

Dated: September 24, 2018.
Leslie Kux,
Associate Commissioner for Policy.
 [FR Doc. 2018–21146 Filed 9–27–18; 8:45 am]
BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 520, 522, 524, and 558

[Docket No. FDA–2018–N–0002]

New Animal Drugs; Withdrawal of Approval of New Animal Drug Applications

AGENCY: Food and Drug Administration, HHS.

ACTION: Notification of withdrawal.

SUMMARY: The Food and Drug Administration (FDA) is withdrawing approval of 12 new animal drug applications (NADAs) at the sponsor’s request because these products are no longer manufactured or marketed.

DATES: Withdrawal of approval is effective October 9, 2018.

FOR FURTHER INFORMATION CONTACT:

Sujaya Dessai, Center for Veterinary Medicine (HFV–212), Food and Drug Administration, 7519 Standish Pl., Rockville, MD 20855, 240–402–5761, *sujaya.dessai@fda.hhs.gov*.

SUPPLEMENTARY INFORMATION: Virbac AH, Inc., 3200 Meacham Blvd., Ft. Worth, TX 76137, has requested that FDA withdraw approval of the NADAs listed in the following table because the products are no longer manufactured or marketed:

File No.	Product name	21 CFR section
011–779 ...	PURINA PIGEMIA 100 (colloidal ferric oxide).	522.1182
040–205 ...	PURINA Horse Wormer Medicated (thiabendazole).	520.2380a
042–116 ...	PURINA 6 DAY WORM-KILL Feed Premix (coumaphos).	558.185
043–215 ...	PURINA GRUB-KILL Pour-on Cattle Insecticide (famphur).	524.900
046–700 ...	STATYL Medicated Premix (nequinatate).	558.365
091–260 ...	PULVEX WORM CAPS (piperazine phosphate monohydrate).	520.1804
097–258 ...	PURINA BAN-WORM for Pigs (pyrantel tartrate).	558.485
102–942 ...	PULVEX Multipurpose Worm Caps (dichlorophene, tol-uene).	520.580
113–748 ...	PURINA PIGEMIA Oral (iron dextran complex).	520.1182
135–941 ...	CHECK-R-TON BM (pyrantel tartrate).	558.485

File No.	Product name	21 CFR section
136–116 ...	PURINA WORM-A-REST™ Litter Pack Premix (fenbendazole).	520.905d
140–869 ...	PURINA SAF-T-BLOC BG Medicated Feed Block (poloxalene, 6.6%).	520.1840

Therefore, under authority delegated to the Commissioner of Food and Drugs, and in accordance with § 514.116 *Notice of withdrawal of approval of application* (21 CFR 514.116), notice is given that approval of NADAs 011–779, 040–205, 042–116, 043–215, 046–700, 091–260, 097–258, 102–942, 113–748, 135–941, 136–116, and 140–869, and all supplements and amendments thereto, is hereby withdrawn, effective October 9, 2018.

Elsewhere in this issue of the **Federal Register**, FDA is amending the animal drug regulations to reflect the voluntary withdrawal of approval of these applications.

Dated: September 24, 2018.
Leslie Kux,
Associate Commissioner for Policy.
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DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Parts 1308, 1312

[Docket No. DEA–486]

Schedules of Controlled Substances: Placement in Schedule V of Certain FDA-Approved Drugs Containing Cannabidiol; Corresponding Change to Permit Requirements

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Final order.

SUMMARY: With the issuance of this final order, the Acting Administrator of the Drug Enforcement Administration places certain drug products that have been approved by the Food and Drug Administration (FDA) and which contain cannabidiol (CBD) in schedule V of the Controlled Substances Act (CSA). Specifically, this order places FDA-approved drugs that contain CBD derived from cannabis and no more than 0.1 percent tetrahydrocannabinols in schedule V. This action is required to satisfy the responsibility of the Acting Administrator under the CSA to place a drug in the schedule he deems most appropriate to carry out United States obligations under the Single Convention

on Narcotic Drugs, 1961. Also consistent therewith, DEA is adding such drugs to the list of substances that may only be imported or exported pursuant to a permit.

DATES: Effective September 28, 2018.

FOR FURTHER INFORMATION CONTACT:

Kathy L. Federico, Regulatory Drafting and Policy Support Section (DPW), Diversion Control Division, Drug Enforcement Administration; Mailing Address: 8701 Morrisette Drive, Springfield, Virginia 22152; Telephone: (202) 598–6812.

SUPPLEMENTARY INFORMATION:

Background and Legal Authority

The United States is a party to the Single Convention on Narcotic Drugs, 1961 (Single Convention), and other international conventions designed to establish effective control over international and domestic traffic in controlled substances. 21 U.S.C. 801(7). The Single Convention entered into force for the United States on June 24, 1967, after the Senate gave its advice and consent to the United States’ accession. *See* Single Convention, 18 U.S.T. 1407. The enactment and enforcement of the Controlled Substances Act (CSA) are the primary means by which the United States carries out its obligations under the Single Convention.¹ Various provisions of the CSA directly reference the Single Convention. One such provision is 21 U.S.C. 811(d)(1), which relates to scheduling of controlled substances.

As stated in subsection 811(d)(1), if control of a substance is required “by United States obligations under international treaties, conventions, or protocols in effect on October 27, 1970, the Attorney General 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 [subsections 811(a) or 812(b)] and without regard to the procedures prescribed by [subsections 811(a) and (b)].” This provision is consistent with the Supremacy Clause of the U.S. Constitution (art. VI, sec. 2), which provides that all treaties made under the authority of the United States “shall be the supreme Law of the Land.” In accordance with this constitutional

¹ *See* S. Rep. No. 91–613, at 4 (1969) (“The United States has international commitments to help control the worldwide drug traffic. To honor those commitments, principally those established by the Single Convention on Narcotic Drugs of 1961, is clearly a Federal responsibility.”); *Control of Papaver Bracteatum*, 1 Op. O.L.C. 93, 95 (1977) (“[A] number of the provisions of [the CSA] reflect Congress’ intent to comply with the obligations imposed by the Single Convention.”).

mandate, under section 811(d)(1), Congress directed the Attorney General (and the Administrator of DEA, by delegation)² to ensure that compliance by the United States with our nation's obligations under the Single Convention is given top consideration when it comes to scheduling determinations.

Section 811(d)(1) is relevant here because, on June 25, 2018, the Food and Drug Administration (FDA) announced that it approved a drug that is subject to control under the Single Convention. Specifically, the FDA announced that it approved the drug Epidiolex for the treatment of seizures associated with two rare and severe forms of epilepsy, Lennox-Gastaut syndrome and Dravet syndrome, in patients two years of age and older. www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm611046.htm. Epidiolex is an oral solution that contains cannabidiol (CBD) extracted from the cannabis plant. This is the first FDA-approved drug made from the cannabis plant.³ Now that Epidiolex has been approved by the FDA, it has a currently accepted medical use in treatment in the United States for purposes of the CSA. Accordingly, Epidiolex no longer meets the criteria for placement in schedule I of the CSA. *See* 21 U.S.C. 812(b) (indicating that while substances in schedule I have no currently accepted medical use in treatment in the United States, substances in schedules II–V do); *see also United States v. Oakland Cannabis Buyers' Cooperative*, 532 U.S. 483, 491–92 (2001) (same). DEA must therefore take the appropriate scheduling action to remove the drug from schedule I.

In making this scheduling determination, as section 811(d)(1) indicates, it is necessary to assess the relevant requirements of the Single Convention. Under the treaty, cannabis, cannabis resin, and extracts and tinctures of cannabis are listed in Schedule I.⁴ The cannabis plant

contains more than 100 cannabinoids. Among these are tetrahydrocannabinols (THC) and CBD.⁵ Material that contains THC and CBD extracted from the cannabis plant falls within the listing of extracts and tinctures of cannabis for purposes of the Single Convention.⁶ Thus, such material, which includes, among other things, a drug product containing CBD extracted from the cannabis plant, is a Schedule I drug under the Single Convention.

Parties to the Single Convention are required to impose a number of control measures with regard to drugs listed in Schedule I of the Convention. These include, but are not limited to, the following:

- Limiting exclusively to medical and scientific purposes the production, manufacture, export, import, distribution of, trade in, use and possession of such drugs. Article 4.
- Furnishing to the International Narcotics Control Board (INCB) annual estimates of, among other things, quantities of such drugs to be consumed for medical and scientific purposes, utilized for the manufacture of other drugs, and held in stock. Article 19.
- Furnishing to the INCB statistical returns on the actual production, utilization, consumption, imports and exports, seizures, and stocks of such drugs during the prior year. Article 20.
- Requiring that licensed manufacturers of such drugs obtain quotas specifying the amounts of such drugs they may manufacture to prevent excessive production and accumulation beyond that necessary to satisfy legitimate needs. Article 29.
- Requiring manufacturers and distributors of such drugs to be licensed. Articles 29 & 30.
- Requiring medical prescriptions for the dispensing of such drugs to patients. Article 30.
- Requiring importers and exporters of such drugs to be licensed and requiring each individual importation or exportation to be predicated on the issuance of a permit. Article 31.

cannabis resin are among the drugs listed in Schedule IV of the Single Convention.

⁵ There are numerous isomers of cannabidiol, which will be referred to here collectively as "CBD."

⁶ Although the Single Convention does not define the term "extract," the ordinary meaning of that term would include a product, such as a concentrate of a certain chemical or chemicals, obtained by a physical or chemical process. *See, e.g., Webster's Third New International Dictionary* 806 (1976). Thus, the term extract of cannabis would include any product that is made by subjecting cannabis material to a physical or chemical process designed to isolate or increase the concentration of one or more of the cannabinoid constituents.

• Prohibiting the possession of such drugs except under legal authority. Article 33.

• Requiring those in the legitimate distribution chain (manufacturers, distributors, scientists, and those who lawfully dispense such drugs) to keep records that show the quantities of such drugs manufactured, distributed, dispensed, acquired, or otherwise disposed of during the prior two years. Article 34.

Because the CSA was enacted in large part to satisfy United States obligations under the Single Convention, many of the CSA's provisions directly implement the foregoing treaty requirements. None of the foregoing obligations of the United States could be satisfied for a given drug if that drug were removed entirely from the CSA schedules. At least one of the foregoing requirements (quotas) can only be satisfied if the drug that is listed in Schedule I of the Single Convention is also listed in schedule I or II of the CSA because, as 21 U.S.C. 826 indicates, the quota requirements generally apply only to schedule I and II controlled substances.

The permit requirement warrants additional explanation. As indicated above, the Single Convention obligates parties to require a permit for the importation and exportation of drugs listed in Schedule I of the Convention. This permit requirement applies to a drug product containing CBD extracted from the cannabis plant because, as further indicated above, such a product is a Schedule I drug under the Single Convention. However, under the CSA⁷ and DEA regulations, the import/export permit requirement does not apply to all controlled substances. Rather, a permit is required to import or export any controlled substance in schedule I and II as well as certain controlled substances in schedules III, IV, and V. *See* 21 U.S.C. 952 and 953; 21 CFR 1312.11, 1312.12, 1312.21, 1312.22. Thus, in deciding what schedule is most appropriate to carry out the United States' obligations under the Single Convention with respect to the importation and exportation of Epidiolex, I conclude there are two options:

(i) Control the drug in schedule II, which will automatically require an

⁷ The provisions of federal law relating to the import and export of controlled substances—those found in 21 U.S.C. 951 through 971—are more precisely referred to as the Controlled Substances Import and Export Act (CSIEA). However, federal courts and DEA often use the term "CSA" to refer collectively to all provisions from 21 U.S.C. 801 through 971 and, for ease of exposition, this document will do likewise.

² 28 CFR 0.100.

³ The drug Marinol was approved by the FDA in 1985. Marinol contains a *synthetic* form of dronabinol (an isomer of tetrahydrocannabinol) and thus is not made from the cannabis plant.

⁴ The text of the Single Convention capitalizes schedules (e.g., "Schedule I"). In contrast, the text of the CSA generally refers to schedules in lower case. This document will follow this approach of using capitalization or lower case depending on whether the schedule is under the Single Convention or the CSA.

It should also be noted that the schedules of the Single Convention operate somewhat differently than the schedules of the CSA. Unlike the CSA, the Single Convention imposes additional restrictions on drugs listed in Schedule IV that go beyond those applicable to drugs listed in Schedule I. All drugs in Schedule IV of the Single Convention are also in Schedule I of the Convention. Cannabis and

import/export permit under existing provisions of the CSA and DEA regulations or

(ii) control the drug in schedule III, IV, or V, and simultaneously amend the regulations to require a permit to import or export Epidiolex.

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)).⁸ 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.⁹ 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.

As noted, this order placing the Epidiolex formulation in schedule V will only comport with section 811(d)(1) if all importations and exportations of the drug remain subject to the permit requirement. Until now, since the Epidiolex formulation had been a schedule I controlled substance, the importation of the drug from its foreign production facility has always been subject to the permit requirement. To ensure this requirement remains in place (and thus to prevent any lapse in compliance with the requirements of the Single Convention), this order will amend the DEA regulations (21 CFR 1312.30) to add the Epidiolex formulation to the list of nonnarcotic schedule III through V controlled substances that are subject to the import and export permit requirement.

Finally, a brief explanation is warranted regarding the quota requirement in connection with the Single Convention. As indicated above, for drugs listed in Schedule I of the Convention, parties are obligated to require that licensed manufacturers of such drugs obtain quotas specifying the amounts of such drugs they may manufacture. The purpose of this treaty requirement is to prevent excessive production and accumulation beyond that necessary to satisfy legitimate needs. Under this scheduling order, the United States will continue to meet this obligation because the bulk cannabis material used to make the Epidiolex formulation (as opposed to the FDA-approved drug product in finished dosage form) will remain in schedule I of the CSA and thus be subject to all applicable quota provisions under 21 U.S.C. 826.¹⁰

Requirements for Handling FDA-Approved Products Containing CBD

As noted, until now, Epidiolex has been a schedule I controlled substance. By virtue of this order, Epidiolex (and any generic versions of the same formulation that might be approved by the FDA in the future) will be a schedule V controlled substance. Thus, all persons in the distribution chain who handle Epidiolex in the United States (importers, manufacturers, distributors, and practitioners) must comply with the requirements of the CSA and DEA regulations relating to schedule V controlled substances. As

further indicated, any material, compound, mixture, or preparation *other than Epidiolex* that falls within the CSA definition of marijuana set forth in 21 U.S.C. 802(16), including any non-FDA-approved CBD extract that falls within such definition, remains a schedule I controlled substance under the CSA.¹¹ Thus, persons who handle such items will continue to be subject to the requirements of the CSA and DEA regulations relating to schedule I controlled substances.

Regulatory Analyses

Administrative Procedure Act

The CSA provides for an expedited scheduling action where control of a drug is required by the United States’ obligations under the Single Convention. 21 U.S.C. 811(d)(1). Under such circumstances, the Attorney General must “issue an order controlling such drug under the schedule he deems most appropriate to carry out such obligations,” without regard to the findings or procedures otherwise required for scheduling actions. *Id.* (emphasis added). Thus, section 811(d)(1) expressly requires that this type of scheduling action not proceed through the notice-and-comment rulemaking procedures governed by the Administrative Procedure Act (APA), which generally apply to scheduling actions; it instead requires that such scheduling action occur through the issuance of an “order.”

Although the text of section 811(d)(1) thus overrides the normal APA considerations, it is notable that the APA itself contains a provision that would have a similar effect. As set forth in 21 U.S.C. 553(a)(1), the section of the APA governing rulemaking does not apply to a “foreign affairs function of the United States.” An order issued under section 811(d)(1) may be considered a foreign affairs function of the United States because it is for the express purpose of ensuring that the

⁸ In the House Report to the bill that would become the CSA (H. Rep. No. 91–1444, at 36 (1970)), this issue is explained as follows:

Under subsection [811(d)], where control of a drug or other substance by the United States is required by reason of its obligations under [the Single Convention], the bill does not require that the Attorney General seek an evaluation and recommendation by the Secretary of Health, Education, and Welfare, or pursue the procedures for control prescribed by the bill but he may include the drug or other substance under any of the five schedules of the bill which he considers most appropriate to carry out the obligations of the United States under the international instrument, and he may do so without making the specific findings otherwise required for inclusion of a drug or other substance in that schedule.

⁹ HHS most recently updated its medical and scientific evaluation and scheduling recommendation for the Epidiolex formulation by letter to DEA dated June 13, 2018.

¹⁰ At present, the cannabis used to make Epidiolex is grown in the United Kingdom and the drug is imported into the United States in finished dosage form.

¹¹ Nothing in this order alters the requirements of the Federal Food, Drug, and Cosmetic Act that might apply to products containing CBD. In announcing its recent approval of Epidiolex, the FDA Commissioner stated:

[W]e remain concerned about the proliferation and illegal marketing of unapproved CBD-containing products with unproven medical claims. . . . The FDA has taken recent actions against companies distributing unapproved CBD products. These products have been marketed in a variety of formulations, such as oil drops, capsules, syrups, teas, and topical lotions and creams. These companies have claimed that various CBD products could be used to treat or cure serious diseases such as cancer with no scientific evidence to support such claims.

www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm611047.htm.

United States carries out its obligations under an international treaty.

Executive Order 12866, 13563, and 13771, Regulatory Planning and Review, Improving Regulation and Regulatory Review, and Reducing Regulation and Controlling Regulatory Costs

This action is not a significant regulatory action as defined by Executive Order 12866 (Regulatory Planning and Review), section 3(f), and the principles reaffirmed in Executive Order 13563 (Improving Regulation and Regulatory Review), and, accordingly, this action has not been reviewed by the Office of Management and Budget (OMB).

This order is not an Executive Order 13771 regulatory action.

Executive Order 12988, Civil Justice Reform

This action meets the applicable standards set forth in sections 3(a) and 3(b)(2) of Executive Order 12988 to eliminate drafting errors and ambiguity, minimize litigation, provide a clear legal standard for affected conduct, and promote simplification and burden reduction.

Executive Order 13132, Federalism

This action does not have federalism implications warranting the application of Executive Order 13132. This action does not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government.

Executive Order 13175, Consultation and Coordination With Indian Tribal Governments

This action does not have tribal implications warranting the application of Executive Order 13175. The action does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal government and Indian tribes, or on the distribution of power and responsibilities between the Federal government and Indian tribes.

Regulatory Flexibility Act

The Regulatory Flexibility Act (RFA) (5 U.S.C. 601–612) applies to rules that are subject to notice and comment under section 553(b) of the APA or any other law. As explained above, the CSA exempts this order from the APA notice-and-comment rulemaking provisions. Consequently, the RFA does not apply to this action.

Paperwork Reduction Act of 1995

This action does not impose a new collection of information requirement under the Paperwork Reduction Act of 1995. 44 U.S.C. 3501–3521. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Congressional Review Act

As noted above, this action is an order, not a rulemaking. Accordingly, the Congressional Review Act (CRA) is inapplicable, as it applies only to rules. However, the DEA has submitted a copy of this final order to both Houses of Congress and to the Comptroller General, although such filing is not required under the Small Business Regulatory Enforcement Fairness Act of 1996 (CRA), 5 U.S.C. 801–808.

List of Subjects

21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

21 CFR Part 1312

Administrative practice and procedure, Drug traffic control, Exports, Imports, Reporting requirements.

For the reasons set out above, DEA amends 21 CFR parts 1308 and 1312 as follows:

PART 1308—SCHEDULES OF CONTROLLED SUBSTANCES

■ 1. The authority citation for part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b), 956(b) unless otherwise noted.

■ 2. In § 1308.15, add paragraph (f) to read as follows:

§ 1308.15 Schedule V.

* * * * *

(f) *Approved cannabidiol drugs.* (1) A drug product in finished dosage formulation that has been approved by the U.S. Food and Drug Administration that contains cannabidiol (2-[1R-3-methyl-6R-(1-methylethyl)-2-cyclohexen-1-yl]-5-pentyl-1,3-benzenediol) derived from cannabis and no more than 0.1 percent (w/w) residual tetrahydrocannabinols 7367

(2) [Reserved]

* * * * *

PART 1312—IMPORTATION AND EXPORTATION OF CONTROLLED SUBSTANCES

■ 3. The authority citation for part 1312 is revised to read as follows:

Authority: 21 U.S.C. 821, 871(b), 952, 953, 954, 957, 958.

■ 4. In § 1312.30, revise the introductory text and add paragraph (b) to read as follows:

§ 1312.30 Schedule III, IV, and V non-narcotic controlled substances requiring an import and export permit.

The following Schedule III, IV, and V non-narcotic controlled substances have been specifically designated by the Administrator of the Drug Enforcement Administration as requiring import and export permits pursuant to sections 201(d)(1), 1002(b)(2), and 1003(e)(3) of the Act (21 U.S.C. 811(d)(1), 952(b)(2), and 953(e)(3)):

* * * * *

(b) A drug product in finished dosage formulation that has been approved by the U.S. Food and Drug Administration that contains cannabidiol (2-[1R-3-methyl-6R-(1-methylethyl)-2-cyclohexen-1-yl]-5-pentyl-1,3-benzenediol) derived from cannabis and no more than 0.1 percent (w/w) residual tetrahydrocannabinols.

Dated: September 21, 2018.

Uttam Dhillon,

Acting Administrator.

[FR Doc. 2018–21121 Filed 9–27–18; 8:45 am]

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DEPARTMENT OF HOMELAND SECURITY

Coast Guard

33 CFR Part 100

[Docket No. USCG–2018–0795]

Special Local Regulations for Marine Events; San Francisco Bay Navy Fleet Week Parade of Ships and Blue Angels Demonstration, San Francisco, CA

AGENCY: Coast Guard, DHS.

ACTION: Notice of enforcement of regulation.

SUMMARY: The Coast Guard will enforce the special local regulations in the navigable waters of the San Francisco Bay for the San Francisco Bay Navy Fleet Week Parade of Ships and Blue Angels Demonstration from October 4 through October 7, 2018. This action is necessary to ensure the safety of event participants and spectators. During the enforcement period, unauthorized