The Food and Drug Administration Won't Budge on Cannabis and Hemp

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After discussing two recent announcements by the Food and Drug Administration relating to cannabis or cannabinoid compounds and products, the authors contend that Congress must take action to end the stalemate between federal and state laws and the "purgatory of FDA selective enforcement."

Two recent announcements by the Food and Drug Administration (FDA) affirm that the agency will not compromise—or create new standards—in evaluating or permitting cannabis or cannabinoid compounds and products, and particularly cannabidiol (CBD). Congress must take action to end the stalemate between federal and state laws and the purgatory of FDA selective enforcement.

Guidance on Cannabis Research: More of the Same

The FDA recently published its guidance entitled, "Cannabis and Cannabis-Derived Compounds: Quality Considerations for Clinical Research."[1] The guidance only minimally updated the FDA's 2020 version. Two takeaways from this guidance are (1) the guidance applies only to "products that meet the legal definition of a drug under the FD&C Act," and (2) except for clinical research products, hemp and cannabis are not distinct categories based on federal legality; generally, the FDA's concerns for both substances are the same.

The Federal Register Notice summarizes the guidance's purpose:

> This guidance outlines FDA's current thinking on several topics relevant to the development of cannabis and cannabis-derived human drugs, including the source of cannabis for clinical research; general quality considerations for developing human drugs that contain cannabis and cannabis-derived compounds; and calculation of percent delta-9 tetrahydrocannabinol

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(THC) in botanical raw materials, intermediates, drug substances, and drug products to determine their control status. This guidance is being issued to support clinical research for development of cannabis and cannabis-derived human drugs.[2]

The FDA Guidance Relates to Drug Products

Notably, the FDA made clear that the guidance applies only to drugs. Its website posting notes: "The recommendations in this guidance are intended for 'products that meet the legal definition of a drug under the FD&C Act,' i.e., 'any product that is intended to diagnose, cure, mitigate, prevent, or treat a disease, or any product (other than food) intended to affect the structure or any function of the body,' including 'any product (including one that contains cannabis or cannabis-derived compounds) marketed with a claim of therapeutic benefit, or with any other disease-related claim.'"[3]

Understanding what qualifies as a "claim" is critical because many products sold in the current state cannabis markets or hemp isomers markets make claims that would qualify them as drugs under the FDA's purview.

Federal Illegality Only Impacts the FDA's Thinking on Sourcing

The FDA acknowledges that (1) "Cannabis and cannabis-derived compounds (i.e., compounds that occur naturally in the Cannabis sativa L plant) have been the subject of interest from consumers, industry, researchers, the public, and regulators," and (2) the 2018 Farm Bill's removal of hemp from the definition of "marihuana" as a controlled substance has legal implications. The FDA emphasizes, however, that the distinction does not matter for FDA standards beyond sourcing: "drugs that contain cannabis and cannabis-derived compounds 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."

Researchers generally can legally use "hemp" as long as it is "deemed to be of adequate quality by FDA when reviewed as part of an [Investigational New Drug Application]." The guidance notes that "CFR 990 and the changes made by the 2018 Farm Bill allow hemp, as defined in the bill (i.e., cannabis at or below 0.3 percent

delta-9 THC on a dry weight basis), to serve as a source of cannabis and cannabis-derived compounds for drug development."

For "marijuana" (cannabis with more than 0.3% delta-9 THC), researchers must use cannabis/extracts/products from the Drug Supply Program at the University of Mississippi or from the other Drug Enforcement Administration (DEA)–registered bulk manufacturers.[4] The guidance also warns that, even if a researcher starts with cannabis defined as hemp, the cannabis could become the controlled substance marijuana if the final product contains more than 0.3% delta-9 THC, and therefore would need to meet all of the Controlled Substances Act (CSA) and DEA standards. While the guidance provides additional directions on calculating THC content, it disclaims the FDA's intent to get involved with enforcement around whether a researcher's "hemp" triggers the CSA; that is, for the DEA: "FDA does not enforce the CSA or regulations within DEA's jurisdiction."

The FDA Again Points the Industry to Its 2016 Guidance on Botanical Drugs

The guidance points to the 2016 guidance for "Botanical Drug Development,"[5] and makes additional recommendations for researchers developing drugs with cannabis, including using a chemical fingerprint (i.e., an assay) to ensure that each batch is consistent and tested for pesticides. The guidance notes that "highly purified substances of botanical origin" are equivalent to conventional synthetic chemicals, but an isolate with a "different impurity profile" from a synthetic would not be. The guidance recommends that researchers develop assays to measure amounts of specific cannabinoids and their impact on bodily functions in humans and animals. Specificity is key, and reliance on public information about cannabinoids may not be sufficient. The guidance comments that generally "chemical composition information found in published studies of test materials is not adequate for bridging to a proposed botanical drug product because the particular botanical drug product under review may differ from that of the published study."

The FDA Issues a Warning Shot to Inhaler and Other Device Manufacturers

Additionally, any product used with an inhaler or other device (such as the vaporizer pens prevalent in both the hemp isomer

and state cannabis markets) would be considered a "combination product" with additional regulatory requirements. This means that the hardware will come under similar scrutiny to the extracts contained within: "Sponsors and applicants should consider selection of a container closure system or device constituent part carefully. As drug development progresses, applicants pursuing FDA approval should generate adequate characterization information and safety assessment data for extractable and leachable compounds to support a marketing application."

The FDA Reminds Manufacturers That the Substance Abuse Potential Is Still Relevant

During the FDA approval process, a new drug may need to be rescheduled on the CSA, for which the FDA needs additional data to help evaluate the drug's abuse potential. On this subject, the guidance states: "FDA's review of the [new drug application] may include an abuse potential assessment to inform drug product labeling and to provide DEA with a scientific and medical evaluation of the drug's abuse potential to allow for drug scheduling or rescheduling under the CSA, if necessary."

Announcement on CBD: The FDA Needs Congress to Act

The FDA also has finally issued its long-awaited announcement on legal pathways for CBD products.[6] Having been ordered to find regulatory pathways for CBD on an expedited basis following the 2018 Farm Bill, now—over four years later—the FDA is reporting back that it cannot do so and is kicking the issue back to Congress.

The FDA Remains Unpersuaded by the Scientific Data

The FDA remains unpersuaded by the scientific data, even after having approved Epidiolex and considered the submitted studies/data. The announcement states: "Given the available evidence, it is not apparent how CBD products could meet safety standards for dietary supplements or food additives. For example, we have

not found adequate evidence to determine how much CBD can be consumed, and for how long, before causing harm."

This should not come as a surprise; the FDA sticks strictly to the Federal Food, Drug, and Cosmetic Act's statutory authority and regulatory requirements. In the announcement, the FDA recognizes as a solution "some risk management tools," including "clear labels, prevention of contaminants, CBD content limits, and measures, such as minimum purchase age, to mitigate the risk of ingestion by children," but concludes that it lacks the authority to implement that pathway. It needs Congress to act.

The FDA Will Not Be More Lenient with CBD for Animals

The FDA also expressed concern about animals and the food supply: "CBD also poses risks to animals, and people could be unknowingly exposed to CBD through meat, milk and eggs from animals fed CBD. Because it is not apparent how CBD products could meet the safety standard for substances in animal food, we also do not intend to pursue rulemaking allowing the use of CBD in animal food."

Conclusion

On the heels of Congress' failure to pass any cannabis reform during the two years when Democrats controlled both chambers of Congress and the White House, the FDA has exacerbated the federal government's blockade on progressing on cannabis and CBD. The two recent proclamations reiterate the agency's unwillingness to take any action, other than warning letters, in the face of approximately $40 billion in annual sales of state-legal cannabis and hemp products. The FDA has made clear what many have suspected for a while—that Congress needs to choose between helping to implement the rule of law in these emerging state-legal industries or standing idle, thus letting uncertainty and even lawlessness prevail.

Notes

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2. https://public-inspection.federalregister.gov/2023-01286.pdf.
3. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/cannabis-and-cannabis-derived-compounds-quality-considerations-clinical-research-guidance-industry.
4. https://www.deadiversion.usdoj.gov/drugreg/marihuana.htm?source=email.
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