May 30, 2023

The Honorable Bernie Sanders
The Honorable Bill Cassidy
Committee on Health, Education, Labor and Pensions
United States Senate
Washington, DC 20510

The Honorable Cathy McMorris Rodgers
The Honorable Frank Pallone
Committee on Energy and Commerce
United States House of Representatives
Washington, DC 20515

Dear Chairs and Ranking Members,

We are writing to share our concerns about a recent review article authored by FDA staff entitled "Review of the Oral Toxicity of Cannabidiol (CBD)."[1] The article claims to be a summary of the data and information in the scientific literature regarding toxicological concerns associated with CBD consumption, and purports to provide a "thorough toxicological hazard identification." It concludes the "data clearly establish CBD's potential for adverse health effects when consumed without medical supervision by the general population" and that "multiple oral toxicity studies raise serious safety questions about the potential for reproductive and developmental toxicity effects."

However, the review article fails to provide a full picture of the available data on CBD, and instead focuses primarily on studies using high-dose CBD formulations – ignoring the growing body of evidence demonstrating the safety of CBD at lower amounts, such as those typically found in CBD dietary supplements and foods sold at retail, and across a range of CBD-containing ingredients. Even essential nutrients like Vitamin D can be both beneficial and toxic depending on the dose.

As outlined below, there are multiple toxicity studies published between 2020 and 2023 demonstrating the safety of CBD at these lower amounts, as well as other studies we expect to be published soon. Combined with the low number of adverse events associated with CBD products and real-world, observational data that also points to the safety of CBD, the totality of the evidence paints a much different picture than what is presented by the FDA in the review article. The FDA continues t

[1] Gingrich, J., Choudhuri, S., Cournoyer, P., Downey, J., Muldoon Jacobs, K. Review of the oral toxicity of cannabidiol (CBD). April 2023:113799. doi: https://doi.org/10.1016/j.fct.2023.113799.

ignore this key data, and we share the concerns voiced by other trade organizations that the review article does not provide useful information to the public and more importantly consumers.[2]

- Three published toxicity studies on three different types of hemp extract, conducted as part of independent GRAS affirmations, have consistently demonstrated the safety of CBD at serving sizes typically found in products sold at retail.[3]
- A fourth toxicity study published in 2023 on CBD isolate also reported positive findings with respect to CBD's safety.[4]
- A fifth toxicity study published in 2023 evaluating the effects CBD isolate has established safe intake levels related to male and female developmental and reproductive toxicity, which addresses an important data gap identified by FDA.[5]
- Unpublished studies presented confidentially to FDA yielded additional positive safety findings, with three studies using hemp extract and three using CBD isolate. Most of these studies are expected to be published in 2023-2024.
- Another toxicity study with additional safety was data submitted to FDA in conjunction with a Citizen Petition, further demonstrating the safety of another CBD-containing hemp extract.[6]
- A further study, based on Phase II and phase III clinical trials utilizing full and broad-spectrum hemp extracts, up to 150 mg of hemp extract daily was not associated with elevated liver tests, notable drug interactions, or adverse events.[7]
- Observational data and the results of another study provide additional evidence of CBD's safety in over 4,000 participants collectively:

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[2] Letter from Council for Responsible Nutrition to FDA Commissioner Robert Califf (May 4, 2023), https://www.crnusa.org/sites/default/files/pdfs/comments-pdfs/CRN-Letter-FDA-CBD-oral-tox-review050423.pdf.

[3] An Assessment of the Genotoxicity and Subchronic Toxicity of a Supercritical Fluid Extract of the Aerial Parts of Hemp (2018), https://doi.org/10.1155/2018/8143582; Safety Assessment of a Hemp Extract using Genotoxicity and Oral Repeat-Dose Toxicity Studies in Sprague-Dawley Rats (2020), https://doi.org/10.1016/j.toxrep.2020.02.014; Toxicological safety of VOHO Hemp Oil; a supercritical fluid extract from the aerial parts of hemp (2022), https://doi.org/10.1371/journal.pone.0261900.

[4] Oral toxicity evaluation of cannabidiol (2023), https://doi.org/10.1016/j.fct.2023.113778.

[5] Reproductive and developmental toxicity evaluation of cannabidiol (2023), https://doi.org/10.1016/j.fct.2023.113786.

[6] Citizen Petition from Daniel Fabricant, Ph.D. on behalf of Natural Products Association, Docket No. FDA-2022-P-0600, https://www.npanational.org/wp-content/uploads/2022/02/CBD-CP-on-CBD.pdf.

[7] Presented confidentially to FDA. Pregnant women were excluded from the studies.

- A 2021 observational study conducted by Validcare in over 800 participants using CBD products showed no increase in the prevalence of elevated liver function tests when compared to a population with a similar incidence of medical conditions.[8]
- Another Validcare study of over 1,000 participants, completed in March 2022, showed that CBD is not associated with elevated liver tests, low testosterone levels, or daytime drowsiness.[9]
- The results of a Radicle Sciences study published in November 2022 and using 2,800 participants reported only minor side effects (e.g., gas, headache) in less than 10% of participants, with no severe side effects.[10]

We are also concerned that CBD is being held to a much higher standard than other dietary supplement ingredients. The existing regulatory framework for dietary supplements is intended to ensure these products do not pose an *unreasonable or significant* risk of illness or injury, and includes the necessary risk management tools to achieve this purpose including mandatory GMPs, new dietary ingredient notification requirements, and mandatory serious adverse event reporting – contrary to the FDA's claims that its current authorities "provide only limited tools for managing many of the risks associated with CBD products."[11]

We welcome the opportunity to discuss this additional data with you and would be happy to answer any questions.

Sincerely,

Jonathan Miller
General Counsel
US Hemp Roundtable

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[8] Observed Impact of Long-term Consumption of Oral Cannabidiol on Liver Function in Healthy Adults (2021), https://www.liebertpub.com/doi/10.1089/can.2021.0114.

[9] https://hempsupporter.com/news/new-study-demonstrates-cbds-strong-safety-profile-amplifies-calls-for-fda-regulation.

[10] The Safety and Effectiveness of Commercially Available Cannabidiol Products for Health and Well-Being: A Randomized, Multi-Arm, Open-Label Waitlist-Controlled Trial (2022), https://doi.org/10.1089/imr.2022.0081.

[11] FDA Concludes that Existing Regulatory Frameworks for Foods and Supplements are Not Appropriate for Cannabidiol, Will Work with Congress on a New Way Forward (Jan. 26, 2023), https://www.fda.gov/news-events/press-announcements/fda-concludes-existing-regulatory-frameworks-foods-and-supplements-are-not-appropriate-cannabidiol.

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