Appendix B

FDA determined that the earliest evidence of cannabidiol (CBD) potentially being marketed as a food or dietary supplement is August 1, 2011. In making this determination, FDA searched patent information from the U.S. Patent & Trademark Office's patent database, relevant scientific literature databases, the Old Dietary Ingredient List, FDA's New Dietary Ingredient internal database, relevant food databases, Internet (for marketing evidence), and internal FDA drug databases for "cannabidiol," "CBD," and their synonyms.

Working from that date (i.e., August 1, 2011), FDA then conducted an evaluation to determine whether (1) CBD has been authorized for clinical investigation[1] as a new drug; (2) substantial clinical investigations of CBD have been instituted; and (3) the existence of such investigations has been made public (section 201(ff)(3)(B)(ii)).

FDA conducted a search of internal sources for investigational new drug (IND) files with a product name of "cannabidiol," "CBD," and/or other terms that FDA determined are synonyms of "cannabidiol" and "CBD." Based on this review, we identified seven INDs that are authorized with the earliest authorized IND dated in the mid-1970s. Five of the seven INDs were authorized before August 1, 2011; cumulatively, the studies associated with these five INDs involved 2,140 subjects. We then searched external sources (i.e., National Library of Medicine's (NLM) clinical trial registry (www.clinicaltrials.gov), medical literal (PubMed) limited to human clinical trials, and an Internet search for articles or company press releases related to clinical trials) for clinical trials that appeared to correspond to IND files identified by a search of our internal sources. Based on a review of these internal and external sources, which included a review of clinical trial protocols for some of the identified INDs, we determined that substantial clinical investigations of CBD have been instituted. We also found that these investigations have been made public because all but one of the INDs appear to be listed in NLM's clinical trial registry. The remaining trial not found in NLM's clinical trial registry was made public via disclosure at a conference and was also described in a public database.

In summary, based on our review and employing the above methodology, FDA concludes that cannabidiol is 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. Further, we conclude that such authorization had already occurred prior to August 1, 2011. FDA has therefore concluded that cannabidiol products are excluded from the definition of "dietary supplement" under section 201(ff)(3)(B)(ii) of the FD&C Act.

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[1] FDA does not affirmatively approve or authorize an Investigational New Drug application (IND). Rather, INDs are authorized by operation of law (see 21 CFR 312.40(b)). FDA's actions with respect to the initiation of trials under an IND are passive in the sense that an IND goes into effect if FDA takes no action. A clinical investigation of an investigational new drug becomes authorized on the date the IND goes into effect. Per our regulations at 21 CFR 312.40(b), an IND goes into effect:

(1) Thirty days after FDA receives the IND, unless FDA notifies the sponsor that the investigations described in the IND are subject to a clinical hold under § 312.42; or
(2) On earlier notification by FDA that the clinical investigations in the IND may begin. FDA will notify the sponsor in writing of the date it receives the IND.