

JOHN J. COLEMAN, M.A., M.S., PH.D.

(b) (6)

Citizen Petition

June 4, 2020

Division of Dockets Management
Food and Drug Administration
U.S. Department of Health and Human Services
Room 1061
5630 Fishers Lane
Rockville, MD 20852

To the Commissioner of Food and Drugs:

The undersigned submits this petition pursuant to 21 CFR §10.30 (*Citizen Petition*) and the relevant provisions of the Federal Food, Drug, and Cosmetic Act and the Administrative Procedure Act to request the Commissioner of Food and Drugs to amend the label (aka Prescribing Information, aka Instructions for Use) for Epidiolex®. Specifically, the Commissioner is asked to change the language in subparagraph 9.1 of the label that states, “EPIDIOLEX is not a controlled substance,” to correctly and accurately indicate that “EPIDIOLEX is a Schedule V controlled substance.”

A. Action Requested

This petition respectfully requests the Commissioner to correct or amend, as necessary, the FDA-approved label for Epidiolex, an approved human drug containing cannabidiol (CBD). This drug is marketed in the United States by Greenwich Biosciences, Inc. (Greenwich), Carlsbad, CA 92008. The current FDA-approved label for Epidiolex was issued to Greenwich as “Revised: 04/2020.” (See Exhibit 1, attached)

Existing wording in Epidiolex label:

9 DRUG ABUSE AND DEPENDENCE
9.1 Controlled Substance
EPIDIOLEX is not a controlled substance.

Proposed amendment petitioned by the undersigned:

9 DRUG ABUSE AND DEPENDENCE
9.1 Controlled substance
EPIDIOLEX is a Schedule V controlled substance

B. Statement of Grounds

On June 25, 2018, The FDA approved a new drug application for Epidiolex, a drug the agency described in its press release as the “First Drug Comprised of an Active Ingredient Derived from Marijuana to Treat Rare, Severe Forms of Epilepsy.” (See Exhibit 2, attached) The ingredient in Epidiolex that is derived from marijuana is cannabidiol (CBD), a non-psych psychoactive cannabinoid.

Prior to the FDA’s approval of Epidiolex, all cannabinoids identified in marijuana, including CBD, were designated Schedule I controlled substances under the Controlled Substances Act (CSA).¹ The approval of medical use for the Epidiolex formulation of CBD meant that this drug and this cannabinoid (CBD) could no longer be listed in Schedule I, a category exclusively reserved for drugs that, *inter alia*, are not approved for medical use in the United States.²

The usual process for placing a drug under control requires a collaborative action between the FDA and the Drug Enforcement Administration (DEA) as authorized by the CSA.³ This process includes the completion of a medical and scientific evaluation of the drug or other substance along with a recommendation by the Secretary of the Department of Health and Human Services (HHS) to the Attorney General to control or not to control the drug or other substance.⁴

Under the customary CSA process for scheduling a drug, both agencies are expected to agree on a Schedule when control is justified by the determination of abuse potential as evidenced by the medical and scientific evaluations carried out by each agency. If the Secretary recommends that a drug or other substance not be controlled, this recommendation is *binding* on the Attorney General.⁵

However, because Epidiolex contains a cannabinoid ingredient, its control is governed by a different provision in the CSA that requires the Attorney General to issue an Order controlling a drug when control is required by an international treaty, convention, or protocol.⁶ CBD, as an “extract” of cannabis (marijuana), is a controlled substance under the provisions of the Single Convention on Narcotic Drugs, an international treaty to which the United States is a party and which entered into force for the United States on June 24, 1967.⁶

Because Article VI, sect. 2, of the United States Constitution provides that all treaties made under the authority of the United States “shall be the supreme Law of the Land,” the CSA directs the Attorney General to ensure compliance with treaty obligations when it comes to drug control and scheduling decisions.⁶

On September 28, 2018, the administrator of the DEA, pursuant to the authority delegated by the Attorney General, issued a Final Order under 21 USC §811(d), placing FDA-approved drugs containing CBD in Schedule V of the CSA.⁶ (See Exhibit 3) In the Final Order, the DEA administrator stated:

It bears emphasis that where, as here, control of a drug is required by the Single Convention, the DEA Administrator “shall issue an order controlling such drug under the schedule he deems most appropriate to carry out such obligations, *without regard to the findings required by [21 U.S.C. 811 (a) or 812(b)] and without regard to the procedures prescribed by [21 U.S.C. 811 (a) or (b)].*” 21 U.S.C. 811(d)(1) (emphasis added). Thus, in such circumstances, the Administrator is not obligated to request a medical and scientific evaluation or scheduling recommendation from the Department of Health and

Human Services (HHS) (as is normally done pursuant to section 811(b)). Nonetheless, DEA did seek such an evaluation and recommendation from HHS with respect to the Epidiolex formulation. In responding to that request, HHS advised DEA that it found the Epidiolex formulation to have a very low potential for abuse and, therefore, recommended that, if DEA concluded that control of the drug was required under the Single Convention, Epidiolex should be placed in schedule V of the CSA. Although I am not required to consider this HHS recommendation when issuing an order under section 811(d)(1), because I believe there are two legally viable scheduling options (listed above), both of which would satisfy the United States' obligations under the Single Convention, I will exercise my discretion and choose the option that most closely aligns to the HHS recommendation. Namely, I am hereby ordering that the Epidiolex formulation (and any future FDA-approved generic versions of such formulation made from cannabis) be placed in schedule V of the CSA. [emphasis as in original text, internal footnote to statutory authority omitted]⁶

To date (June 4, 2020), there has been no modification or change to the DEA's Final Order placing FDA-approved CBD products, including Epidiolex, in Schedule V of the CSA.

Yet, the FDA-approved labeling for Epidiolex, including the most recently revised version (04/2020), clearly but incorrectly states, "EPIDIOLEX is not a controlled substance." This not only is contrary to the HHS recommendation referred to above in the DEA administrator's Final Order, but also legally groundless and likely to mislead prescribers and patients to ignore the health risks associated with using Schedule V controlled substances.

The placement of a drug or other substance under the control of the CSA is an important element in the overall protection of public health. The supply chain for controlled substances requires registration by the DEA of entities at every juncture to prevent diversion of regulated drugs from legitimate to illegitimate channels. In addition, the DEA's aforementioned Final Order revised 21 CFR §1312.30, to require DEA-issued import and export permits for finished CBD drug products approved by the FDA.^{6,7}

Thus, as this brief analysis shows, the incorrect designation by FDA of Epidiolex as not being a controlled substance not only misleads prescribers and patients on the health risks of this drug, but also contradicts and may interfere with the lawful control and security of the import and export of Epidiolex and other FDA-approved CBD products.

In view of the forgoing analysis and grounds, the undersigned respectfully requests that the Commissioner correct the label for Epidiolex to reflect that it is a Schedule V controlled substance.

C. Environmental Impact

Petitioner asserts a categorial exclusion for this matter under the appropriate chapter and subparagraph of Title 21, Code of Federal Regulations.

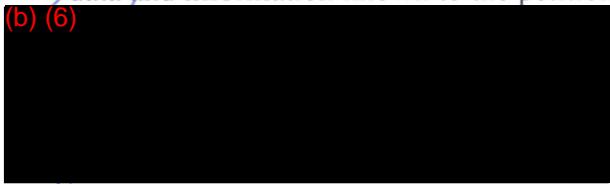
D. Economic Impact

Upon review and request by the Commissioner, as authorized, an economic impact analysis will be provided by the petitioner.

E. Certification

The undersigned certifies that, to the best knowledge and belief of the undersigned, this Petition includes all information and views on which the Petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the Petition.

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/ John J. Coleman, MA, MS, PhD

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References cited

1. United States Code. Controlled Substances Act, Title II, 21 USC 812; *Schedules of controlled substances*, Pub.L. 91-513, 84 Stat. 1242. 1970.
2. Controlled Substances Act. Title 21, United States Code, § 812(b)(1). 1970.
3. Controlled Substances Act, Title 21, United States Code, Sec. 811(b), Evaluation of drugs and other substances. 1970.
4. Controlled Substances Act, Title 21, United States Code, Sec. 811, Authority and criteria for classification of substances. 1970.
5. Controlled Substances Act, Title 21, United States Code, Sec. 811(d), International treaties, conventions, and protocols requiring control; procedures respecting changes in drug schedules of Conventions on Psychotropic Substances. 1970.
6. Federal Register. Schedules of Controlled Substances: Placement in Schedule V of Certain FDA-Approved Drugs Containing Cannabidiol; Corresponding Change to Permit Requirements [Vol. 83, No. 189; 83 FR 48950]. 2018.
7. Code of Federal Regulations. 21 CFR 1312.30 Schedule III, IV, and V (nonnarcotic controlled substances requiring an import and export permit). 2020.

Appendix

Exhibit 1: Copy of current FDA-approved label for Epidiolex

Exhibit 2: Copy of June 25, 2018 press release by FDA announcing approval of Epidiolex

Exhibit 3: DEA Final Order, dated September 28, 2018, placing all FDA-approved CBD drugs in Schedule V

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