4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 15

[Docket No. FDA-2019-N-1482]

Scientific Data and Information about Products Containing Cannabis or Cannabis-Derived Compounds; Public Hearing; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public hearing; request for comments.

SUMMARY: The Food and Drug Administration (FDA, the Agency, or we) is announcing a public hearing to obtain scientific data and information about the safety, manufacturing, product quality, marketing, labeling, and sale of products containing cannabis or cannabis-derived compounds.

DATES: The public hearing will be held on May 31, 2019, from 8 a.m. to 6 p.m. Submit requests to make oral presentations and comments at the public hearing by May 10, 2019. Electronic or written comments will be accepted until July 2, 2019. See the SUPPLEMENTARY INFORMATION section for registration and information.

ADDRESSES: The public hearing will be held at FDA White Oak Campus,10903 New Hampshire Ave., Building 31 Conference Center, the Great Room (rm. 1503), Silver Spring, MD 20993. Entrance for the public hearing participants (non-FDA employees) is through Building 1, where routine security check procedures will be performed. For parking and security information, please refer to

https://www.fda.gov/AboutFDA/WorkingatFDA/BuildingsandFacilities/WhiteOakCampusInformation/ucm241740.htm.

FDA is establishing a docket for public comment on this hearing. The docket number is FDA-2019-N-1482. The docket will close on July 2, 2019. Submit either electronic or written comments on this public hearing by July 2, 2019. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before July 2, 2019. The https://www.regulations.gov electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of July 2, 2019. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: https://www.regulations.gov. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to https://www.regulations.gov will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on https://www.regulations.gov.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2019-N-1482 for "Scientific Data and Information about Products Containing Cannabis or Cannabis-Derived Compounds; Public Hearing; Request for Comments." Received comments, those filed in a timely manner (see ADDRESSES), will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at https://www.regulations.gov or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in our

consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on https://www.regulations.gov. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to https://www.regulations.gov and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Beth F. Fritsch, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 32, Rm. 5308, Silver Spring, MD 20993, 301-796-8451, StakeholderEngagement@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background and Purpose of Hearing

Cannabis is a plant of the Cannabaceae family and contains more than 80 biologically active chemical compounds. The most commonly known compounds are delta-9-

tetrahydrocannabinol (THC) and cannabidiol (CBD). Parts of the *Cannabis sativa* plant have been controlled under the Federal Controlled Substances Act (CSA) since 1970 under the drug class "Marihuana" (21 U.S.C. 802(16).[1] "Marihuana" is listed in Schedule I of the CSA due to its high potential for abuse, which is attributable in large part to the psychoactive effects of THC, and the absence of a currently accepted medical use for marijuana in the United States. Cannabis and cannabis-derived products have been the subject of increasing interest by consumers, industry, researchers, the public, and regulators. Regulatory oversight of products containing cannabis or cannabis-derived compounds is complex and involves multiple Federal and State agencies.

The legality of cannabis has been changing over time at both the State and Federal levels. Currently, 33 States and Washington, D.C., allow "medical" use of marijuana under State law and 14 additional States have State law "medical" programs that are limited to CBD products. In addition, 10 States and Washington, D.C., have legalized marijuana for recreational use under State law, and 13 additional States have decriminalized recreational marijuana possession under State law in some form.

At the Federal level, the Agriculture Improvement Act of 2018, Pub. L. 115-334 (the 2018 Farm Bill), was signed into law on December 20, 2018. Among other things, this new law changes certain Federal authorities relating to the production and marketing of hemp, defined as the plant *Cannabis sativa L*. and any part of that plant, including the seeds thereof and all derivatives, extracts, cannabinoids, isomers, acids, salts, and salts of isomers, whether growing

[1] Under the CSA, the term "marihuana" means all parts of the plant *Cannabis sativa L*., whether growing or not; the seeds thereof; the resin extracted from any part of such plant; and every compound, manufacture, salt, derivative, mixture, or preparation of such plant, its seeds or resin. Such a term does not include hemp or the mature stalks of such plant, fiber produced from such stalks, oil or cake made from the seeds of such plant, any other compound, manufacture, salt, derivative, mixture, or preparation of such mature stalks (except the resin extracted therefrom), fiber, oil, or cake, or the sterilized seed of such plant which is incapable of germination.

or not, with a delta-9 tetrahydrocannabinol concentration of not more than 0.3 percent on a dry weight basis. These changes include removing hemp from the CSA, which means that cannabis plants and derivatives that contain no more than 0.3 percent THC on a dry weight basis are no longer controlled substances under Federal law.

The 2018 Farm Bill explicitly preserved FDA's authority to regulate products containing cannabis or cannabis-derived compounds under the Federal Food, Drug, and Cosmetic Act (FD&C Act) and section 351 of the Public Health Service Act.[2] In doing so, Congress recognized FDA's important public health role with respect to all the products it regulates. Therefore, because the 2018 Farm Bill did not change FDA's authorities, cannabis and cannabis-derived products are subject to the same authorities and requirements as FDA-regulated products containing any other substance, regardless of whether the products fall within the definition of "hemp" under the 2018 Farm Bill.

FDA is aware that some companies are marketing products containing cannabis and cannabis-derived compounds in ways that violate the FD&C Act. FDA has taken action against companies illegally selling cannabis and cannabis-derived products that put the health and safety of consumers at risk. For example, FDA has issued warning letters[3] to companies illegally selling CBD products that were intended to prevent, diagnose, mitigate, treat, or cure serious diseases, such as cancer, and that had not obtained new drug approvals. Selling unapproved drug products with unsubstantiated therapeutic claims is not only a violation of the law, but also can put patients at risk as the marketing of unproven treatments raises significant public health concerns. Patients and other consumers may be influenced not to use approved therapies to treat serious and even fatal diseases.

[2] For a discussion of FDA's legal authorities, see section IV of this notice.
[3] https://www.fda.gov/NewsEvents/PublicHealthFocus/ucm484109.htm

FDA's warning letters also cited food products to which CBD had been added and CBD products marketed as dietary supplements. As discussed below, under current law, such products violate the FD&C Act because CBD is an active ingredient in an approved drug and has been the subject of substantial clinical investigations. Allowing drug ingredients in foods can undermine the drug approval process and diminish commercial incentives for further clinical study of the relevant drug substance. It also raises questions about the safety to consumers of exposure from broader consumption of such ingredients.

While the use of cannabis and cannabis-derived products, including hemp and hemp-derived products, has increased dramatically in recent years, questions remain regarding the safety considerations raised by the widespread use of these products. These questions could impact the approaches we consider taking in regulating the development and marketing of products. For example, a 2017 report by the National Academies of Sciences, Engineering, and Medicine[4] reviewed the scientific literature published since 1999 about what is known about the health impacts of cannabis and cannabis-derived products and identified the need for additional research. In addition, during its review of the marketing application for EPIDIOLEX, a CBD oral solution indicated for the treatment of seizures associated with Lennox-Gastaut syndrome and Dravet syndrome in patients 2 years of age and older that was approved in 2018, FDA identified certain safety concerns (see FDA's drug approval package at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/210365Orig1s000TOC.cfm). Specifically, at doses of 20 milligrams per kilogram of body weight per day (mg/kg/day) of EPIDIOLEX in clinical trials, there was a potential for liver injury, evidenced by elevated transaminase levels. This is a potentially serious risk that can be managed when the product is

[4] http://www.nationalacademies.org/hmd/Reports/2017/health-effects-of-cannabis-and-cannabinoids.aspx.

taken under medical supervision in accordance with the FDA approved labeling for the product, but it is less clear how this risk might be managed if this substance is used far more widely, without medical supervision, and not in accordance with FDA-approved labeling. Other serious treatment-emergent adverse events reported in clinical studies of EPIDIOLEX included somnolence and lethargy; and hypersensitivity reactions. Common adverse reactions included decreased appetite, diarrhea, and sleep disorders.

Given the substantial interest in this topic and Congressional interest in fostering the development of appropriate hemp products under the 2018 Farm Bill, while also preserving FDA's ability to protect the public health, FDA is holding a public hearing. The goal of the hearing is to obtain additional scientific data and other information related to cannabis and cannabis-derived compounds, both from botanical and synthetic sources, to inform our regulatory oversight of these products. FDA does not intend for this hearing to produce any decisions or new positions on specific regulatory questions, but this hearing is expected to be an important step in our continued evaluation of cannabis and cannabis-derived compounds in FDA-regulated products.

II. Participating in the Public Hearing

Registration: To register to attend the public hearing, either in person or by webcast, on "Scientific Data and Information about Products Containing Cannabis or Cannabis-Derived Compounds" please register at https://www.fda.gov/NewsEvents/MeetingsConferencesWorkshops/ucm634550.htm. Please provide complete contact information for each attendee, including name, title, affiliation, address, email, and telephone and whether you want to attend in person or by webcast.

Request for Presentations: During online registration, you may indicate if you wish to make a formal presentation (with accompanying slide deck) or present oral comments during the public hearing session (with no slide deck) and which topic(s) you would like to address. FDA will do its best to accommodate requests to make public presentations. We are seeking to have a broad representation of ideas and issues presented at the meeting. Individuals and organizations with common interests are urged to consolidate or coordinate their presentations. Following the close of registration, FDA will determine the amount of time allotted to each presenter and the approximate time each presentation is to begin and will select and notify participants by May 21, 2019. All requests to make presentations must be received by the close of registration on May 10, 2019, Eastern Time.

If selected for a formal oral presentation (with a slide deck), each presenter must submit an electronic copy of their presentation (PowerPoint or PDF) to Stakeholderengagement@fda.hhs.gov with the subject line "Scientific Data and Information about Products Containing Cannabis or Cannabis-Derived Compounds" on or before May 28, 2019. No commercial or promotional material will be permitted to be presented or distributed at the public hearing.

Persons notified that they will be presenters are encouraged to arrive at the hearing room early and check in at the onsite registration table to confirm their designated presentation time. Actual presentation times may vary based on how the meeting progresses in real time. An agenda for the hearing and any other background materials will be made available 5 days before the hearing at https://www.fda.gov/NewsEvents/MeetingsConferencesWorkshops/ucm634550.htm.

Those without internet or email access can register and/or request to participate by contacting Beth F. Fritsch by the above dates (see FOR FURTHER INFORMATION CONTACT).

Streaming Webcast of the Public Hearing: For those unable to attend in person, FDA will provide a live webcast of the hearing. To join the hearing via the webcast, please go to https://collaboration.fda.gov/cannabispart15.

Transcripts: Please be advised that as soon as a transcript is available, it will be accessible at https://www.fda.gov/NewsEvents/MeetingsConferencesWorkshops/ucm634550.htm. It may be viewed at the Dockets Management Staff (see ADDRESSES) and also will be available at https://www.regulations.gov.

III. Issues for Consideration and Request for Data and Information

We encourage public comments and presentations at the public hearing. In submitting comments, data, and information to the docket, please identify available references for the data and information, as well as the general category area and specific question number listed below.

A. Health and Safety Risks

As noted above, there are many unanswered questions about the safety of cannabis and cannabis-derived products. To inform FDA's regulatory oversight of these products, especially as we consider whether it is appropriate to exercise our authority to allow the use of CBD in dietary supplements and other foods, we are interested in obtaining information, including data and studies, on, among other things:

1. Based on what is known about the safety of products containing cannabis and cannabis-derived compounds, are there particular safety concerns that FDA should consider regarding its regulatory oversight and monitoring of these products? For example:
    - What levels of cannabis and cannabis-derived compounds cause safety concerns?
    - How does the mode of delivery (e.g., ingestion, absorption, inhalation) affect the safety and exposure to cannabis and cannabis-derived compounds?
    - How do cannabis and cannabis-derived compounds interact with other substances (e.g., drug ingredients)?
2. Are there special human populations (e.g., children, adolescents, pregnant and lactating women) or animal populations (e.g. species, breed, or class) that should be considered when assessing the safety of products containing cannabis and cannabis-derived compounds?
3. What are the characteristics of a successful system to collect representative safety information at the national or State level about products containing cannabis and cannabis-derived compounds?
    - Are there systems that currently exist for the collection of this information (other than FDA's systems)?
    - Are there particular safety concerns related to the overlap of therapeutic dose levels from approved drug products, with potential exposure from other uses (e.g., from food, dietary supplements, cosmetics)? Please identify any safety concerns and include relevant data or studies.
4. What endpoints or outcomes would define a maximal acceptable daily intake from all products?

- What margin of exposure would represent an appropriate and safe level from anticipated cumulative exposure? Does that margin of exposure vary based on the form of consumption (e.g., from ingestion, absorption, inhalation)? Please explain your reasoning and include relevant data or studies.
- What mechanisms would be available to help ensure that this margin of exposure was maintained at a level sufficiently protective of public health?

5. Are there any data known that would support the safe use of cannabis and cannabis-related compounds in general food use (including dietary supplements), including data regarding exposure levels to cannabis and cannabis-related compounds in foods (including dietary supplements) that would be acceptable from a food safety perspective?
    - What data are available about residues of cannabis-derived compounds in human foods (e.g., meat, milk, or eggs) that come from animals that consume cannabis or cannabis-derived compounds? Are there residue levels that should be tolerated in these foods? Please provide data or other information to support your reasoning.
6. How does the existing commercial availability of food products containing cannabis-derived compounds such as CBD (which may in some cases be lawful at the State level but not the Federal level) affect the incentives for, and the feasibility of, drug-development programs involving such compounds?
    - How would the incentives for, and the feasibility of, drug development be affected if food products containing cannabis-derived compounds, such as CBD, were to become widely commercially available? How would this change if FDA established thresholds on acceptable levels of cannabinoids, including CBD, in the non-drug

products it regulates? What else could FDA do to support drug development from cannabinoids?

B. Manufacturing and Product Quality

Please provide data and information on how products containing cannabis or cannabis-derived compounds (other than those marketed as drugs in compliance with the FD&C Act) are currently manufactured, including information about methods for ensuring product quality and consistency. More specifically, we are interested in obtaining information on, among other things:

1. Are there particular standards needed to address any safety issues related to the manufacturing, processing, and holding of products containing cannabis and cannabis-derived compounds (e.g., genotoxic impurities, degradation of active compounds)? Please identify or describe those standards.
2. Are there particular standards or processes needed to ensure manufacturing quality and consistency of products containing cannabis or cannabis-derived compounds, including standards applied to evaluate product quality? Please identify or describe those standards.
3. What validated analytical testing is needed to support the manufacturing of safe and consistent products?
4. Are there any currently used standardized definitions for the ingredients in cannabis products (e.g., "hemp oil")? If standardized definitions would be helpful, what terms should be defined and what should the definition(s) be?
5. What are the functional purposes of adding cannabis-derived compounds, such as CBD, to foods (e.g., nutritive value, technical effect), both in terms of manufacturer intent and

consumer perceptions and/or expectations? To the extent a compound is added to food to achieve a particular functional purpose, what evidentiary support is available to demonstrate that the addition of such compound has the intended or perceived effect?

C. Marketing/Labeling/Sales

FDA is interested in information about how products containing cannabis or cannabis-derived compounds, other than drug products approved by FDA for human or animal use, are marketed, labeled, and sold. More specifically, we seek information on, among other things:

1. How should consumers be informed about the risks associated with such products (e.g., directions for use, warnings)? What specific risks should consumers be informed about? Are there any subpopulations for which additional warnings or restrictions are appropriate? Please explain your reasoning.
2. What conditions, restrictions, or other limitations on the manufacturing and distribution of these products have been put in place under State or local law, particularly with respect to food products containing cannabis-derived compounds such as CBD (which may, in some cases, be lawful at the State level but not the Federal level)? What other conditions, restrictions, or other limitations might be appropriate to ensure adequate consumer information and to protect the public health?
3. What statutory or regulatory restrictions are in place under State or local law to warn about the use of these products by certain vulnerable human populations (e.g., children, adolescents, pregnant and lactating women) or animal populations (e.g. species, breed, or class)? Are there other steps that should be taken to warn about use by vulnerable populations? Please identify such steps and how they would apply to a particular subpopulation.

4. What other information should FDA consider in the labeling of specific product categories of cannabis and cannabis-derived products?

IV. FDA Legal Authorities

There are FD&C Act provisions that are relevant to the legality of cannabis or cannabis-derived products. To help in understanding the context of the public hearing and current FDA actions, a synopsis of FDA legal authorities is provided below.

A. Human Drugs

A drug is an article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals (section 201(g) of the FD&C Act (21 U.S.C. 321(g)). A drug is also defined as an article (other than food) intended to affect the structure or any function of the body of man or other animals. Thus, the determination of whether a product is a drug turns in part on the "intended use" of the product.

By statute, it is a prohibited act to introduce a new drug into interstate commerce unless it has an approved marketing application (New Drug Application (NDA) or Abbreviated New Drug Application (ANDA)) (section 301(d) of the FD&C Act (21 U.S.C. 331(d)). FDA reviews the data submitted in a marketing application to evaluate whether a drug product meets the statutory standards for approval. To conduct clinical research that can lead to an approved new drug, including research using materials from plants such as cannabis, researchers submit an Investigational New Drug (IND) application to FDA, as described in 21 CFR Part 312.

FDA has approved several drug products that contain compounds found in cannabis. Most recently, FDA has approved EPIDIOLEX,[5] which contains the purified drug substance CBD for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet

[5] https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/210365Orig1s000TOC.cfm

syndrome in patients 2 years of age and older. We also have approved MARINOL and SYNDROS for therapeutic uses in the United States, including for the treatment of anorexia associated with weight loss in AIDS patients. MARINOL and SYNDROS include the active ingredient dronabinol, a synthetic THC which is considered the psychoactive component of marijuana. Another FDA-approved drug, CESAMET, contains the active ingredient nabilone, which has a chemical structure similar to THC and is synthetically derived.

B. Human Foods/Dietary Supplements

By statute, any substance intentionally added to food is a food additive, and therefore subject to premarket review and approval by FDA, unless the substance is generally recognized as safe (GRAS) by qualified experts under the conditions of its intended use, or the use of the substance is otherwise excepted from the definition of a food additive (sections 201(s) and 409 of the FD&C Act (21 U.S.C. 321(s) and 348)). Three hemp seed ingredients--hulled hemp seeds, hemp seed protein, and hemp seed oil--have gone through the FDA GRAS process and can be legally marketed in human foods for certain uses without food additive approval, provided they comply with all other requirements. More specifically, these three ingredients were the subject of a GRAS notice in which the submitter concluded that the ingredients were GRAS for specific uses in human foods. FDA evaluated these notices and had no questions[6] regarding the submitter's conclusions.

No other cannabis-derived compounds have been the subject of a food additive petition, an evaluated GRAS petition, or have otherwise been approved for use in food by FDA. Food

[6] https://www.fda.gov/Food/NewsEvents/ConstituentUpdates/ucm628910.htm

companies that wish to use cannabis or cannabis-derived compounds in their foods are subject to the relevant laws and regulations that relate to the food additive[7] and GRAS[8] processes.

In addition, it is prohibited by statute to introduce or deliver for introduction into interstate commerce any food (including any animal food) to which has been added a substance which is an active ingredient in a drug product approved under section 505 of the FD&C Act (21 U.S.C. 355) or a drug for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public (section 301(*ll*) of the FD&C Act (21 U.S.C. 331(*ll*)). There are exceptions, including when the drug was marketed in food before the drug was approved or before the substantial clinical investigations involving the drug had been instituted or, in the case of animal food, that the drug is a new animal drug approved for use in animal food and used according to the approved labeling. Based on available evidence, FDA has concluded[9] that it is a prohibited act to introduce or deliver for introduction into interstate commerce any food (including any animal food) to which THC or CBD has been added. When this statutory prohibition applies to a substance, the substance cannot be added to any food that is sold into interstate commerce unless the Secretary of the Department of Health and Human Services (the Secretary),[10] in the Secretary's discretion, has issued a regulation approving the use of the substance in the food (section 301(*ll*)(2) of the FD&C Act. To date, no such regulation has been issued for any substance.

For similar reasons, FDA has determined that products that contain THC or CBD cannot be marketed as dietary supplements.[11] By statute, if an ingredient is approved as a new drug

[7] https://www.fda.gov/Food/IngredientsPackagingLabeling/FoodAdditivesIngredients/default.htm
[8] https://www.fda.gov/Food/IngredientsPackagingLabeling/GRAS/
[9] https://www.fda.gov/newsevents/publichealthfocus/ucm421168.htm#legal
[10] The authority to make this determination has been delegated to FDA.
[11] https://www.fda.gov/newsevents/publichealthfocus/ucm421168.htm#dietary_supplements

under section 505 of the FD&C Act or has been 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, then products containing that substance are excluded from the statutory definition of a dietary supplement (sections 201(ff)(3)(B)(i) and (ii) of the FD&C Act. There is an exception if the substance was "marketed as" a dietary supplement or as a food before the new drug investigations were authorized. Based on available evidence, FDA has concluded that this is not the case for THC or CBD. There is also an exception if FDA has issued a regulation finding that the article would be lawful under the FD&C Act (section 201(ff)(3)(B) of the FD&C Act). At this time, no such regulation has been issued.

Some ingredients are derived from parts of the cannabis plant that may not contain THC or CBD, in which case those ingredients might fall outside the scope of this exclusion, and therefore might be able to be marketed as dietary supplements. However, the product must still comply with all other applicable laws and regulations governing dietary supplement products. For example, manufacturers and distributors who wish to market dietary supplements that contain "new dietary ingredients" (i.e., dietary ingredients that were not marketed in the United States in a dietary supplement before October 15, 1994) generally must notify FDA[12] about these ingredients (section 413(d) of the FD&C Act (21 U.S.C. 350b(d)). Generally, the notification must include information demonstrating that a dietary supplement containing a new dietary ingredient will reasonably be expected to be safe under the conditions of use recommended or suggested in the labeling. A dietary supplement is adulterated if it contains a new dietary ingredient for which there is inadequate information to provide reasonable assurance that the

[12] https://www.fda.gov/Food/DietarySupplements/NewDietaryIngredientsNotificationProcess/ucm109764.htm

ingredient does not present a significant or unreasonable risk of illness or injury (section 402(f)(1)(B) of the FD&C Act (21 U.S.C. 342(f)(1)(B)).

Numerous other legal requirements apply to food and dietary supplement products, including requirements relating to CGMPs, labeling, allergens, and various provisions of the FDA Food Safety Modernization Act. Information about these requirements, and about FDA requirements across all product areas, can be found on FDA's website, https://www.fda.gov.

C. Animal Food and Drugs

FDA regulates animal food in a variety of ways, including by approving safe food additives and establishing standards for animal food contaminants. FDA has not reviewed any food additive petitions for cannabis-derived animal feed, nor have any cannabis-derived feed ingredients been the subject of a GRAS determination by FDA, a GRAS notice that underwent FDA evaluation and received a "no questions" response, or otherwise been approved for use in animal feed by FDA. Animal food companies that wish to use cannabis or cannabis-derived compounds in their animal food products are subject to the relevant laws and regulations that relate to the food additive and GRAS processes. With respect to THC and CBD specifically, as discussed above, it is a prohibited act under section 301(*ll*) of the FD&C Act , to introduce or deliver for introduction into interstate commerce any animal food to which THC or CBD has been added.

As stated above, a drug is an article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals (section 201(g) of the FD&C Act. A drug is also defined as an article (other than food) intended to affect the structure or any function of the body of man or other animals. Thus, the determination of whether a product is a drug turns in part on the "intended use" of the product.

Currently, there are no legally marketed new animal drugs that contain cannabis or cannabis-derived compounds. A new animal drug is deemed "unsafe" under section 512(a) of the FD&C Act (21 U.S.C. 360b(a)), and may not be sold into interstate commerce under section 301(a) of the FD&C Act), unless it has an approved new animal drug application (NADA), abbreviated NADA (ANADA), conditional approval (CNADA) or index listing. FDA reviews the data submitted in a marketing application to evaluate whether an animal drug product meets the statutory standards for approval. To conduct clinical research that can lead to an approved new animal drug, including research using materials from plants such as cannabis, researchers establish an Investigational New Animal Drug (INAD) file with FDA, and comply with the requirements described in 21 CFR Part 511.

D. Cosmetics

Under the FD&C Act, cosmetic products and ingredients are not subject to premarket approval by FDA, except for most color additives. Certain cosmetic ingredients are prohibited or restricted by regulation,[13] but currently that is not the case for any cannabis or cannabis-derived ingredients. Ingredients not specifically addressed by regulation must nonetheless comply with all applicable requirements, and no ingredient--including a cannabis or cannabis-derived ingredient--can be used in a cosmetic if it causes the product to be adulterated or misbranded in any way. A cosmetic generally is adulterated if it bears or contains any poisonous or deleterious substance which may render it injurious to users under the conditions of use prescribed in the labeling, or under such conditions of use as are customary or usual (section 601(a) of the FD&C Act (21 U.S.C. 361(a)).

E. Tobacco Products

[13] https://www.fda.gov/Cosmetics/GuidanceRegulation/LawsRegulations/ucm127406.htm

The Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act) (Pub. L. 111-31) was enacted on June 22, 2009, amending the FD&C Act and providing FDA with the authority to regulate tobacco products. Specifically, the Tobacco Control Act amends the FD&C Act by adding a new chapter that provides FDA with authority over tobacco products. Section 901(b) of the FD&C Act (21 U.S.C. 387a(b)), as amended by the Tobacco Control Act, states that the new chapter in the FD&C Act (chapter IX--Tobacco Products) (21 U.S.C. 387 through 387u) applies to all cigarettes, cigarette tobacco, roll-your-own tobacco, smokeless tobacco, and any other tobacco products that the Secretary by regulation deems to be subject to chapter IX. In the *Federal Register* of May 10, 2016 (81 FR 28973), FDA issued a final rule deeming all products that meet the statutory definition of "tobacco product" in section 201(rr) of the FD&C Act (21 U.S.C. 321(rr)), except accessories of deemed tobacco products, to be subject to FDA's tobacco product authority (the deeming rule). The products now subject to FDA's tobacco product authority include electronic nicotine delivery systems (sometimes referred to as vapes, vaporizers, or electronic cigarettes, among other terms), cigars, waterpipes (hookah), pipe tobacco, nicotine gels, dissolvables that were not already subject to the FD&C Act, and other tobacco products that meet the statutory definition of "tobacco product" (other than accessories) that may be developed in the future. The term "tobacco product" means any product made or derived from tobacco that is intended for human consumption, including any component, part, or accessory of a tobacco product (except for raw materials other than tobacco used in manufacturing a component, part, or accessory of a tobacco product) (section 201(rr)(1) of the FD&C Act. For example, an e-liquid mixture that contains both a cannabis-derived ingredient and nicotine made or derived from tobacco, and that is intended for human consumption, would likely be subject to FDA's chapter IX authorities.

Numerous legal requirements apply to tobacco products, including legal requirements that relate to new tobacco products that are to be introduced, or delivered for introduction into interstate commerce. Other requirements relate to registration and listing, and sales and distribution, among other things. For more information on these topics, including the statutory standards that must be met for FDA to permit new tobacco products to be marketed, we encourage interested parties to go to the Center for Tobacco Products' web page at https://www.fda.gov/TobaccoProducts/Labeling/RulesRegulationsGuidance/ucm246129.htm.

F. Medical Devices

An article is a device if it is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar related article which is intended for use in the diagnosis of disease or other conditions, or in the cure mitigation, treatment, or prevention of disease, or is intended to affect the structure or any function of the body of man (section 201(h) of the FD&C Act). A device is also defined as not achieving its primary intended purposes through chemical action in or on the body of man and which is not dependent upon being metabolized for the achievement of its primary intended purpose (Id.). For example, an article that is used to aid intake of a product that contains cannabis or a cannabis-derived compound could be properly classified as a device if it meets all aspects of the above definition.

The FD&C Act establishes a comprehensive system for the regulation of medical devices intended for human use. The FD&C Act categorizes medical devices into one of three classes based on their risks and the extent of the regulatory controls needed to provide reasonable assurance of their safety and effectiveness (see section 513 of the FD&C Act (21 U.S.C. 360c)). The three categories of devices are class I (general controls), class II (special controls), and class

III (premarket approval). Class I devices generally pose the lowest risk to the patient and/or user and class III devices pose the highest risk.

The class to which a device is assigned determines, among other things, the type of premarket submission required for FDA authorization to market. In general, if a device is classified as class I or II, and if it is not exempt, manufacturers must obtain FDA clearance of a premarket notification (also referred to as a 510(k) submission) (see sections 510(k) and 513(i) of the FD&C Act (21 U.S.C. 360(k) and 360c(i))). For class III devices, manufacturers generally must obtain FDA approval of a premarket approval application (PMA) (see section 515 of the FD&C Act (21 U.S.C. 360e)). It is a prohibited act to market a device without its requisite premarket approval (see section 501(f)(1) of the FD&C Act (21 U.S.C. 351)).

V. Notice of Hearing Under 21 CFR Part 15

The Commissioner of Food and Drugs is announcing that this public hearing will be held in accordance with part 15 (21 CFR part 15). The hearing will be conducted by a presiding officer, who will be accompanied by FDA senior management from relevant program areas. Under § 15.30(f), the hearing is informal and the rules of evidence do not apply. No participant may interrupt the presentation of another participant. Only the presiding officer and panel members can pose questions; they can question any person during or at the conclusion of each presentation. Public hearings under part 15 are subject to FDA's policy and procedures for electronic media coverage of FDA's public administrative proceedings (21 CFR part 10, subpart C).

Under § 10.205, representatives of the media may be permitted, subject to certain limitations, to videotape, film, or otherwise record FDA's public administrative proceedings,

including presentations by participants. Persons attending FDA's public hearings are advised that FDA is not responsible for providing access to electrical outlets.

The hearing will be transcribed as stipulated in § 15.30(b) (see Supplementary Information). To the extent that the conditions for the hearing, as described in this notice, conflict with any provisions set out in part 15, this notice acts as a waiver of those provisions as specified in § 15.30(h).

Dated: March 28, 2019.

Lowell J. Schiller,

Acting Associate Commissioner for Policy.

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