CADCA

CADCA Response to Congressional RFI on CBD

Question 2: How has the market changed since the passage of the 2018 Farm Bill?
A major unintended consequence of the 2018 Farm Bill has been the manufacture and proliferation of synthetic and semi-synthetic cannabinoids derived from hemp. These products can have intoxicating, psychoactive and hallucinogenic effects and are widely sold in gas stations, convenience stores and head shops across the nation. These products exist in a legal gray area due to the loophole created by the 2018 Farm Bill. This loophole needs to be permanently closed.

Recommendation: Psychoactive synthetic and semi-synthetic cannabinoids need to be removed 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.

Justification

- The legalization of hemp has resulted in unintended consequences, i.e., the proliferation of "look-a-like," "imitation" or "marijuana like" products such as delta-9 THC, delta-10 THC and THC-O, as well as numerous other synthetic and semi-synthetic cannabinoids. As written, the definition of hemp in the 2018 Farm Bill allows for the continuous engineering of new synthetic and semi-synthetic cannabinoids, including delta-6 THC, delta-11 THC, THC-A, THC-P, THC-V, THC-JD, PHC, HHC, HHC-P and HXC. Therefore, over time, there has been a vast growth in the number and potency of these products, as can be seen at Delta8Resellers.com (link below). This website is a representative example of the current state of the semi-synthetic cannabinoid market. There is a wide range of different cannabinoid substances sold, the number of which steadily increases over time. Few to none of these substances beyond delta-8 THC have been analyzed in a peer-reviewed or evidence-supported way for either short-term safety effects or long-term use. These chemicals are essentially designer drugs, and we are unsure of the health impacts of using them at any age. The rapid growth in the number of these products makes regulation almost impossible to achieve as can be seen at the website below. We have watched the availability of the products offered exponentially increase over time.
    - https://delta8resellers.com/shop/
    - LoParco, C.R., Rossheim, M.E., Walters, S. T., Zhou, Z., Olsson, S., & Sussman, S. (2023). Delta-8 tetrahydrocannabinol: a scoping review and commentary. Addiction, 118(6):1011–28. doi: 10.1111/add.16142 https://pubmed.ncbi.nlm.nih.gov/36710464/
    - Rossheim, M.E., LoParco, C., Henry, D., Trangenstein, P.J., & Walters, S.T. (2023). Delta-8, Delta-10, HHC, THC-O, THCP, and THCV: What should we call these products? Journal of Studies on Alcohol and Drugs. doi: 10.15288/jsad.23-00008 https://pubmed.ncbi.nlm.nih.gov/36971760/
- Synthetic and semi-synthetic cannabinoids are chemically synthesized from the CBD in hemp through processes which have resulted in impurities and dangerous chemicals being left behind in the final product such as strong acids and residual heavy metals.

    - Erickson, B.E. (2021 August 30). Delta-8-THC craze concerns chemists. C&EN: Chemical and Engineering News. https://cen.acs.org/biological-chemistry/natural-products/Delta-8-THC-craze-concerns/99/i31

- These psychoactive synthetic and semi-synthetic cannabinoids can be smoked or added to vapes and edibles and are commonly sold at gas stations, smoke shops, convenience stores, bodegas and online. These products are readily available to children.
- Recent research has shown that the use of THC-O could risk inciting another wave of e-cigarette or vaping product use-associated lung injury (EVALI). EVALI is thought to be caused by the inhalation of Vitamin E acetate, which, when heated, releases a powerful lung toxicant called ketene. Vaping THC-O may also release ketene and damage the lungs of users.

    - Kary, T. (2021 June 2). Pot producers are pushing to clamp down on delta-8 THC. Bloomberg. https://www.bloomberg.com/news/articles/2021-06-02/a-pot-knockoff-sometimes-made-with-household-acid-draws-scrutiny
    - Benowitz, N.L., Havel, C., Jacob, P., O'Shea, D.F., Wu, D., Fowles, J. (2022 December 12). Vaping THC-0 acetate: Potential for another EVALI epidemic. Journal of Medical Toxicology, Vol. 19. pp. 37-39. https://doi.org/10.1007/s13181-022-00921-3

- These products are purposely named, packaged and marketed in ways that make them particularly attractive and dangerous to kids. For example, many delta-8 THC products display bright colored cartoon characters and names which are specifically designed to appeal to children such as "Grape Ape", "Girl Scout Cookie", "Pineapple Express," "S'mores Chocolate", "Space Gods" and "Rainbow Sourbelts".

    - Partnership to End Addiction. (n.d.). Delta-8 THC: What you need to know about 'cannabis light'. Partnership to End Addiction. https://drugfree.org/article/delta-8-thc/


COURTESY: VA AG OFFICE
Cheetos
Doritos
NACHO CHEESE
TEAR AND SHARE
MEDICATED
Onion Flavored Rings
Crawlers
SOUR
VERY BERRY
BARIBU
Peach
Nerds
SOUR
INFUSED
Gushers
600 MG DELTA 8
SOUR TROPICAL
500 mg
MEDICATED
Nerds
GOTTA-HAVE-GRAPE
SUPER POTENT FORMULA
60 MINUTE
ACTIVATION TIME
NEW
ORIGINAL
Kittle
Gummies
SHARING
NET WT 1.0 OZ (28g)

Figure 1: Delta-8 products are purposely named, packaged, and marketed in ways that make them attractive to kids. (https://www.ftc.gov/news-events/news/press-releases/2023/07/ftc-sends-cease-desist-letters-fda-companies-selling-edible-products-containing-delta-8-thc)

Images courtesy of Joy Gonnerman, Cindy Hayford, and Diana OToole.

- Synthetic and semi-synthetic cannabinoids are available in all states, even those that have banned some of these products, such as delta-8.
    - LoParco, C.R., Rossheim, M.E., Walters, S. T., Zhou, Z., Olsson, S., & Sussman, S. (2023). Delta-8 tetrahydrocannabinol: a scoping review and commentary. Addiction, 118(6):1011–28. doi: 10.1111/add.16142 https://pubmed.ncbi.nlm.nih.gov/36710464/
    - Rossheim, M.E., LoParco, C., Henry, D., Trangenstein, P.J., & Walters, S.T. (2023). Delta-8, Delta-10, HHC, THC-O, THCP, and THCV: What should we call these products? Journal of Studies on Alcohol and Drugs. doi: 10.15288/jsad.23-00008 https://pubmed.ncbi.nlm.nih.gov/36971760/

Question 5: How should CBD and/or cannabinoid-containing hemp products be defined? What compounds should be included and excluded from a regulatory framework?

a. Should Congress or FDA limit the amount of intoxicating or potentially intoxicating substances produced by *Cannabis sativa L.* in food and dietary supplements? Which substances, if any, warrant greater concern? How should these substances of concern be addressed? What products, if any, should not be allowed on the market?

Recommendation: The definition of hemp should be changed to prohibit the manufacture or sale of intoxicating hemp products, such as delta-8 THC. CADCA is working to get the following language in the 2023

Farm Bill to amend the Agricultural Marketing Act of 1946 to modify the definition of hemp as follows: "The term 'hemp' does not include any synthetic derivative of hemp (as defined in subparagraph (A)), including delta-8 tetrahydrocannabinol and delta-10 tetrahydrocannabinol". Congress should disallow any amounts of intoxicating or potentially intoxicating substances in food and dietary supplements. Synthetic and semi-synthetic cannabinoids and THC derived from hemp are of greatest concern and should not be allowed on the market.

Justification

- Synthetic and semi-synthetic cannabinoids carry risks of harm, especially for young people. These products contain chemical contaminants and harsh solvents are often used in the process of creating them. Potency limits for synthetic and semi-synthetic cannabinoid products are rare, despite evidence that using higher potency products carries a greater risk of harm. Not only are potency limits rare, but a number of these substances are psychoactive and can be hallucinogenic as well.
    - LoParco, C.R., Rossheim, M.E., Walters, S. T., Zhou, Z., Olsson, S., & Sussman, S. (2023). Delta-8 tetrahydrocannabinol: a scoping review and commentary. Addiction, 118(6):1011–28. doi: 10.1111/add.16142 https://pubmed.ncbi.nlm.nih.gov/36710464/
    - Murray, E. (2022, March 22). The Risks Involved with Using THC-0. *Addiction Center*. https://www.addictioncenter.com/community/risks-thc
- Synthetic and semi-synthetic cannabinoids are consumed accidentally by children, as evidenced by the large number of calls to poison control centers involving minors due to poor labeling and a lack of childproof containers.
    - United States Food and Drug Administration (FDA). (2022). 5 Things to Know about Delta-8 Tetrahydrocannabinol – Delta-8 THC. https://www.fda.gov/consumers/consumer-updates/5-things-know-about-delta-8-tetrahydrocannabinol-delta-8-thc
- Synthetic and semi-synthetic cannabinoids are often marketed and packaged in ways that appeal to children and mimic the names of brands that appeal to them, such as Cap'n Crunch, Cocoa Puffs, Froot Loops, Nerds Ropes, Starbursts and Sour Patch Kids.
    - https://www.fda.gov/food/alerts-advisories-safety-information/fda-warns-consumers-about-accidental-ingestion-children-food-products-containing-thc
- Side effects of synthetic and semi-synthetic cannabinoid use can include disorientation, sedation, anxiety, agitation, tachycardia (increased heart rate), hypertension, dyspnea (labored breathing), nausea, vomiting, hyperglycemia (high blood sugar), hypokalemia (low potassium), seizures, impaired vision, hearing and touch and hyperreflexia (increased or overactive reflex response).
    - Malaca, S., Busardo, F.P., Nittari, G., Sirignano, A., Ricci, G. (2022). Fourth generation of synthetic cannabinoid receptor agonists: a review on the latest insights. *Current Pharmaceutical Design, Vol. 28* pp. 2603-2617. https://pubmed.ncbi.nlm.nih.gov/34781870/

b. How should Congress or FDA identify appropriate limits for THC and other cannabinoids in finished products? Relatedly, how should a framework account for "total THC," including tetrahydrocannabinol acid (THCA) in FDA's regulation of intermediate and finished products?

Recommendation: THC is still illegal at the federal level. Congress needs to obey federal law and these products should not contain any THC or other psychoactive substances.

Justification

- The 2018 Farm Bill stipulates that hemp must have no more than 0.3% THC. However, when synthetic or semi-synthetic cannabinoids are made into products like gummies or beverages, 0.3% THC can become 5-10mg of THC, which can cause users to get high. Even in states that have not legalized marijuana, like Iowa, the THC in hemp is being used to produce and sell products containing enough

THC that can get users impaired. These products are being marketed as legal in states because they are derived from the THC in hemp. (See Figure 2).

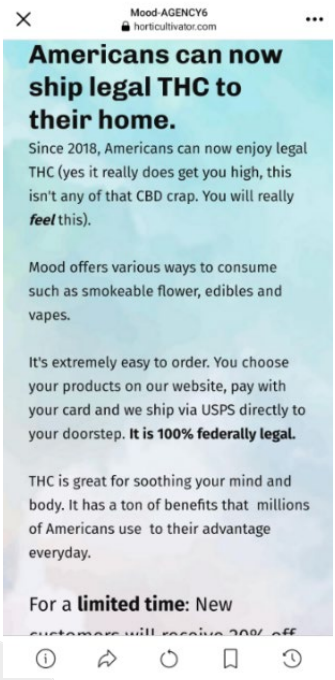

Figure 2: Synthetic and semi-synthetic cannabinoid products are now being marketed as legal (courtesy Joy Gonnerman)

- KCCI Des Moines. (2023 June 15). Des Moines brewery offers THC-infused beverage. *KCCI Des Moines.* https://www.kcci.com/article/des-moines-lua-brewing-offers-thc-infused-beverage/44197080#

- One example is “Iowa’s first cannabis-infused social beverage”, from Lua brewery called “Climbing Kites”, which contains up to 5mg THC per can. (See Figure 3).
  - Clayworth, J. (2023 June 13). Iowa’s first cannabis-infused drink hits the market. *Axios Des Moines.* https://www.axios.com/local/des-moines/2023/06/13/cannabis-marijuana-legal-drink-iowa-lua-desmoines

Figure 3: “Climbing Kites” – Iowa’s first cannabis social beverage.

c. Should FDA regulate the manufacture and sale of "semisynthetic derivatives," or "biosynthetic cannabinoids," which are still scheduled under the CSA?

Recommendation: Synthetic, semi-synthetic or biosynthetic cannabinoids that are still scheduled under the CSA should not be manufactured or sold. These products need to be removed from the market, rather than regulated.

Justification

- Synthetic, semi-synthetic or biosynthetic cannabinoids can be contaminated with strong acids, toxins and residual heavy metals.
    - Erickson, B.E. (2021 August 30). Delta-8-THC craze concerns chemists. *C&EN: Chemical and Engineering News.* https://cen.acs.org/biological-chemistry/natural-products/Delta-8-THC-craze-concerns/99/i31
- These products can be psychoactive, hallucinogenic and can be three times more potent than delta-9 THC. These products should be prohibited, rather than regulated.
    - Murray, E. (2022, March 22). The Risks Involved with Using THC-0. *Addiction Center*. https://www.addictioncenter.com/community/risks-thc

Question 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 those novel compounds?

Novel synthetic and semi-synthetic cannabinoid compounds have negative public health impacts.

Justification

- These novel compounds are psychoactive. Delta-8 THC is psychoactive and can get users high, although it is described as "diet weed". Scientists are still learning about delta-10 THC, but it is also psychoactive and causes feelings of euphoria.
    - Kaufman, A. (2023 April 15). Battle over delta-8 is heating up nationally. Here's what to know about the 'diet weed'. USA Today. https://www.usatoday.com/story/news/health/2023/04/15/what-is-delta-8/11521735002/
- THC-O can have hallucinatory effects and can be three times more potent than delta-9 THC.
    - Murray, E. (2022, March 22). The Risks Involved with Using THC-O. Addiction Center. https://www.addictioncenter.com/community/risks-thc
- Research also supports that the use of these products is associated with acute psychiatric, lung, chest and heart disorders, as well as injuries and poisonings.
    - Leas, E.C., Harati, R.M., Satybaldiyeva, N., Morales, N.E., Huaker, S.L., Mejorado, T., & Grant, I. (2023 2023). Self-reported adverse events associated with Delta-8-Tetrahydrocannabinol (Delta-8-THC) Use. Journal of Cannabis Research, 5(15). doi: 10.1186/s42238-023-00191-y https://jcannabisresearch.biomedcentral.com/articles/10.1186/s42238-023-00191-y
- The harmful effects of synthetic and semi-synthetic cannabinoids were first reported in the U.S. in 2009. Poison control centers have found the rat poison brodifacoum in these products.
- Symptoms of poisonings from these products include back and side pain as well as unexplained bleedings (blood in urine, bleeding from previous wounds, bleeding from the gums, etc.).
    - National Poison Data System, America's Poison Centers. https://www.aapcc.org/track/synthetic-cannabinoids

b. How have FDA and state regulators enforced against products containing these compounds?

Recommendation: FDA and FTC have sent warning letters to companies that have most egregiously used copyright infringements to look like highly recognizable trademarked products such as Doritos, Cheetos and Nerds. (See Figure 4). However, there are thousands of these products being sold across the country including in states that have specifically made these illegal.

Figure 4: Examples of synthetic and semi-synthetic cannabinoid products that infringe on copyrights. https://www.ftc.gov/news-events/news/press-releases/2023/07/ftc-sends-cease-desist-letters-fda-companies-selling-edible-products-containing-delta-8-thc

Justification

- State regulators in New York have banned synthetic and semi-synthetic cannabinoids such as delta-8 THC; however, these products are sold across the state in bodegas, convenience stores and gas stations. In Iowa, the cannabis-infused beverage "Climbing Kites", which contains up to 5mg THC is available despite marijuana being illegal in the state. (See Figure 3).
    - Clayworth, J. (2023 June 13). Iowa's first cannabis-infused drink hits the market. *Axios Des Moines.* https://www.axios.com/local/des-moines/2023/06/13/cannabis-marijuana-legal-drink-iowa-lua-desmoines
- Deceptive marketing of unproven health claims raises significant public health concerns because patients and other consumers may use these products rather than FDA approved medications and therapies.
    - FDA. (2023 July 5). FDA regulation of cannabis and cannabis-derived products, including cannabidiol (CBD). *FDA.* https://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-including-cannabidiol-cbd

c. How should Congress consider the inclusion of these products in a regulatory framework for cannabinoid hemp products if at all?

Recommendation: Psychoactive synthetic and semi-synthetic cannabinoids need to be prohibited, rather than regulated.

Justification

- States like New York have issued bans, and, in Iowa, these products are illegal, however, they are still sold. (See Figures 1, 3 and 4). These products have not been evaluated or approved by the FDA for safe use. Therefore, a federal ban should be implemented to strengthen statewide bans and protect public health.

- FDA. (2022 May 4). 5 things to know about delta-8 tetrahydrocannabinol – delta-8 THC. *FDA.* https://www.fda.gov/consumers/consumer-updates/5-things-know-about-delta-8-tetrahydrocannabinol-delta-8-thc

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 this knowledge. Please include in your answer any relevant information about safety with regard to specific populations, such as children and pregnant individuals.

Synthetic and semi-synthetic cannabinoids are unregulated and have limited laboratory testing. These products present a great public health and safety risk.

Justification

- Most states do not require testing for chemical contaminants, even though synthetic and semi-synthetic cannabinoids are commonly synthesized using harsh solvents known to be hazardous to human health.
- Potency limits are rare, despite conclusive evidence that more potent products carry higher risk of harm.
  - LoParco, C.R., Rossheim, M.E., Walters, S. T., Zhou, Z., Olsson, S., & Sussman, S. (2023). Delta-8 tetrahydrocannabinol: a scoping review and commentary. Addiction, 118(6):1011–28. doi: 10.1111/add.16142 https://pubmed.ncbi.nlm.nih.gov/36710464/
- Research supports that synthetic and semi-synthetic cannabinoid use is associated with acute psychiatric, lung, chest and heart disorders, as well as injuries and poisonings.
  - Leas, E.C., Harati, R.M., Satybaldiyeva, N., Morales, N.E., Huaker, S.L., Mejorado, T., & Grant, I. (2023). Self-reported adverse events associated with Delta-8-Tetrahydrocannabinol (Delta-8-THC) Use. Journal of Cannabis Research, 5(15). doi: 10.1186/s42238-023-00191-y https://jcannabisresearch.biomedcentral.com/articles/10.1186/s42238-023-00191-y
- Synthetic and semi-synthetic cannabinoids are also very new, so we do not know all the short- and long-term risks from use. These products are consumed accidentally by children, as evidenced by the large number of calls to Poison Control Centers involving minors because of poor labeling and a lack of child-proof containers.
- As of July 31, 2023, poison centers have received 372 calls for synthetic and semi-synthetic cannabinoid-related exposure cases.
  - United States Food and Drug Administration (FDA). (2022). 5 Things to Know about Delta-8 Tetrahydrocannabinol – Delta-8 THC. https://www.fda.gov/consumers/consumer-updates/5-things-know-about-delta-8-tetrahydrocannabinol-delta-8-thc
  - National Poison Data System, America's Poison Centers. https://www.aapcc.org/track/synthetic-cannabinoids