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INTER-AMERICAN DRUG ABUSE CONTROL COMMISSION

C I C A D

Secretariat for Multidimensional Security

SIXTY-EIGHTH REGULAR SESSION OF CICAD
December 9 - 11, 2020
Bogotá, D.C., Colombia

OEA/Ser.L/XIV.2.68
CICAD/doc.2573/20
10 December 2020
Original: English

FDA ROLE IN REGULATION OF CANNABIS PRODUCTS

U.S. FOOD & DRUG ADMINISTRATION

FDA Role in Regulation of Cannabis Products

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December 11, 2020

FDA Responsibilities

Regulated Products include:

Human Foods (e.g., conventional foods, dietary supplements, food additives)

Drugs (including prescription and non-prescription)

Biologics (e.g., vaccines, blood and blood products)

Medical Devices (e.g., tongue depressors, pacemakers)

Electronic Products that give off radiation (e.g., microwave oven, X-ray equipment)

Cosmetics (e.g., skin moisturizers, lipsticks, eye and facial make-up, nail polish, cleansing shampoos)

Veterinary Products (e.g., animal foods, animal drugs)

Tobacco Products (e.g., cigarettes, smokeless tobacco)

Picture: https://pixabay.com/vectors/us-united-states-russia-map-1907526/

FDA Authority

Federal Food, Drug & Cosmetic Act (FD&C Act)	• Federal law enacted by Congress • Along with other federal laws it establishes legal framework within which FDA operates
FDA regulations	• Develops regulations based on law set forth in FD&C Act or other laws under which FDA operates • FDA regulations can be found in Title 21 of the Code of Federal Regulations (21 CFR)
FDA guidance	• Follows procedures required by its "Good Guidance Practice" regulation to issue FDA Guidance • Describe FDA's current thinking on a regulatory issue

FDA Basics: https://www.fda.gov/aboutfda/transparency/basics/ucm194909.htm

FDA Role in Regulation of Cannabis Products

Cannabis-derived compounds

- Compounds occurring naturally in the plant – like **CBD** and **THC**
- These compounds are extracted directly from the plant
- Can be used to manufacture drug products
- Example: highly-purified CBD extracted from the plant
- Agency approved one cannabis-derived drug product: Epidiolex (cannabidiol)

CANNABIS

- *Cannabis sativa* L. is a plant that contains over 80 different naturally occurring compounds called "cannabinoids"
- Two well-known cannabinoids:
  - **Cannabidiol (CBD)**
  - **Tetrahydrocannabinol (THC)**
- Plants are grown to produce varying concentrations of cannabinoids – **THC** or **CBD**
- These plant variations are called cultivars

Cannabis-related compounds

- These synthetic compounds are created in a laboratory
- Can be used to manufacture drug products
- Some synthetic compounds may also occur naturally in the plant and some may not
- Examples: Synthetically-derived dronabinol (also naturally occurring) and nabilone (not naturally occurring)
- Agency approved 3 synthetic cannabis-related drug products: Marinol & Syndros (dronabinol), Cesamet (nabilone)

FDA and Cannabis: Research and Drug Approval Process

Regulatory Landscape

- **Federal/state coordination** is necessary:
  - States
  - Health and Human Services (HHS)
  - Department of Justice (DOJ) & Drug Enforcement Administration (DEA)
  - U.S. Department of Agriculture (USDA)
  - Office of National Drug Control Policy (ONDCP)
  - Other federal partners

Regulatory Landscape : The Agriculture Improvement Act of 2018 (Farm Bill)

- Gives US Department of Agriculture (USDA) **authority** to issue federal regulations and guidelines concerning hemp production. **Individual States or tribes** desiring primary regulatory authority over hemp production must submit a plan to USDA

- **Removed hemp from the definition of marijuana** in the Controlled Substances Act (CSA)
  - Hemp: defined as cannabis (*Cannabis sativa* L.), and derivatives of cannabis, with extremely low (not more than 0.3 percent on a dry weight basis) concentrations of THC

- **Marijuana is still regulated by DEA** under Schedule 1 of the CSA

The Farm Bill's Impact on FDA Authorities

- **FDA's authorities** under the FDCA and section 351 of the PHS Act were **specifically preserved by the Farm Bill**

- Cannabis and cannabis-derived products are **subject to the same authorities and requirements** as FDA-regulated products **containing any other substance**
  - Allows hemp to serve as a source of cannabis and cannabis-derived compounds for drug development if they **do not contain delta-9 THC at more than 0.3 percent by dry weight**

Overview of FDA Drug Authority

- Under the FD&C Act:
  - Any product, including a cannabis product (hemp or otherwise), that is **marketed with a claim of therapeutic benefit, or with any other disease claim, is considered to be a drug**
  - A new drug must be approved by the FDA for its intended use before it may be introduced into interstate commerce

THC and CBD: Active ingredients in approved drugs

- Sec. 301(ll) of the FD&C Act (21 U.S.C. § 331)- paraphrased
  - It is **prohibited** to introduce into interstate commerce any food that contains an active ingredient (such as **THC or CBD**) in an approved drug product or in a potential drug for which substantial clinical investigations have been instituted and made public.

- CBD and THC **cannot** be added to foods under the FD&C Act
  - This prohibition applies regardless of whether the substances are hemp-derived

- CBD and THC products **are excluded** from the definition of dietary supplements under FD&C Act Section 201(ff)(3)(B)(i) and (ii)

FDA Internal Agency Working Groups

Marijuana Working Group

- **Focused on** products containing cannabis or cannabis-derived compounds **in general**.
- **Surveillance, enforcement, and policy options** for products containing cannabis or cannabis-derived compounds.

CBD Working Group

- Explore **potential pathways** for dietary supplements, conventional foods, veterinary products, and cosmetics containing **CBD** to be lawfully marketed
- Consider what the impact of such marketing would be on the **public health**.
- **Consider whether statutory or regulatory changes** might be needed.

Cannabis Drug Development

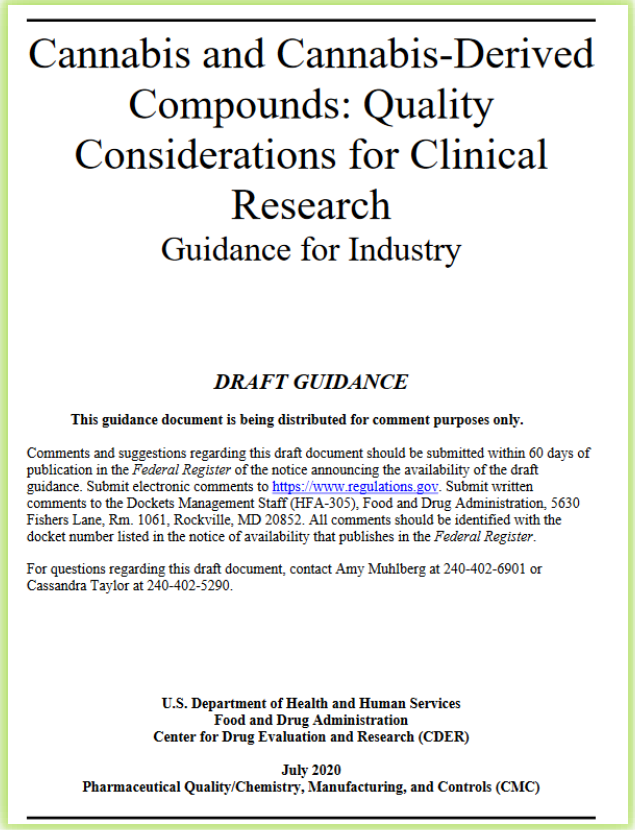
- When used under clinical trial, cannabis and cannabis-derived compounds must meet all FDA requirements for IND applications, which includes 3 broad areas
  1. Animal Pharmacology and Toxicology Studies
  2. Manufacturing Information
  3. Clinical Protocols and Investigator Information

- Development of drugs has focused on using compounds in cannabis: CBD, THC

- **Four products approved**:
  1. Marinol (dronabinol) (1985): nausea from cancer chemotherapy →Schedule III
  2. Cesamet (nabilone) (1985 (2006)): nausea & neuropathic pain → Schedule II
  3. Syndros (dronabinol) (2016): nausea from cancer chemotherapy → Schedule II
  4. Epidiolex (CBD) (2018): for childhood seizures & TSC → No longer controlled

Cannabis Drug Development Draft Guidance

- On July 21st, 2020 FDA published Draft Guidance Cannabis and Cannabis-Derived Compounds: Quality Considerations for Clinical Research
- Cannabis and cannabis-derived compounds can be used in clinical research
  - Under an Investigational New Drug (IND) application to study a specific therapeutic indication



Cannabis and Cannabis-Derived Compounds: Quality Considerations for Clinical Research

Guidance for Industry

DRAFT GUIDANCE

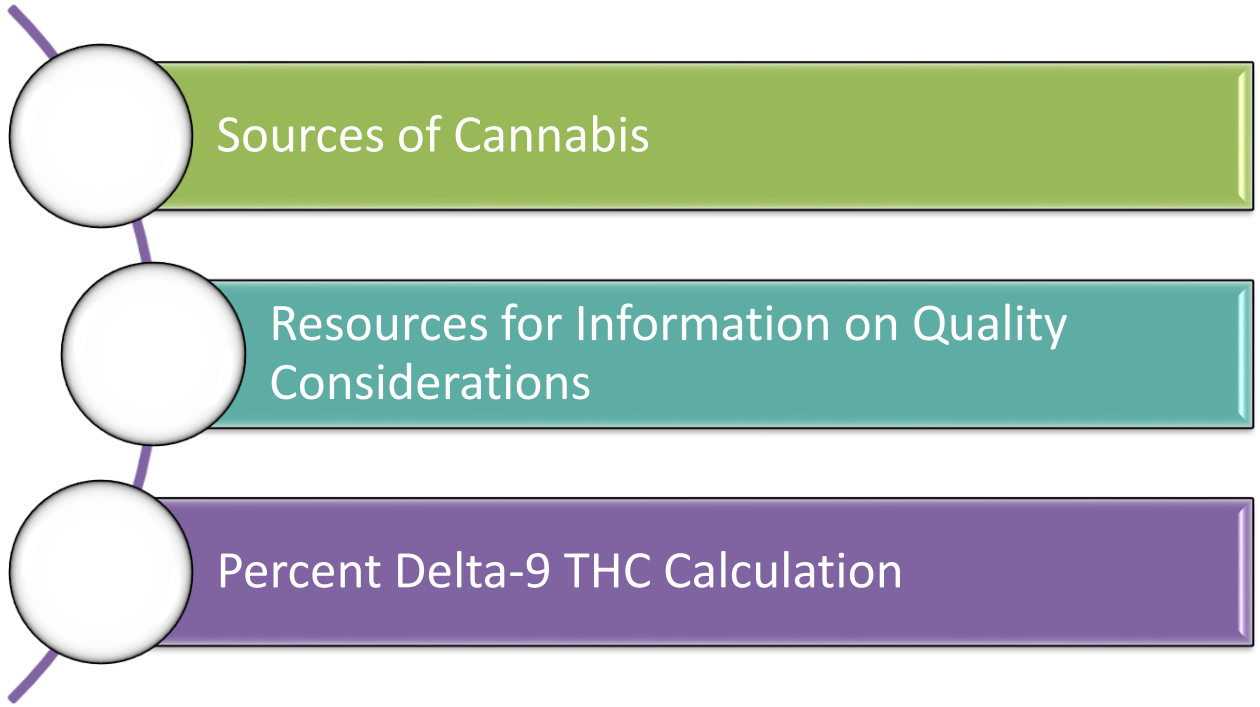
This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact Amy Muhlberg at 240-402-6901 or Cassandra Taylor at 240-402-5290.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

July 2020
Pharmaceutical Quality/Chemistry, Manufacturing, and Controls (CMC)



FDA Authority Over Foods for Humans and Animals & Food Additives

Foods:

- Exceptions to §301(ll):
  - If article was **marketed in food before the drug was approved** or **before the substantial clinical investigations** involving the drug had been authorized.
    - *Note: FDA has examined the available evidence and concluded that this exception does not apply*
  - FDA can also create an exception to 301(ll) through **notice and comment rulemaking**.
- All ingredients in human and animal food must be **approved food additives or GRAS** for their intended use in the intended species.

Food Additives:

- At this time, there are **no approved food additive uses** for any substances derived from hemp and we are **unaware of any basis to conclude that CBD is GRAS** for its use in human or animal food.
  - This includes a lack of available safety data related to-food producing animal use (residues in meat, milk, eggs).

FD&C Act §201(ff)(3)(B): Dietary Supplements

- Under sections 201(ff)(3)(B)(i) and (ii) of FDCA, if a substance (such as THC or CBD) is an active ingredient in a drug product that has been approved under FDCA §505, 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 outside the definition of a dietary supplement**.

- CBD and THC products are therefore **excluded from the definition of dietary supplement** under the FDCA regardless of whether the substances are hemp-derived.

FDA Authority over Cosmetics

- **No premarket approval** required for cosmetic products and ingredients, with the exception of color additives.
- Must not be **adulterated**
  - Safe for consumers when used according to the directions in labeling and under customary/usual conditions of use.
- Must not be **misbranded**
- **Topical products**, including those that contain **CBD**, intended to affect the structure or any function of the body, or to be used in the diagnosis, cure, mitigation, treatment, or prevention **of disease**, **are drugs**, even if they are also cosmetics (dual classification is common).
  - New drugs must be approved.

Other FDA Activities: Warning Letters Related to CBD Products

- FDA issued **numerous Warning Letters** from 2015 to present, including after passage of the Farm Bill:
  - Unapproved new drugs [§§201(p), 301(d), and 505(a)]
  - Misbranded drugs [§§301(a) and 502(f)(1)]
  - Illegally marketed food [§301(ll), 402(a)(2)(C)(i), and 301(a)]
  - Illegally marketed supplements [§201(ff)(3)(B)]
  - Unapproved new animal drugs [§§301(a) and 501(a)(5)]

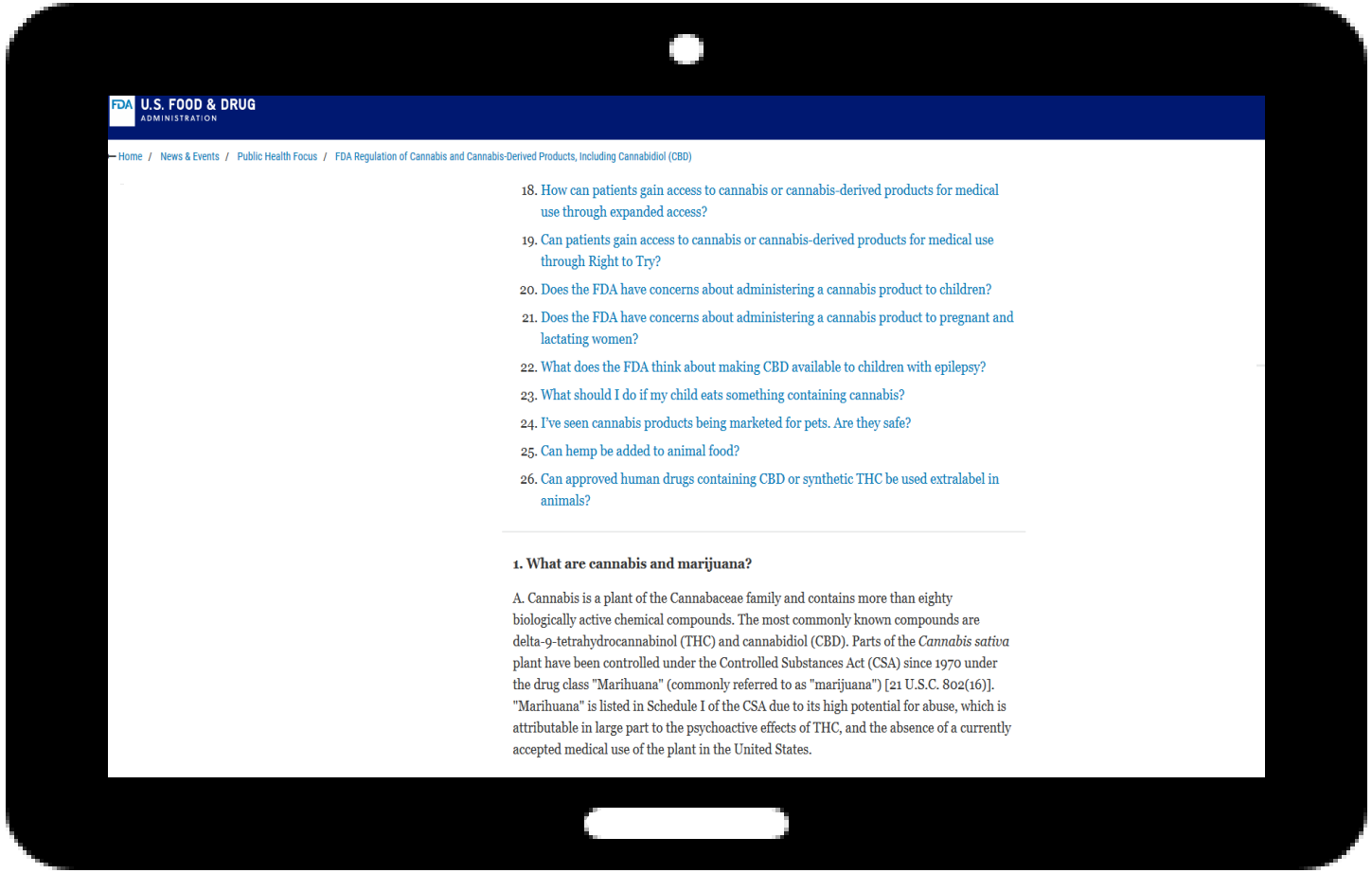
- FDA **posted lab results** for dozens of CBD products cited in the warning letters.
  - In many cases, the CBD content did not match the labeled claims and some products did not contain any CBD

FDA Resources

FDA Regulation of Cannabis and Cannabis-Derived Products, Including Cannabidiol (CBD)

On this page:

- Consumer Information
- FDA Communications
- Regulatory Resources
- Questions and Answers



Summary and Conclusions

- FDA has a well-defined role to play in the regulation and development of products containing cannabis and cannabis-derived compounds
- FDA continues to support scientific and rigorous testing and approval of drugs derived from cannabis and to support **robust scientific research** into understanding the **therapeutic uses and safety** of non-drug cannabis products
- FDA is actively exploring potential **regulatory pathways** for the **lawful marketing** of appropriate cannabis-derived products
- FDA is **committed to protect and promote the public health** with respect to products containing cannabis and cannabis-derived compounds, including enforcement action when needed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