July 23, 2021

Mr. Tim Orr
Charlotte's Web, Inc.
1600 Pearl Street
Boulder, Colorado 80302

Dear Mr. Orr:

This letter is to inform you that the notification that you submitted pursuant to 21 United States Code (U.S.C.) § 350b(a)(2) (section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act (the Act)), was received and filed by the Food and Drug Administration (FDA or we) on March 31, 2021. Additional information was received on May 7, May 12, and June 21, 2021. The amendment received on May 12, 2021, was deemed a substantive amendment, which reset the filing date to May 12, 2021, as per 21 CFR 190.6(d). Your notification concerns the new dietary ingredient (NDI) "Charlotte's Web Full Spectrum Hemp Extract" (CW FSHE) (hereinafter "NDI 1202") that you intend to market in a dietary supplement tincture.

According to your notification, the conditions of use are: "The proposed maximum daily intake of dietary supplement tincture is two (2) servings per day. Each 0.15 mL serving of the tincture provides 12.9 mg of the CW FSHE extract (9.75 mg CBD). Suggested daily intake is 0.30 mL of the tincture providing 25.8 [mg of the] CW FSHE [extract] (19.5 mg CBD). Duration of use is intermittent. Target population is adults (18+ years) with instructions to consult your physician before use if you are pregnant, nursing, have or suspect a medical condition or are taking any medications. Also includes instructions to keep out of the reach of children."

Under 21 U.S.C. § 350b(a), the manufacturer or distributor of a dietary supplement containing a new dietary ingredient that has not been present in the food supply as an article used for food in a form in which the food has not been chemically altered must submit to FDA, at least 75 days before the dietary ingredient is introduced or delivered for introduction into interstate commerce, information that is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such new dietary ingredient will reasonably be expected to be safe. FDA reviews this information to determine whether it provides an adequate basis for such a conclusion. Under 21 U.S.C. § 350b(a)(2), there must be a history of use or other evidence of safety establishing that the new dietary ingredient, when used under the condition recommended or suggested in the labeling of the dietary supplement, will reasonably be expected to be safe. If this requirement is not met, the dietary supplement is considered to be adulterated under 21 U.S.C. § 342(f)(1)(B) because there is inadequate information to provide reasonable assurance that the new dietary ingredient does not present a significant or unreasonable risk of illness or injury.

FDA has carefully considered the information in your notification and other available information and determined that your NDI 1202 cannot be used in dietary supplements pursuant to the dietary supplement exclusion provision in 21 U.S.C. § 321(ff)(3)(B) (section 201(ff)(3)(B) of the Act). The definition of a dietary supplement is set forth in 21 U.S.C. § 321(ff) (section 201(ff) of the Act), which states in relevant part:

> (ff) The term 'dietary supplement' . . . (3) does . . . (B) not include – (i) an article that is approved as a new drug under section 355 of this title . . . or (ii) an article 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,
>
> which was not before such approval . . . or authorization marketed as a dietary supplement or as a food unless the Secretary, in the Secretary's discretion, has issued a regulation, after notice and comment, finding that the article would be lawful under this chapter.

FDA has concluded that CBD products are excluded from the dietary supplement definition under 21 U.S.C. § 321(ff)(3)(B) (section 201(ff)(3)(B) of the Act). CBD is the active ingredient in the approved drug product, Epidiolex. Furthermore, the existence of substantial clinical investigations involving CBD has been made public. FDA has also determined that CBD was not marketed as a dietary supplement or conventional food before it was authorized for investigation as a new drug.[1] FDA has concluded based on the record that your NDI 1202 is carefully designed to ensure consistent levels of CBD, and that it is produced from your proprietary (b) (4) that provide robust levels of CBD. In addition, your NDI 1202 contains a significant amount of CBD per mL and you also appear to market "full-spectrum hemp extract"-containing products as CBD products. Looking at the totality of the record, FDA has concluded that your NDI 1202 is a CBD product and thus is subject to the exclusion from the definition of dietary supplement under 21 U.S.C. § 321(ff)(3)(B). Accordingly, your product may not be marketed as or in a dietary supplement.

We also conclude that, even if your NDI 1202 was not excluded from the definition of dietary supplement, the agency has concerns about the adequacy of safety evidence included in your submission as a basis for concluding that a dietary supplement containing NDI 1202 will reasonably be expected to be safe under the conditions of use described in your notification. The notification included some evidence intended to show adequate history of safe use and also included reports of safety studies. These categories of evidence had deficiencies on their own and, even when all of the evidence was considered as a whole, the notification failed to show that the NDI will reasonably be expected to be safe. For example, your submission provided two years of marketing for NDI 1202 as evidence of history of use, which is insufficient to establish the safety of your ingredient when used under the proposed conditions of use. Furthermore, FDA was unable to accept your proposed no-observed adverse effect level (NOAEL), which was based on the publication by Dziwenka et al., 2020, because the publication included inadequate information for the purposes of assessing the reliability of the conclusions in the publication.

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[1] *See* "FDA Regulation of Cannabis and Cannabis-Derived Products, Including Cannabidiol (CBD)," available at https://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-including-cannabidiol-cbd#dietarysupplements

FDA requested that you provide the agency with the supporting or underlying data that formed the basis for the Dziwenka et al. 2020 study, but you did not provide FDA with this data. In addition, none of the clinical and pre-clinical studies that you provided adequately address certain reported toxicity endpoints of CBD such as hepatotoxicity and reproductive toxicity. For these reasons, the information in your submission indicates that, even if your NDI 1202 were not excluded from the definition of a dietary supplement, your notification does not provide an adequate basis to conclude that a dietary supplement containing the ingredient, when used under the proposed conditions of use, would reasonably be expected to be safe. Therefore, if it were a dietary supplement, a product containing your NDI 1202 may be adulterated under 21 U.S.C. § 342(f)(1)(B) (section 402(f)(1)(B) of the Act).

If you have additional or new information that has a bearing on the issues discussed in this letter, you may present it to FDA for our consideration.

Your notification will be kept confidential for 90 days after the filing date of May 12, 2021. After the 90-day date, the notification will be placed on public display at www.regulations.gov as new dietary ingredient notification report number 1202. Prior to that date, you may wish to identify in writing specifically what information you believe is trade secret or confidential commercial information and include an explanation of the basis for this belief.

If you have any questions concerning this matter please contact Jeanne Skanchy, R.Ph, by email at NDITEAM@fda.hhs.gov.

Sincerely,

Cara Welch -S Digitally signed by Cara Welch -S
Date: 2021.07.23 16:21:11 -04'00'

Cara Welch, Ph.D.
Acting Director
Office of Dietary Supplement Programs
Center for Food Safety and Applied Nutrition