



440 1st St. NW, Ste. 520,
Washington, D.C. 20001
(202) 223-0101, Fax (202) 223-0250
NPAnational.org

March 14, 2019

Dockets Management Staff (HFA-305)

U.S. Food and Drug Administration

5630 Fishers Lane, Rm. 1061

Rockville, MD 20852

RE: Docket No. FDA-2019-N-0767 for "International Drug Scheduling; Convention on Psychotropic Substances; Single Convention on Narcotic Drugs; World Health Organization; Scheduling Recommendations; Dronabinol (delta-9-tetrahydrocannabinol) and its Stereoisomers; Cannabis, Cannabis Resin, Extracts and Tinctures; Cannabidiol Preparations; and Pharmaceutical Preparations of Cannabis; Requests for Comments" (Publication Date: March 1, 2019)

Dear FDA Desk Officer:

The Natural Products Association (NPA) is submitting this letter as general comment to docket FDA-2019-N-0767 (Docket Name: International Drug Scheduling; Convention on Psychotropic Substances; Single Convention on Narcotic Drugs; World Health Organization; Scheduling Recommendations; Dronabinol (delta-9-tetrahydrocannabinol) and its Stereoisomers; Cannabis, Cannabis Resin, Extracts and Tinctures; Cannabidiol Preparations; and Pharmaceutical Preparations of Cannabis; Requests for Comments). The NPA was founded in 1936 to promote and protect the unique values and shared interests of retailers and suppliers of natural nutritional foods and natural products, including conventional foods, medical foods, dietary supplements, and foods for special dietary use. The NPA is a non-profit 501(c)(6)

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association whose mission is to advocate for the rights of consumers to have access to products that will maintain and improve their health, and for the rights of retailers and suppliers to sell these products. We are the oldest and largest trade association in the natural products industry representing over 1,100 members accounting for almost 10,000 retail, manufacturing, wholesale, and distribution locations of natural products, including foods, dietary supplements, homeopathic products, and health/beauty aids. Many of our members have an interest in selling, manufacturing, or distributing cannabidiol (CBD) as a food or dietary supplement product once it is permitted by FDA’s Center for Food Safety and Applied Nutrition (CFSAN). Therefore, NPA has an interest to submit comments on this topic. Thank you for the opportunity to comment.

Background

On March 1, 2019, FDA submitted a federal register notice involving cannabidiol for stakeholder notice and comment. The FDA is providing interested persons with the opportunity to submit comments about the World Health Organization (WHO) recommendations to impose international manufacturing and distributing restrictions, under international treaties, on certain substances. The comments received will be considered in preparing the United States’ position on these proposals for a meeting of the United Nations Commission on Narcotic Drugs (CND) in Vienna, Austria, March 18-22, 2019. As a party to the 1971 Convention on Psychotropic Substances, whenever the CND proposes to add, transfer, or remove a drug from one of the schedules, the Secretary of State must transmit notification of this process to the Secretary of Health and Human Services (Secretary of HHS) and allow for public notice and comment. Regarding cannabidiol preparations (prepared from hemp or hemp-derived), WHO and its Expert Committee on Drug Dependence (ECDD) prepared a health hazard evaluation, which is

referenced here.¹ Cannabidiol while found in cannabis and cannabis resin, was not found to have the same psychoactive properties and results in no potential for abuse and no potential to produce dependence. It was also not found to present with significant ill effects upon ingestion. At its 40th Meeting, the ECDD considered this critical review of cannabidiol and recommended that preparations considered to be pure cannabidiol should not be scheduled within the International Drug Control Conventions. A footnote to the entry for cannabis and cannabis resin in Schedule 1 of the Single Convention on Narcotic Drugs (1961) was proposed to read “Preparations containing predominantly cannabidiol and not more than 0.2 percent of delta-9-tetrahydrocannabinol are not under international control.”

Regulatory Status of CBD in the US

FDA contains a page on their website titled “FDA and Marijuana”. FDA clearly states that “FDA has concluded that THC and CBD products are excluded from the dietary supplement definition under sections 201(ff)(3)(B)(i) and (ii) of the Federal Food, Drug and Cosmetic Act (FD&C Act), respectively. Under those provisions, if a substance (such as THC or CBD) is an active ingredient in a drug product that has been approved under 21 U.S.C. § 355 (section 505 of the FD&C Act), or has been authorized for investigation as a new drug for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public, then products containing that substance are outside the definition of a dietary supplement. FDA considers a substance to be "authorized for investigation as a new drug" if it is the subject of an Investigational New Drug application (IND) that has gone into effect. Under FDA’s regulations (21 CFR 312.2), unless a clinical investigation meets the limited criteria in that regulation, an IND is required for all clinical investigations of products that are subject to section

¹ World Health Organization. (2017). Cannabidiol (CBD) Pre-Review Report Agenda Item 5.2. Expert Committee on Drug Dependence. Thirty-ninth Meeting. Geneva, 6-19 November 2017.

505 of the FD&C Act. Moreover, the page goes on to add further clarity that “[t]here is an exception to sections 201(ff)(3)(B)(i) and (ii) if the substance was “marketed as” a dietary supplement or as a conventional food BEFORE the drug was approved or before the new drug investigations were authorized, as applicable. However, based upon available evidence, FDA has concluded that this is not the case for THC or CBD. NPA is also aware of the twenty (20) or more warning letters FDA has issued to companies marketing CBD as a dietary supplement.

Despite the agency’s actions and message, the market for CBD products in the US is surging. According to a recent report issued by New Frontier Data, the U.S. CBD industry grew by nearly 40% in 2017, reaching \$367 Million in annual sales across hemp-derived and marijuana-derived markets. At present the only federally approved CBD product is Epidiolex, a pharmaceutical product manufactured by GW Pharma and approved by FDA in 2018.

Growth of Hemp-Derived CBD Products in the Marketplace

The time for enforcement of CBD would have been several years ago when it was not as prevalent in the market. While CBD was a technically a federally “scheduled” substance prior to the passage of the 2018 Farm Bill in December, sales of CBD products continued to rise. Several states allow access to CBD oil and/or high-CBD strains of marijuana. To date, marijuana is legal in nine states and the District of Columbia for recreational use; CBD is legal with varying restrictions in 46 states.”² We would expect sales to continue to rise with the recent passage of the Farm Bill, which removed considerable regulatory risk from the Drug Enforcement Agency to firms selling

² Washington Post – Step right up for this cannabis cure, October 19, 2018
https://www.washingtonpost.com/opinions/step-right-up-for-this-cannabis-cure/2018/10/19/1eff6f66-d3da-11e8-8c22-fa2ef74bd6d6_story.html?utm_term=.b2263f3a8b72

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CBD in interstate commerce. As more firms engage in discussions over whether to manufacture/sell hemp-derived CBD, the lack of enforcement in this area has been troubling.

FDA Should Exhibit Enforcement Discretion Regarding Hemp-Derived CBD Products (Dietary Supplements) in the Marketplace

While NPA understands with intimate knowledge and remain respectful of the agency’s limited resources and vast priorities when it comes to safeguarding the nation’s food and drug supply, NPA and its member companies are concerned over what appears to be an absence of establishing a deterrent in this instance. Firms may weigh the regulatory risk of receiving a warning letter vs. the potential profitability and gains realized in sales of CBD products across state lines. Warning letters do not appear to serve as a severe enough punishment or deterrent in this regard.

The Agency was established to provide protection from harms in the marketplace. FDA has ample and adequate authority to regulate the marketplace, especially one, in this instance, that by its own word are products not eligible to be lawfully marketed. Yet this market of unlawful CBD products is surging, creating a problem that does indeed involve conscious opponents, and which even in considering resource constraints seems to be an approach of willful ignorance or learned helplessness. Understanding that no situation is one size fits all at the agency, it is unclear as to what the principles are here from the agency’s tradition of upholding the Federal Food Drug and Cosmetic Act. Taking final agency action on some of the largest CBD players and developing an enforcement strategy would go a long way to closing this perceived loophole and belief that CBD is permitted to be sold in interstate commerce as a dietary supplement.

FDA’s Internal Policy on CBD Should Be Made Public

FDA seems to be disinterested in pursuing CBD enforcement due to limited resources, the health hazard evaluation by WHO and its ECDD showing no effect on dependence, the magnitude of CBD products found in the marketplace, and a general belief that a public health concern over marijuana and hemp-derived CBD products lacks merit. If that is the case, FDA’s internal policy on enforcement discretion should be made public. The agency has made clear, as a matter of course, that when issues do not rise to the level of said priority, they are subject to enforcement discretion. This is important for established manufacturers and retailers who are facing the question every day as to why such products continue to be available for sale but not by those who have taken the FDA’s word to heart. If CBD enforcement is not a priority for the Agency, then such a formal signal from the FDA would allow for reputable firms to begin establishing standards for qualification, identity, and ethical conduct. These activities would help keep irresponsible or incompetent players out of the market, thereby enhancing the credibility and reputation of the established firms, limiting the potential for consumer harm.

Precedence for Allowing a Drug Constituent as Part of a Food (Dietary Supplement)

While FDA can formally remove the current exclusion of CBD as a dietary ingredient for use in dietary supplement through a petition by the Secretary for Health and Human Services, there is precedence for allowing drug constituents as naturally-occurring components in foods (dietary supplements). For example, red yeast rice contains the naturally-occurring HMG-CoA reductase inhibitor lovastatin (Mevacor®), which is an FDA-approved drug for lowering lipids. Red yeast rice is a permissible dietary ingredient for use in dietary supplements, just as CBD is a derived constituent from hemp, an herb or other ingredient, as described in 201(ff)(1)(C). In addition, reserpine, one of the first FDA-approved treatments for high blood pressure, can be found in *Rauvolfia* herbs like *Rauvolfia vomitoria* (devil’s pepper) and

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Rauvolfia serpentina (Indian snakeroot). *Rauvolfia* herbs are botanicals and fit under 201(ff)(1)(C) of the FD&CA. These are just two examples where FDA has allowed for a dietary supplement to be sold in which the supplement contains an FDA-approved drug as a naturally-occurring constituent.

New Dietary Ingredient (NDI) Notification as Critical Component of CBD Regulatory Pathway to Market

FDA should either formalize their internal policy on CBD enforcement in a meaningful way for the public or create a pathway that would remove the exclusion clause in 201(ff), specifically for CBD products, so that they can be eligible dietary ingredients for use in dietary supplements and other foods. NPA would like to point out that removal of the exclusion clause for CBD by the Secretary of HHS would not eliminate other regulatory barriers for any other new dietary ingredient introduced into the market after October 15, 1994, the implementation date for the Dietary Supplement Health and Education Act of 1994 (DSHEA). The New Dietary Ingredient (NDI) provision in DSHEA would become the final arbiter as to whether a given hemp-derived CBD extract would be permitted to be sold in interstate commerce in the U.S. This would require an NDI notification to be submitted to FDA within 75 days of marketing of any dietary supplement containing hemp-derived CBD extracts to ensure that the product(s) have a “reasonable expectation of safety” within the meaning of the FD&C Act. The NDI safety dossier would cover the identity of the ingredient, formulation specifications, limits on contaminants, and safety of the CBD ingredient. The NDI pathway to market could not be ignored by a company selling hemp-derived CBD products.

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Conclusion

Finally, NPA submitted a letter to FDA Commissioner Gottlieb on October 24, 2018 echoing these discussion points. While we have yet to hear back from FDA on our October letter, our Association and our member companies would welcome the opportunity to meet with the Agency further to discuss a workaround solution to allow CBD to be sold in dietary ingredients or any other ways we could address this very serious issue. Thanks for your consideration of this matter.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Dan Fabricant". The signature is fluid and cursive, with the first name "Dan" and the last name "Fabricant" clearly distinguishable.

Daniel Fabricant, Ph.D.

CEO and President, Natural Products Association