

August 18, 2023

The Honorable Bernie Sanders
Chair
Senate, Education, Labor and
Pensions Committee
428 Dirksen Senate Office Building
Washington, DC 20510

The Honorable Cathy McMorris Rodgers
Chair
House Energy and Commerce Committee
2125 Rayburn House Office Building
Washington, DC 20515

The Honorable Bill Cassidy
Ranking Member
Senate, Education, Labor and
Pensions Committee
428 Dirksen Senate Office Building
Washington, DC 20510

The Honorable Frank Pallone
Ranking Member
House Energy and Commerce Committee
2322 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Sanders, Chairwoman McMorris Rodgers, Senator Cassidy and Congressman Pallone:

On behalf of the American Academy of Addiction Psychiatry (AAAP), thank you for the opportunity to provide input in response to the Request for Information regarding the Food and Drug Administration's regulation of cannabidiol (CBD).

AAAP is a professional organization representing specialists in addiction psychiatry and other healthcare professionals who treat patients with substance use disorders (SUDs). AAAP's primary mission is to educate healthcare professionals in the prevention and treatment of SUDs and co-occurring psychiatric disorders. AAAP is focused on working with the Administration, Congress, and experts in the field of addiction treatment to develop and implement science-based policies and programs to accomplish our shared goal of expanding SUD treatment, ending the opioid misuse and overdose epidemic, addressing co-occurring mental health conditions, and providing effective treatments for our patients and their families. From that perspective, we offer the following comments in response to the RFI's questions.

Question 2: How has the market changed since the passage of the 2018 Farm Bill?

Since the 2018 Farm Bill was enacted, the availability and popularity of CBD has increased significantly. A variety of CBD formulations are widely available for sale through cannabis dispensaries, online stores and typical retail outlets such as convenience stores and drug stores.

Consumer sales have soared as sellers tout the potential therapeutic benefits of their products, citing – largely without evidence – pain relief, anxiety reduction and anti-inflammatory effects. CBD is sold in a variety of products including topically in lotions, creams and oils, edible products such as candy, gummies and tea, cosmetics, fabrics and even products for pets.¹ Forbes reports that in 2014, CBD accounted for \$107 million in product sales – by 2022, that number jumped to \$1.9 billion.

As CBD's availability and popularity has increased, the rate of accidental poisonings, particularly among children, has also increased. From April 1, 2019 to March 31, 2020, the first year in which CBD was identified uniquely as a substance in the National Poison Data System, poison control centers handled 1,581 cases involving exposures to CBD-containing products. Patients under age 13 made up 44% of reported exposures. The most frequently reported symptoms included mild central nervous system depression (10.3%),

¹ <https://www.samhsa.gov/resource/ebp/advisory-cbd-potential-harms-side-effect-unknowns>

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tachycardia (5.7%), dizziness/vertigo (5.3%), vomiting (4.9%), nausea (4.5%), and agitation (4.4%). 13% of cases were coded as having "moderate" or "severe" medical outcomes. Fortunately, no fatalities were reported.¹

In short, following the enactment of the 2018 Farm Bill, the CBD market has been on a significant upward trajectory accompanied by an increase in accidental exposures and little evidence showing the medical benefit.

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

As noted above, the commercial CBD market has exploded amid a lack of standards and safety regulations. A [Forbes Health poll](#) conducted last year found that 60% of the 2,000 respondents had tried a CBD product.

However, consumers are unknowingly putting themselves at risk for potentially serious side effects which may include liver injury, interaction with other medications, and male reproductive toxicity, among others.² Moreover, little is known about long-term side effects on brain development and function and the effects of cumulative exposure (i.e if a person used a CBD lotion and then ingested a CBD gummy on a daily basis).³

In the absence of regulation, it has become impossible for consumers to know if the product they are buying is accurately labeled. For example, one study found that 26% of products had less CBD content than labeled, while another study found that 31% of tested products contained more than 110% than what was labeled.^{4,5}

Another concern is variable rates of THC in CBD products, especially in products not accurately labeled as containing the substance. The *Journal of the American Medical Association* published a letter summarizing the results of "undercover" CBD purchases. Of 84 samples tested, THC was detected in 21%.⁶ As a result of misleading or inaccurate labeling, children and adolescents who consume these products are at risk for cannabis intoxication and adults may unknowingly have detectable THC in their systems. Purity may also be a concern as non-FDA regulated THC products may have contaminants including pesticides and heavy metals.⁷

In brief, the lack of national standards has resulted in a wild west marketplace that is potentially putting consumers at risk of long-term health consequences.

² <https://pubmed.ncbi.nlm.nih.gov/33975134/>

³ <https://www.fda.gov/consumers/consumer-updates/what-you-need-know-and-what-were-working-find-out-about-products-containing-cannabis-or-cannabis>

⁴ <https://www.samhsa.gov/resource/ebp/advisory-cbd-potential-harms-side-effect-unknowns>

⁵ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5818782/>

⁶ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9169299/>

⁷ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7723146/>

⁸ <https://www.fda.gov/consumers/consumer-updates/what-you-need-know-and-what-were-working-find-out-about-products-containing-cannabis-or-cannabis>

Question 4: Please comment on the concerns FDA has raised with regard to 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.

We agree with FDA that synthetic and semisynthetic cannabinoids derived from hemp do not meet the criteria for approval through existing pathways for food or supplements. However, we believe an appropriate pathway currently exists: the process for the approval of prescription medications.

Under the Federal Food, Drug, and Cosmetic (FD&C) Act, any product claiming to have therapeutic or medicinal use (other than food) is considered a drug. Drugs must receive premarket approval by FDA through the New Drug Application (NDA) process or conform to a “monograph” for a particular drug category as established by FDA’s over-the-counter (OTC) drug review. Since CBD was not an ingredient considered under the OTC drug review, CBD cannot be distributed or sold in interstate commerce as a drug.

However, as discussed above, a multitude of companies have made unsubstantiated claims of CBD diagnosing, curing, mitigating, treating, or preventing diseases. [Some](#) have gone further by claiming that CBD was effective in treating teething and ear pain in infants, autism, ADHD, and dementia (i.e. Parkinson’s and Alzheimer’s).

While there is much still to be learned about CBD and long-term consequences associated with its use, we do have knowledge about potential short-term side effects. In a meta-analysis, the most common adverse effects were gastrointestinal symptoms (59.5%). Other adverse effects in order of decreasing incidence include somnolence (16.7%), loss of appetite (16.5%), increased ALT/AST (12.8%), and fatigue (11.4%). Most common side effects overall include drowsiness, sedation, fatigue, dizziness, headache, diarrhea, nausea, decreased appetite, and abdominal discomfort. Other common adverse drug effects include sleep disturbances, infection and anemia.⁸

As demonstrated by the approval of Epidiolex for the treatment of Lennox-Gastaut and Dravet’s Syndrome, CBD may provide important therapeutic benefits. However, in the absence of a rigorous review process, consumers are being left vulnerable to the potential side effects of these products without a truly informed understanding of their benefits. An appropriate remedy to this situation is for the FDA to regulate products in the same manner that other drugs are considered as part of the government’s responsibility to ensure consumer safety. For currently existing CBD products, FDA should consider mechanisms to improve accuracy in branding and marketing claims, and to ensure purity of available CBD.

Question 11: What is currently known about the safety and risk-benefit profile of CBD and other hemp derived cannabinoids? What safety and toxicity data are available to support the knowledge. Please include in your answer any relevant information about safety with regard to specific populations, such as children and pregnant individuals.

A significant need exists for more research to understand dosing, efficacy, and tolerability in humans of CBD products. The FDA has [outlined](#) numerous unknowns about the effects of CBD, including what the effects are of CBD on children’s developing brains, developing fetuses and breastfed newborns. What we do know is that CBD can be stored in breastmilk and it can easily cross the placental barrier. As a result,

⁹ <https://www.mdpi.com/1999-4923/14/12/2598>

some of the possible effects could include improper development of the immune system and microbiome of the fetus.⁹

More broadly, FDA [noted](#) that only limited data is available about CBD's safety and that such data points to potential risks which include liver injury, drug interactions, and male reproductive toxicity.

Question 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 discussed above, utilizing the NDA process would provide for the opportunity to study these products and their potential harms and benefits. FDA [outlines](#) that the goals of an NDA are to, "provide enough information to permit FDA reviewer to reach the following key decisions:

- Whether the drug is safe and effective in its proposed use(s), and whether the benefits of the drug outweigh the risks.
- Whether the drug's proposed labeling (package insert) is appropriate, and what it should contain.
- Whether the methods used in manufacturing the drug and the controls used to maintain the drug's quality are adequate to preserve the drug's identity, strength, quality, and purity."

These are the core questions that need to be answered about CBD: is it safe, is it effective, do the risks outweigh the benefits, what information do consumers need to make an informed choice, is the manufacturing process appropriate and safe? We urge FDA to treat CBD products like drugs, not supplements, and recommend the utilization of this established process for the consideration of CBD products.

In addition, as Congress is working to reauthorize the Farm Bill, we recommend the removal of psychoactive synthetic and semi-synthetic cannabinoids from the market by changing the definition of hemp in the Farm Bill to prohibit any "synthetic derivative of hemp...including delta-8 tetrahydrocannabinol and delta-10 tetrahydrocannabinol." The creation of these synthetic and semi-synthetic cannabinoids was not the intent of the Farm Bill and runs counter to existing drug policies related to designer drugs and novel psychoactive chemical compounds. Because of the vast proliferation, immense variety and potency of these products – from delta-8 and delta-10 to the hundreds of synthetic and semi-synthetic cannabinoids that are available now - regulation is impossible. There is potential for an unlimited number of derivations of these psychoactive synthetic and semi-synthetic products to be created.

Conclusion

Thank you again for the opportunity to comment on this important issue. Please do not hesitate to contact us if we can serve as a resource to you and your staff.

Sincerely,



Larissa Mooney, MD

¹⁰ Cannabinoid exposure during pregnancy and its impact on immune function." *Cellular and Molecular Life Sciences* 76 (2019): 729-743.