats was identified (Moore et al., 2023) that reports, of the four minor cannabinoids tested, delta(8) THC had the highest likely exposure as demonstrated by the area under the curve. Moore et al. additionally note that delta(8) THC accumulates in the plasma, and is detected in brain tissue; demonstrating its ability to cross the blood-brain-barrier.

Two articles investigated self-reported adverse events following delta(8) THC consumption to the FDA Adverse Event Reporting System (FAERS) (Leas et al., 2023; Simon et al., 2023) and through an online forum (Leas et al., 2023). The authors note that the most frequent adverse events reported were dyspnea, respiratory disorder, and seizure (in FAERS) and psychiatric disorders (online forum). They further noted that these data indicate a potential safety concern, and that the prevalence for adverse events reported to be associated with cannabis versus delta(8) THC were similar, suggesting an overlap in those event reports.

One literature review discusses the current state of knowledge on synthetic delta(8) THC and concludes that US consumers are ingesting mislabeled products, and raises concern over fatalities linked to vaping-associated lung injury (Geci et al., 2022).

Two clinical case reports discuss unintentional delta(8) THC consumption in pediatric patients. In the first, two children were admitted to the pediatric intensive care following consumption of delta(8) THC products that resembled candy; both patients were discharged approximately 45 hrs. after ingestion (Bradley et al., 2023). In the second, four pediatric

patients experiencing confusion, somnolence, seizure-like activity hypotension, and tachycardia presented to the hospital after consumption of retail-store obtained delta(8) THC products (Shaker et al., 2023).

Additionally, FDA has published a statement to consumers that delta(8) THC products have not been evaluated or approved for safe use in any context, and such products may pose serious health risks (FDA, 2022).

Conclusion

Based on the updated literature search, no new data and information was identified that would change the conclusion as stated in our memorandum dated December 2, 2021.

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