FDA and Marijuana: Questions and Answers

1. How is marijuana therapy being used by some members of the medical community?

A. The FDA is aware that marijuana or marijuana-derived products are being used for a number of medical conditions including, for example, AIDS wasting, epilepsy, neuropathic pain, treatment of spasticity associated with multiple sclerosis, and cancer and chemotherapy-induced nausea.

2. Why hasn't the FDA approved marijuana for medical uses?

A. To date, the FDA has not approved a marketing application for marijuana for any indication. The FDA generally evaluates research conducted by manufacturers and other scientific investigators. Our role, as laid out in the Federal Food, Drug, and Cosmetic (FD&C) Act, is to review data submitted to the FDA in an application for approval to assure that the drug product meets the statutory standards for approval.

The FDA has approved Epidiolex, which contains a purified drug substance cannabidiol, one of more than 80 active chemicals in marijuana, for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2 years of age and older. That means the FDA has concluded that this particular drug product is safe and effective for its intended indication.

The agency also has 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 delta-9- tetrahydrocannabinol (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.

3. Is marijuana safe for medical use?

A. The study of marijuana in clinical trial settings is needed to assess the safety and effectiveness of marijuana for the treatment of any disease or condition.

The FDA will continue to facilitate the work of companies interested in appropriately bringing safe, effective, and quality products to market, including scientifically-based research concerning the medicinal uses of marijuana.

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?

A. Conducting clinical research using marijuana involves interactions with several federal agencies. This includes: a registration administered by the Drug Enforcement Administration (DEA); obtaining the marijuana for research from the National Institute on Drug Abuse (NIDA), within the National Institutes of Health, or another DEA-registered source; and review by the FDA of an investigational new drug (IND) application and research protocol. Additionally:

- As a Schedule I controlled substance under the Controlled Substances Act, DEA provides researchers with investigator and protocol registrations and has Schedule I-level security requirements at the site marijuana will be studied.

- NIDA provides research-grade marijuana for scientific study. The agency is responsible for overseeing the cultivation of marijuana for medical research and has contracted with the University of Mississippi to grow marijuana for research at a secure facility. Marijuana of varying potencies and compositions is available. DEA also may allow additional growers to register with the DEA to produce and distribute marijuana for research purposes.
- Researchers work with the FDA and submit an IND application to the appropriate division in the Office of New Drugs, in the Center for Drug Evaluation and Research (CDER), depending on the therapeutic indication.

The roles of the three agencies are the same for investigations of marijuana for use as an animal drug product, except that researchers would establish an investigational new animal drug (INAD) file with the Center for Veterinary Medicine to conduct their research, rather than an IND with CDER.

5. Does the FDA object to the clinical investigation of marijuana for medical use?

A. No. The FDA believes that scientifically valid research conducted under an IND application is the best way to determine what patients could benefit from the use of drugs derived from marijuana. The FDA supports the conduct of that research by:

1. Providing information on the process needed to conduct clinical research using marijuana.
2. Providing information on the specific requirements needed to develop a drug that is derived from a plant such as marijuana. In June 2004, the FDA finalized its Guidance for Industry: Botanical Drug Products, which provides sponsors with guidance on submitting IND applications for botanical drug products.
3. Providing specific support for investigators interested in conducting clinical research using marijuana and its constituents as a part of the IND process through meetings and regular interactions throughout the drug development process.
4. Providing general support to investigators to help them understand and follow the procedures to conduct clinical research through the FDA Center for Drug Evaluation and Research's Small Business and Industry Assistance group.

6. What kind of research is the FDA reviewing when it comes to the efficacy of marijuana?

A. The FDA reviews applications to market drug products to determine whether those drug products are safe and effective for their intended indications. The FDA reviews scientific investigations, including adequate and well-controlled clinical trials, as part of the FDA's drug approval process.

The FDA relies on applicants and scientific investigators to conduct research. Our role, as outlined in the Federal Food, Drug, and Cosmetic Act, is to review data submitted to the FDA in a marketing application to determine whether a proposed drug product meets the statutory standards for approval. Additional information concerning research on the medical use of marijuana is available from the National Institutes of Health, particularly the National Cancer Institute (NCI) and NIDA.

7. How can patients get into expanded access program for marijuana for medical use?

A. Manufacturers may be able to make investigational drugs available to individual patients in certain circumstances through expanded access, as described in the FD&C Act and implementing regulations.

8. Does the FDA have concerns about administering a cannabis product to children?

A. We understand that parents are trying to find treatments for their children's medical conditions. However, the use of untested drugs can have unpredictable and unintended consequences. Caregivers and patients can be confident that FDA-approved drugs have been carefully evaluated for safety, efficacy, and quality, and are monitored by the FDA once they are on the market. The FDA continues to support sound, scientifically-based research into the medicinal uses of drug products containing marijuana or marijuana constituents, and will continue to work with companies interested in bringing safe, effective, and quality products to market.

9. Does the FDA have concerns about administering a cannabis product to pregnant and lactating women?

A. The FDA is aware that there are potential adverse health effects with use of marijuana in pregnant or lactating women. Published scientific literature reports potential adverse effects of marijuana use in pregnant women, including fetal growth restriction, low birth weight, preterm birth, small-for-gestational age, neonatal intensive care unit (NICU) admission, and stillbirth. [1, 2, 3] Based on published animal research, there are also concerns that use of marijuana during pregnancy may negatively impact fetal brain development. [4, 5, 6] The American College of Obstetricians and Gynecologists (ACOG) recommends that women who are pregnant or contemplating pregnancy should be encouraged to discontinue marijuana use. In addition, ACOG notes that there are insufficient data to evaluate the effects of marijuana use on breastfed infants; therefore, marijuana use is discouraged when breastfeeding. [7] Pregnant and lactating women should talk with a health care provider about the potential adverse health effects of marijuana use.

10. What is FDA's reaction to states that are allowing marijuana to be sold for medical uses without the FDA's approval?

A. The FDA is aware that several states have either passed laws that remove state restrictions on the medical use of marijuana and its derivatives or are considering doing so. It is important to conduct medical research into the safety and effectiveness of marijuana products through adequate and well-controlled clinical trials. We welcome the opportunity to talk with states who are considering support for medical research of marijuana and its derivatives to provide information on Federal and scientific standards.

11. Has the agency received any adverse event reports associated with marijuana for medical conditions?

A. The agency has received reports of adverse events in patients using marijuana to treat medical conditions. The FDA is currently reviewing those reports and will continue to monitor adverse event reports for any safety signals attributable to marijuana and marijuana products, with a focus on serious adverse effects associated with the use of marijuana.

Information from adverse event reports regarding marijuana use is extremely limited; the FDA primarily receives adverse event reports for approved products. General information on the potential adverse effects of using marijuana and its constituents can come from clinical trials using marijuana that have been published, as well as from spontaneously reported adverse events sent to the FDA. Additional information about the safety and effectiveness of marijuana and its constituents is needed. Clinical trials of marijuana conducted under an IND application could collect this important information as a part of the drug development process.

12. Can products that contain THC or cannabidiol (CBD) be sold as dietary supplements?

A. No. Based on available evidence, FDA has concluded that THC and CBD products are excluded from the dietary supplement definition under sections 201(ff)(3)(B)(i) and (ii) of the FD&C Act,

respectively. Under those provisions, 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. FDA considers a substance to be "authorized for investigation as a new drug" if it is the subject of an Investigational New Drug application (IND) that has gone into effect. Under FDA's regulations (21 CFR 312.2), unless a clinical investigation meets the limited criteria in that regulation, an IND is required for all clinical investigations of products that are subject to section 505 of the FD&C Act.

There is an exception to sections 201(ff)(3)(B)(i) and (ii) 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. However, based on available evidence, FDA has concluded that this is not the case for THC or CBD. For more information on this provision, including an explanation of the phrase "marketed as," see Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues.

FDA is not aware of any evidence that would call into question its current conclusions that THC and CBD products are excluded from the dietary supplement definition under sections 201(ff)(3)(B)(i) and (ii) of the FD&C Act. Interested parties may present the agency with any evidence that they think has bearing on this issue. Our continuing review of information that has been submitted thus far has not called our conclusions into question.

13. Is it legal, in interstate commerce, to sell a food to which THC or CBD has been added?

A. No. Under section 301(ll) of the FD&C Act, it is prohibited to introduce or deliver for introduction into interstate commerce any food (including any 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. 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 feed, that the drug is a new animal drug approved for use in feed and used according to the approved labeling. However, based on available evidence, FDA has concluded that none of these is the case for THC or CBD. FDA has therefore concluded that it is a prohibited act to introduce or deliver for introduction into interstate commerce any food (including any animal food or feed) to which THC or CBD has been added. FDA is not aware of any evidence that would call into question these conclusions. Interested parties may present the agency with any evidence that they think has bearing on this issue. Our continuing review of information that has been submitted thus far has not called our conclusions into question.

14. In making the two previous determinations about THC, why did FDA conclude that THC is an active ingredient in a drug product that has been approved under section 505 of the FD&C Act? In making the two previous determinations about CBD, why did FDA determine that substantial clinical investigations have been authorized for and/or instituted, and that the existence of such investigations has been made public?

A. THC (dronabinol) is the active ingredient in the approved drug products, Marinol capsules (and generics) and Syndros oral solution.

The existence of substantial clinical investigations regarding CBD has been made public. For example, two such substantial clinical investigations include GW Pharmaceuticals' investigations regarding Sativex and Epidiolex. (See Sativex Commences US Phase II/III Clinical Trial in Cancer

Pain and GW Pharmaceuticals Receives Investigational New Drug (IND) from FDA for Phase 2/3 Clinical Trial of Epidiolex in the Treatment of Dravet Syndrome).

15. Will FDA take enforcement action regarding THC and CBD products that are marketed as dietary supplements? What about foods to which THC and CBD has been added?

A. When a product is in violation of the FD&C Act, FDA considers many factors in deciding whether or not to initiate an enforcement action. Those factors include, among other things, agency resources and the threat to the public health. FDA also may consult with its federal and state partners in making decisions about whether to initiate a federal enforcement action.

16. What does the FDA think about making cannabidiol available to children with epilepsy?

A. The FDA has approved Epidiolex, which contains a purified drug substance cannabidiol, one of more than 80 active chemicals in marijuana, for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2 years of age and older. That means the FDA has concluded that this particular drug product is safe and effective for its intended indication.

17. What should I do if my child eats something containing marijuana?

A. It is important to protect children from accidental ingestion of marijuana and products containing marijuana. FDA recommends that these products are kept out of reach of children to reduce the risk of accidental ingestion.

If the parent or caregiver has a reasonable suspicion that the child ingested products containing marijuana, the child should be taken to a physician or emergency department, especially if the child acts in an unusual way or is/feels sick.

18. I've seen marijuana products being marketed for pets. Are they safe?

A. FDA has recently become aware of some marijuana products being marketed to treat diseases in animals. We want to stress that FDA has not approved marijuana for any use in animals, and the agency cannot ensure the safety or effectiveness of these products. For these reasons, FDA cautions pet-owners against the use of such products.

19. Can I give my pet marijuana products for medical purposes, such as to relieve the pain of a sick or dying pet?

A. Marijuana needs to be further studied to assess the safety and effectiveness for medical use in animals. To date, FDA has not approved marijuana for any use in animals (see question and answer #4 above). If your pet is in pain, we urge you to talk with your veterinarian about appropriate treatment options.

20. I gave my pet marijuana and I'm concerned my pet is suffering adverse effects. What should I do?

A. Signs that your pet may be suffering adverse effects from ingesting marijuana may include lethargy, depression, heavy drooling, vomiting, agitation, tremors, and convulsions.

If you have concerns that your pet is suffering adverse effects from ingesting marijuana or any substance containing marijuana, consult your veterinarian, local animal emergency hospital or an animal poison control center immediately.

21. Has the agency received any adverse event reports associated with marijuana for animals?

A. While the agency is aware of reports of pets consuming various forms of marijuana, to date, FDA has not directly received any adverse event reports associated with giving marijuana to animals via our safety reporting portals. However, adverse events from accidental ingestion are well-documented in scientific literature. If you feel your animal has suffered from ingesting marijuana, we encourage you to report the adverse event to the FDA. Please visit Reporting Information about Animal Drugs and Devices to learn more about how to report an adverse event related to an animal food or drug.

22. What is FDA doing about marijuana products currently on the market for pets?

A. FDA is currently collecting information about marijuana and marijuana-derived products being marketed for animals. FDA reminds consumers that these products have not been evaluated by FDA for safety and effectiveness, and we recommend that you talk with your veterinarian about appropriate treatment options for your pet.

23. What is the effect of the Agricultural Improvement Act of 2018 on the FD&C Act?

A. The Agriculture Improvement Act of 2018 changes certain federal authorities relating to the production and marketing of hemp, defined as cannabis (Cannabis sativa L.), and derivatives of cannabis with extremely low (less than 0.3 percent on a dry weight basis) concentrations of the psychoactive compound delta-9-tetrahydrocannabinol (THC). These changes include removing hemp from the Controlled Substances Act, which means that it will no longer be an illegal substance under federal law. However, Congress explicitly preserved the agency's current authority to regulate products containing cannabis or cannabis-derived compounds under the FD&C Act and section 351 of the Public Health Service Act. Please see the FDA's statement on the signing of the Agriculture Improvement Act of 2018.

[1] Gray, et al. Identifying Prenatal Cannabis Exposure and Effects of Concurrent Tobacco Exposure on Neonatal Growth. Clinical Chemistry. 2010; 56(9): 1442-1450.
[2] Gunn, et al. Prenatal Exposure to cannabis and maternal and child health outcomes: a systematic review and meta-analysis. BMJ Open. 2016; 6:e009986.
[3] Hayatbakhsh, et al. Birth Outcomes associated with cannabis use before and during pregnancy. Pediatric Research. 2012; 71 (2): 215-219.
[4] Silva, et al. Prenatal tetrahydrocannabinol (THC) alters cognitive function and amphetamine response from weaning to adulthood in the rat. Neurotoxicol and Teratol 2012; 34(1): 63-71.
[5] Trezza, et al. Effects of perinatal exposure to delta-9-tetrahydrocannabinol on the emotional reactivity of the offspring: a longitudinal behavioral study in Wistar rats. Psychopharmacology (Berl) 2008; 198(4): 529-537.
[6] Campolongo, et al. Perinatal exposure to delta-9-tetrahydrocannabinol causes enduring cognitive deficits associated with alteration of cortical gene expression and neurotransmission in rats. Addict Biol 2007; 12(3-4): 485–495.
[7] http://www.acog.org/Resources-And-Publications/Committee-Opinions/Committee-on-Obstetric-Practice/Marijuana-Use-During-Pregnancy-and-Lactation