APhA
American Pharmacists Association

August 18, 2023

The Honorable Bernie Sanders
Chair, U.S. Senate Committee on
Health, Education, Labor, and Pensions
428 Dirksen Senate Office Building
Washington, DC 20510

The Honorable Cathy McMorris Rodgers
Chair, House Energy &
Commerce Committee
2125 Rayburn House Office Building
Washington, D.C. 20515

The Honorable Bill Cassidy, M.D.
Ranking Member, U.S. Senate Committee
on Health, Education, Labor, and Pensions
455 Dirksen Senate Office Building
Washington, DC 20510

The Honorable Frank Pallone, Jr.
Ranking Member, House Energy &
Commerce Committee
2125 Rayburn House Office Building
Washington, DC 20515

RE: Request for Information: Regarding FDA Regulation of Cannabidiol (CBD)

Submitted via email to CBD@mail.house.gov and CBD@help.senate.gov

Dear Chair Sanders, Ranking Member Cassidy, Chair McMorris-Rodgers, & Ranking Member Pallone:

The American Pharmacists Association (APhA) appreciates the opportunity to submit comments to the U.S. House Energy & Commerce Committee (E&C) and the U.S. Senate Health, Education, Labor, & Pensions (HELP) Committee on your joint request for information regarding the Food and Drug Administration's (FDA) regulation of cannabidiol (CBD). APhA supports efforts by Congress to obtain scientific data and information about the safety, manufacturing, product quality, marketing, labeling, and sale of products containing CBD. APhA believes developing any legislative approach to the regulation of CBD products should include collaboration with clinical researchers and health care providers, including pharmacists, to ensure that the 14 percent of adults using CBD products are using them safely and effectively.

APhA is the only organization advancing the entire pharmacy profession. APhA represents pharmacists, student pharmacists, and pharmacy technicians in all practice settings, including but not limited to community pharmacies, hospitals, long-term care facilities, specialty pharmacies, community health centers, physician offices, ambulatory clinics, managed care organizations, hospice settings, and government facilities. Our members strive to improve medication use, advance patient care, and enhance public health.

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APhA's House of Delegates passed the following policy on cannabis in 2015:

Role of the Pharmacist in the Care of Patients Using Cannabis

1. APhA supports regulatory changes to further facilitate clinical research related to the clinical efficacy and safety associated with the use of cannabis and its various components.
2. APhA encourages health care provider education related to the clinical efficacy, safety, and management of patients using cannabis and its various components.
3. APhA advocates that the pharmacist collect and document information in the pharmacy patient profile about patient use of cannabis and its various components and provide appropriate patient counseling.
4. APhA supports pharmacist participation in furnishing cannabis and its various components when scientific data support the legitimate medical use of the products and delivery mechanisms, and federal, state, or territory laws or regulations permit pharmacists to furnish them.
5. APhA opposes pharmacist involvement in furnishing cannabis and its various components for recreational use.

Request for Information Questions & Answers

Current Market Dynamics

3. How is the lack of national standards for CBD products affecting the market?

Currently, there are very few safeguards to protect consumers from the potential risks of CBD in food and a lack of national standards for CBD products, which is confusing the market and its consumers. Researchers express that CBD products for human consumption have been brought to market with inconsistent guidelines and without proper evidence of effectiveness and safety.

Pathway

4. Please comment on the concerns FDA has raised about regulating most CBD products through existing pathways (i.e., conventional foods, dietary supplements, and cosmetics), and FDA's view that there is a need for a new regulatory pathway for CBD products. If existing regulatory pathways are sufficient for regulating CBD products, please explain how these existing pathways can be used to address the concerns raised by FDA, as appropriate.

Regulating CBD continues to present challenges since FDA does not approve or evaluate supplements for safety and efficacy before they are marketed. Although CBD does not meet the relevant statutory requirements as a food or dietary supplement due to safety concerns, the incorporation of CBD as a drug into foods may be viewed as adulteration. Adulteration is considered a violation of Section 402(a)(3) of the Federal Food, Drug, and Cosmetic Act in that the food has been grown, harvested, packed, or held under such conditions that it is unfit for food.

7. How has the absence of federal regulation over CBD created a market for intoxicating, synthetically-produced compounds, such as Delta-8 THC, THC-O, THC-B, HHC-P, and others?

a) **What is the public health impact of these novel compounds?**
   - Patients and healthcare providers have expressed that there is confusion regarding different dosage forms, variations in state laws, and lack of clear warning labels that highlight CBD content vs. tetrahydrocannabinols (THC) content. CDC released a Health Alert Network (HAN) Health Advisory in 2021 to inform consumers that CBD can be synthetically converted into Delta-8 THC, which is psychoactive and not well understood. Increased reports of adverse events related to delta-8 THC, as well as preliminary reports of the emergence of other similarly produced products derived from cannabis warrant the continued monitoring and tracking of adverse events related to THC.
   - There is limited research in humans on the exact levels of CBD needed before inherent risks become evident, but current literature supports that appropriate laboratory and monitoring of international normalized ratio (INR) in patients receiving concomitant cannabis products with pharmaceuticals is recommended. Animal studies have been conducted citing co-administration of CBD at the dose of 116 mg/kg with acetaminophen resulting in 37.5% mortality associated with liver injury whereas no mortality was observed in the use of CBD-alone or acetaminophen-alone subgroups. The researchers in this study cite a paradoxical effect of CBD/APAP-induced hepatotoxicity, further lending support to the need for increased research on this matter.

b) **How should Congress consider the inclusion of these products in a regulatory framework for cannabinoid hemp products, if at all?**
   - APhA recommends consideration of safety concerns and relevant use information for different forms of CBD (e.g., oil-based solutions, crystalline derivatives (or solid forms), edibles, suppositories, and topicals) into any regulatory framework. APhA also believes there is a need for pharmacokinetic studies that correlate blood levels with therapeutic efficacy and adverse effects for most cannabis and cannabis-derived products. Further research is needed in this area to determine dosing regimens.

8. CBD products are not limited to just ingestible routes of administration—some are interested in products with alternative routes of administration (e.g., inhalable, topical, ophthalmic drops, etc.).

a) **For which non-ingestible routes of administration are consumers interested in consuming CBD products?**
b) **How should a regulatory framework for cannabinoid products account for non-ingestible routes of administration?**

Research is currently lacking regarding specific levels of cannabis and cannabis-derived compounds that cause safety concerns, including drug interactions, and how the mode of delivery (e.g., ingestion, absorption, inhalation, transdermal) affects safety and exposure to cannabis and cannabis-derived compounds, particularly potential long-term effects in various age-group populations. Non-ingestible routes need additional study and should be accounted for in a regulatory framework if warranted by adverse events. Despite certain products being accessible to consumers within states, Federal requirements tend to limit researchers' ability to study more broadly the availability of cannabis and cannabis-derived products.

Federal-State Interaction

9. In the absence of federal regulation or enforcement over CBD products, many states have established state regulatory programs to safeguard public health and create market certainty for industry participants.

a. Which product standards relating to warning labels, minimum age of sale, manufacturing and testing, ingredient prohibitions, adverse event reporting, and others, have states adopted to protect consumer safety?

There are many different state laws addressing cannabis and hemp. For example, in certain states pharmacists may be instructed by their board of pharmacy not to sell cannabis or cannabis-derived products. Alternatively, some states have laws specific to CBD (generally with a specified, low-level of THC) to allow use of products for certain medical purposes not approved by the FDA. A few states have not removed hemp from their state's controlled substances acts, so legality of CBD products differs across states. Therefore, variable interpretations and definitions of state and federal laws may result in limitations regarding both the location of sale and the products that may be sold.

Differences among Federal and state laws may also pose barriers for regulators seeking to identify effective strategies for protecting public health. For example, state-imposed conditions, restrictions, or other limitations (e.g., registries/patient ID cards, medical conditions, patient age, healthcare practitioner involvement) may be applicable to a different scope of products and circumstances between states. As a result, it may be difficult to determine whether a limitation or other conditions could be replicated to mitigate specific risks.

12. What actions, if any, should the Federal government take to better understand the potential benefits or harms of CBD products and other cannabinoids?

As Congress and FDA consider a regulatory framework for cannabis and cannabis-derived products, APhA recommends addressing options to obtain more robust safety data. We also encourage Congress to utilize and promote current systems rather than develop systems unique to cannabis and cannabis-derived products. Making health care practitioners and consumers aware of reporting options and information relevant to include in reports may help increase the quantity and quality of surveillance information.

According to a 2021 Harvard Health article on CBD, animal studies, self-reports, and research in humans suggest that CBD has benefits to reduce anxiety, assist individuals who have trouble falling and staying asleep, alleviating chronic pain, (including inflammation due to arthritis), as well as addiction treatment properties. However, studies also suggest that information on safe quantities of CBD in food in particular is limited and incomplete. With few safeguards to protect consumers from potential risks of CBD in food, a lack of national standards for CBD products is negatively affecting and confusing the market and its consumers. Researchers have expressed concern that CBD products for human consumption have been brought to market with inconsistent guidelines and without proper evidence of effectiveness and safety.

13. How should a new framework for CBD products balance consumer safety with consumer access?

Pharmacists play an essential role in educating and counseling patients about safety concerns with their medications. APhA encourages utilizing pharmacists' expertise to counsel patients on the appropriate use of these products. APhA also encourages communicating to consumers and healthcare providers regarding enforcement activity and information about improper marketing. The use of traditional and enhanced communication routes like professional associations and social media will help reach broader audiences.

14. Some stakeholders have raised concerns that CBD products have inherent risks. What are those inherent risks, and at what levels of CBD do those risks present themselves? What data and other evidence support the existence of such risks, and from which products are such data and evidence derived?

With increased access to CBD containing products, the rate of adverse drug interactions is likely to increase. Cannabidiol has been found to interact and increase concentration levels of medications such as warfarin, cyclosporine, and tacrolimus. Additionally, there is difficulty identifying the amounts of CBD and THC in currently available products. Given the increased recreational use of these products there is concern for higher rates of misuse of these drugs. APhA recommends identifying strategies to prevent misuse of these products and determine the extent this currently occurs and the circumstances under which it occurs. This research will be helpful to identify strategies to prevent misuse.

26. Some suggest requiring labels for CBD products to include "potential THC content." Would THC content be unknown in a particular product? Is there precedent for such a labeling requirement?

Patients and healthcare providers have expressed confusion regarding different dosage forms, variations in state laws, and a lack of clear warning labels that highlight CBD content vs. THC content. A different approach is required to regulate these products as a market for intoxicating, synthetically produced compounds, such as Delta-8 THC, THC-O, THC-B, HHC-P, and others have already been introduced (as mentioned above). APhA believes there are a variety of options to consider in informing consumers about the risks associated with CBD products,

including the directions for use and warning labels. The information conveyed in labeling should be evidence-based and clear for consumers and health care practitioners to understand and apply. In the labeling, APhA recommends considering how to disclose the presence of THC and the amount of both THC and CBD in the marketed product.

28. What specific additional restrictions should apply to CBD products regarding their appeal to or use by children about marketing, packaging, and labeling? Is there precedent in the food, dietary supplement, tobacco, or cosmetics space for restricting certain product features that would make products appealing to children? Please describe.
APhA encourages Congress to review studies on the risks and benefits of cannabis or cannabis-derived products to certain populations (children, elderly, and pregnant or lactating women) and determine how to decrease these risks. For example, child-resistant packaging and standardized labeling could mitigate any risks to these particular populations.

Conclusion
APhA appreciates the opportunity to provide feedback on the joint request for information regarding FDA regulation of CBD. APhA understands the need to balance careful regulatory decision-making with public health protections. However, APhA remains concerned that risks to patients may increase as more unregulated CBD and other similar products come onto market.

Pharmacists play an important role in educating patients and consumers about different products, including CBD products. APhA recommends leveraging the expertise of our nation's pharmacists as you determine the legislative or regulatory pathway forward for CBD products. Integrating pharmacists into these efforts will help to reduce the incidence of misuse of CBD products and protect public health. If you have any questions or need any additional information please contact Heather Boyd, Director, Health Policy at hboyd@aphanet.org.

Sincerely,

Michael Baxter

Michael Baxter
Acting Head of Government Affairs