

FDA Role in Regulation of Cannabis Products

NIDA

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FDA's Policy Interests

- Protecting the public from harmful products
- Protecting the public from fraudulent products with unproven disease claims (which could result in patients foregoing proven treatments)
- Incentivizing rigorous scientific research to support beneficial therapies (through requiring NDAs)
- Protecting human subjects involved in research (through requiring INDs)
- Protecting the integrity of the conventional food supply and dietary supplements
- Respecting the “right to try” unapproved drugs for seriously ill patients



FDA and Cannabis

Regulatory roles under the Federal Food, Drug & Cosmetic Act (FDCA):

- Scientific and regulatory support for research on potential therapeutic uses of cannabis
- Regulation of products (e.g., foods, drugs, cosmetics) from cannabis
- Enforcement actions as necessary against products made from cannabis or containing compounds found in the cannabis plant, particularly those that present human health risks

FDA roles under the Controlled Substances Act (CSA):

- Assisting the Drug Enforcement Administration (DEA) on protocol registration for Schedule I drug research (Under 21 CFR 1301.18 and 1301.32)
- Conducts scientific and medical analysis ('8-factor analysis') to recommend appropriate controls under the CSA (working with NIDA)
 - At DEA request
 - Responding to citizen petitions
 - New approved drug products with need for scheduling action

Regulatory Landscape

- Federal/state coordination is necessary:
 - States
 - DEA
 - FDA
 - USDA
 - Others: SAMHSA, NIDA, ONDCP



Intra-Agency Team

FDA has a cross-Agency team that works on cannabis issues:

- All product divisions represented as well as field inspectorate
- Policy
- Enforcement
- Outreach
- Interagency coordination
 - Federal, state, international

The Farm Bill

- Agriculture Improvement Act of 2018 (Farm Bill) changes some federal authorities related to the production and marketing of hemp.
 - Establishes a state-USDA process and gives USDA the authority to issue federal regulations and guidelines concerning hemp production
 - Hemp is 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
- Removed hemp from the definition of marijuana in the Controlled Substances Act (CSA)
- Marijuana is still regulated by DEA under Schedule 1 of the CSA
 - Note: Epidiolex and certain future FDA approved CBD products have been classified as Schedule V

The Farm Bill - FDA

- FDA's authorities under the FD&C Act 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.

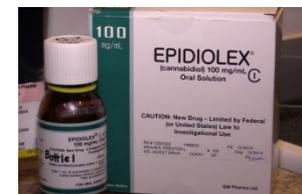


Overview of FDA Drug Authority

- 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.

Drug Development from Cannabis

- Development of drugs has focused on using compounds in cannabis: CBD, THC
- Four products approved:
 - Marinol (dronabinol) (1985): nausea from chemotherapy. Schedule III
 - Cesamet (nabilone) (1985 (2006)): nausea & neuropathic pain. Schedule II
 - Syndros (dronabinol) (2016): nausea from cancer chemotherapy. Schedule II
 - Epidiolex (CBD) (2018): for childhood seizures. Schedule V





FDA Support for Drug Development from the Cannabis Plant

- Regulatory programs and expediting pathways for important drug development
 - Priority Review of NDAs, Fast Track Designation, Breakthrough Therapy Designation
- “FDA and Marijuana” web page includes links to Q&A page, guidance on initiating INDs or DMFs, contact points for Office of New Drugs’ review divisions, small business assistance, and links to NIDA Drug Supply Program and DEA registration site
- Updated final guidance in 2016, ***Botanical Drug Development***, on the use of botanicals (e.g., cannabis) as sources for drugs
 - Focus on quality manufacturing and controls during development

FDA Support for Drug Development (cont'd)



- Botanicals Team available to guide development of drugs from plants
 - Can request Botanicals Team participation, to gain clarity on characterizing an investigational botanical drug to support proposed clinical study or NDA submission
- Controlled Substances Staff available to help with FDA-DEA interactions
 - E.g., issues around abuse potential assessment requirements to support an NDA submission



THC and CBD in Food: 301(II)

- CBD and THC cannot be added to foods under the FD&C Act regardless of whether the substances are hemp-derived.
 - Under section 301(II) of the FD&C Act, it is prohibited to introduce or deliver for introduction into interstate commerce any food (including animal food or feed) to which has been added a substance which is an active ingredient in a drug product that has been approved under 21 U.S.C. § 355 (section 505 of the Act) or a drug for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public.
 - Exception: If article 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 feed, that the drug is a new animal drug approved for use in feed and used according to the approved labeling.
 - FDA has no evidence that this exception applies



Other Applicable Regulatory Requirements for Foods

- All foods are subject to a number of other regulatory requirements related to topics such as:
 - Safety of ingredients
 - Production controls
 - Labeling

Hemp Seed-Derived Ingredients

- FDA completed the evaluation of three GRAS notices related to the use of hemp seed-derived food ingredients in December 2018.
 - Hulled hemp seed, hemp seed protein, hemp seed oil
 - Products have typical food uses
- FDA had no questions about the submitter's conclusion that the ingredients were GRAS for the uses in the notice.
- These products can be legally marketed in human foods for these uses without food additive approval, provided they comply with all other requirements and do not make disease claims.

THC and CBD in Dietary Supplements: 201(ff)(3)(B)

- It is unlawful to market CBD and THC products as, or in, dietary supplements, regardless of whether the substances are hemp-derived.
- CBD and THC products are excluded from the definition of dietary supplements under the FD&C Act
 - Under sections 201(ff)(3)(B)(i) and (ii) of the FD&C Act, if a substance (such as THC or CBD) is an active ingredient in a drug product that has been approved under 21 U.S.C. § 355 (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 outside the definition of a dietary supplement.
 - Exception: If the substance was "marketed as" a dietary supplement or as a conventional food before the drug was approved or before the new drug investigations were authorized, as applicable.
 - FDA has no evidence that this exception applies

Cosmetics

- No premarket approval 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
- If a topical product, including those that contain CBD, is 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, it is a drug, even if it is also a cosmetic (dual classification is common). New drugs must be approved

Current FDA Warning Letters Related to CBD Products



- FDA has issued numerous WLs from 2015 to present
 - Unapproved new drugs [§§201(p), 301(d), and 505(a)]
 - Misbranded drugs [§§301(a) and 502(f)(1)]
 - Illegally marketed food [§301(l)]
 - Illegally marketed supplements [§201(ff)(3)(B)]
- 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

Challenges

Challenges include:

- Rapidly-changing legal frameworks at the federal, state, and local level
- Continually evolving market with many types of products
- Need for more data (e.g., safety)
- Need to support rigorous scientific research into therapeutic uses of products from cannabis
 - Impact of Farm Bill on CBD for research
- Resources



Commissioner Gottlieb Statement

December 20, 2018

- Affirming FDA's commitment to protect and promote the public health with respect to these products, including enforcement action when needed
- Concern about unapproved drugs and about introduction into the food supply
- Soliciting input on how to make legal pathways for the lawful marketing of these products more efficient
- Taking steps to evaluate options for use in foods, including dietary supplements
- Intent to hold a public meeting for stakeholders to share experiences and challenges with these products
 - Including information related to safety
- <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm628988.htm>



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FDA and Marijuana: Questions and Answers

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1. [How is marijuana therapy being used by some members of the medical community?](#)
2. [Why hasn't the FDA approved marijuana for medical uses?](#)
3. [Is marijuana safe for medical use?](#)
4. [How does FDA's role differ from the role of other federal agencies when it comes to the investigation of marijuana for medical use?](#)
5. [Does the FDA object to the clinical investigation of marijuana for medical use?](#)
6. [What kind of research is the FDA reviewing when it comes to the efficacy of marijuana?](#)
7. [How can patients get into expanded access program for marijuana for medical use?](#)
8. [Does the FDA have concerns about administering a cannabis product to children?](#)
9. [Does the FDA have concerns about administering a cannabis product to pregnant and lactating women?](#)
10. [What is FDA's reaction to states that are allowing marijuana to be sold for medical uses without the FDA's approval?](#)

<https://www.fda.gov/NewsEvents/PublicHealthFocus/ucm421168.htm>

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 focus on supporting scientific and rigorous testing and approval of drugs derived from cannabis
- FDA will solicit input on how to make legal pathways for the lawful marketing of these products more efficient
- FDA will continue to protect and promote the public health with respect to these products

