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NDI Notifications For CBD 'Excluded' On Arrival But US FDA Still Explains Where Safety Evidence Fails

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Executive Summary

CFSAN Office of Dietary Supplement Programs tells Charlotte's Web and Irwin Naturals that not providing sufficient evidence of a reasonable assumption of safety for an NDI's intended use wasn't the only reason each notification was rejected.

The US Food and Drug Administration went to the trouble when rejecting two firms' new dietary ingredient notifications for cannabidiol of explaining that the firms didn't provide sufficient safety information after first stating that CBD is unlawful for use as a dietary ingredient anyway.

Both of the letters the Center for Food Safety and Applied Nutrition's Office of Dietary Supplement Programs submitted on 23 July to Charlotte's Web Inc. and to Irwin Naturals Inc. used an "even if" clause to explain that each firm's failure to provide sufficient evidence to support a reasonable assumption of safety of its NDI for the intended use wasn't the only reason the FDA rejected each notification.

Each letter states that "even if [the firm's NDI] 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 [the NDI] will reasonably be expected to be safe under the conditions of use described in your notification."

Both NDIs are excluded, ODSP explains in the letter as FDA officials have said since CBD and other hemp-derived cannabinoids emerged as ingredients in widely available supplements, food and non-drug topicals, because the agency deems the substances drug ingredients.

The letters explain that CBD is the active ingredient in an approved drug, Epidiolex; substantial clinical investigations involving CBD have been made public; and "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."

"After complying with FDA's requests, these companies saw FDA reject their NDI notifications—disregarding published peer-reviewed toxicology studies and years' worth of real-world safety evidence." – CRN CEO Steve Mister

Each of those reasons and all of them combined disqualify hemp-derived CBD and other cannabinoids from meeting the FDA's regulatory definition of a dietary ingredient, rendering them unlawful for use in dietary supplements available in the US.

Unanswered in the letters are questions about whether the synthetic CBD used as the active ingredient in Epidiolex, which was approved in 2018 for treatment of a rare form of pediatric epilepsy, should be considered the same hemp-derived CBD or other cannabinoid that Charlotte's Web, Irwin Naturals and numerous other firms want to use in supplements.

Another question left hanging is how the FDA concluded that US consumers didn't have access to purchase cannabinoid-containing supplements, food and non-drug topicals before the first investigation of any cannabinoid as a new drug was authorized.

HBW Insight submitted questions on those and other points to the FDA and was advised that answers wouldn't be available until 12 August.

Those also are questions that the Council for Responsible Nutrition has. CRN president and CEO Steve Mister says while the FDA fails to keep potentially unsafe cannabinoid supplements off the market, it's rejecting evidence Charlotte's Web and Irwin Naturals provided to market safe products.

The FDA "mischaracterized these products as the same article as a prescription drug and has ignored, dismissed, and downplayed ample evidence that these full-spectrum hemp products can be marketed in a manner that is reasonably expected to be safe," Mister said in a statement to HBW Insight.

"FDA continually asked the companies for meetings and safety data about their products containing full-spectrum hemp extract. After complying with FDA's requests, these companies saw FDA reject their NDI notifications—disregarding published peer-reviewed toxicology studies and years' worth of real-world safety evidence."

Currently Marketed Products' Safety Irrelevant

Like a multitude of large and small businesses in the US, Los Angeles-based Irwin Naturals and Denver-based Charlottes Web, which is a business of Stanley Brothers USA Holdings Inc, already are selling cannabinoid-containing supplements.

Irwin Naturals also sells cannabis-based products through its hydroCanna skin- and hair-care line; Stanley Brothers also markets containing cannabis-derived ingredients under namesake and ReCreate brands.

All of the firms' cannabinoid-containing products are considered unlawful under FDA regulations. However, while it considers opening a regulatory pathway for lawful use, the agency is exercising enforcement discretion to allow sales of cannabinoid-containing supplements that are manufactured and marketed in compliance with all relevant regulations. (Also see "Future Of CBD In Supplements: NDI Notification Looms As Regulatory Path " - HBW Insight, 3 Dec, 2019.)

"Even if [the firm's NDI] was not excluded from the definition of dietary supplement, the agency has concerns about the adequacy of safety evidence … as a basis for concluding that a dietary supplement containing [the NDI] will reasonably be expected to be safe." – ODSP letters

Each letter acknowledges that the firms already market CBD supplements. However, marketing cannabinoid supplements during this period of enforcement discretion doesn't qualify as showing the products are safe, according to the letters signed by acting ODSP director Cara Welch.

The firm's "submission provided two years of marketing for [its NDI] as evidence of history of use, which is insufficient to establish the safety of your ingredient when used under the proposed conditions of use," Welch wrote to Charlotte's Web.

Irwin Naturals' "evidence for history of use was vague and did not provide an adequate description of the cannabis preparations (e.g., composition), serving levels, or frequency and durations of use which makes it difficult to compare this history of use to the proposed conditions of use for your ingredient and establish the safety of your product," Welch advised the firm.

FDA 'Inaction' Doesn't Help Consumers

The FDA, CRN's Mister says, has created a market for hemp-derived cannabinoids in supplements that will be difficult to bring under control.

The agency has had ample time since Congress de-scheduled hemp as a controlled substance as part of the 2018 farm bill to establish regulations for using of hemp-derived ingredients in supplements.

"Meanwhile, the agency has done little to protect consumers from the unregulated marketplace it has created from more than two years of inaction," he said.

"Despite very clear direction from Congress when it removed hemp from the Controlled Substances Act in 2018, FDA seems to have made up its mind not to support CBD in supplements and is now trying to justify it. That's the only logical conclusion to draw from FDA's actions—and its continued inaction. These mixed messages from FDA are unacceptable, and Congress must exercise leadership by stepping in to end it."

Additionally, the agency apparently is ignoring that there is little similarity between the synthetic CBD it approved for use as a drug and the cannabinoids available in many supplements.

"FDA also claimed the full-spectrum ingredients containing CBD and Epidiolex should be considered the same 'article'" but Epidiolex "is a highly concentrated CBD isolate that contains 10 times more CBD than either of the full-spectrum hemp ingredients and plainly is not the same article supplement companies are producing, as CRN has argued for several years," Mister said.

Bills have been introduced in the House and Senate to authorize the FDA to allow cannabinoids' use in supplements; S. 1698 proposes allowing their use in both food and supplements while H.R. 841 limits the use to supplements. (Also see "Mixing Food In Legislation Changing US FDA Cannabinoid Rules Could Choke Its Progress" - HBW Insight, 25 May, 2021.)

Additionally, Senate majority leader Chuck Schumer, D-NY, joined by Democrats Cory Booker, D-NJ, and Ron Wyden, OR, has circulated a draft bill proposing that the FDA establish a safe daily use level for cannabinoids along with changing an the agency's regulation to allow the ingredients' use in supplements. The draft also proposes rules on producing, marketing and possessing marijuana. (Also see "Schumer Includes Cannabinoid Pathway For Supplements In Cannabis Legalization Draft Bill" - HBW Insight, 14 Jul, 2021.)

The House this year passed the Secure and Fair Enforcement "SAFE Banking" Act, H.R. 1996, sponsored by Rep. Ed Perlmutter, D-CO, to allow cannabis- and hemp-related businesses in states with some form of legalized marijuana to access financial institutions by creating protections for depository institutions that provide financial services to the companies. (Also see "Schumer Includes Cannabinoid Pathway For Supplements In Cannabis Legalization Draft Bill" - HBW Insight, 14 Jul, 2021.)