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FDA Passes New Cannabis Guidance for Clinical Research

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Key Takeaways

- **What Happened:** The Food and Drug Administration (FDA) finalized a 2020 draft guidance detailing the agency's recommendations for clinical research for developing cannabis and cannabis-derived human drugs.
- **Who's Impacted:** Those involved in the clinical research of cannabis can rely on this FDA guidance for recommended sources of cannabis for clinical research and resources for information on quality and control status considerations. The guidance also recommends methods for researchers to calculate the THC differences between "hemp" and "cannabis." The guidance helps inform stakeholders, lawmakers, and others in the cannabis industry by addressing certain questions raised about drugs containing cannabis and key FDA regulatory concepts.

Background

On January 24, 2023, the FDA announced new guidance entitled "Cannabis and Cannabis-Derived Compounds: Quality Considerations for Clinical Research." The non-binding guidance discusses three key cannabis-related subjects:

- Sourcing cannabis for clinical research;
- How to calculate percent delta-9 tetrahydrocannabinol (THC) throughout the research cycle; and,
- General quality considerations for developing human drugs that contain cannabis and cannabis-derived compounds.

Generally, to be considered “hemp,” a product must contain less than 0.3 percent delta-9 THC by dry weight. Anything above 0.3 percent delta-9 THC is considered cannabis (or marijuana), a Schedule I controlled substance. Human drugs that contain hemp, cannabis, and cannabis-derived compounds are generally subject to the same authorities and requirements, including quality standards, as FDA-regulated drug products containing any other substance.

The goal of FDA’s latest guidance is to support clinical research for the development of cannabis and cannabis-derived human drugs. The guidance does not address the development of fully synthetic versions of substances that occur in cannabis and does not cover other FDA-regulated products.

Sourcing of Cannabis

The National Institute on Drug Abuse (NIDA) Drug Supply Program was the only legal source for scientists to acquire cannabis for many years. The NIDA Drug Supply Program continues to be a source of cannabis over the 0.3 percent delta-9 THC threshold for clinical research. In 2020, the Drug Enforcement Agency (DEA) adopted new procedures to allow the registration of new manufacturers to plant, grow, cultivate, or harvest cannabis. There was confusion, however, over whether clinical studies could use these new manufacturers. This guidance intends to clarify that confusion and provides that:

- For cannabis over the 0.3 percent delta-9 THC threshold and not part of an investigational new drug (IND) application - the NIDA Drug Supply Program and other sources authorized by DEA to provide Schedule I cannabis materials for research can be used.

- For any cannabis sources (above or below the 0.3 percent threshold) as part of an IND application- other sources can be used subject to the approval of the application.

While the sourcing of cannabis for clinical research has been a clear area of concern for those involved in the clinical research of cannabis, the FDA also provided guidance on more nuanced issues that this sector faces.

Calculation of THC

Farmers and researchers have long been concerned over the calculation of THC, given the unpredictable nature of the plant. Uncontrollable environmental factors as well as extraction and manufacturing processes can affect the THC concentration and push legal hemp into a controlled substance. The guidance recommends that scientists calculate the THC content in their proposed cannabis or cannabis-derived investigational drug product early in the development process to determine their product’s potential abuse liability and control status. The guidance also discusses the best calculation methods throughout the lifecycle of clinical studies.

General Quality Considerations

As part of an IND for any drug, researchers are expected to show that they can consistently manufacture a quality product. In each phase of clinical investigation, they must submit sufficient information to demonstrate the drug’s identity, quality, purity, and potency. The guidance includes

additional principles and recommendations that are particularly relevant for developing drugs that contain cannabis and cannabis-derived compounds:

- Cannabis and cannabis-derived compounds are held to the same regulatory standards as any other botanical raw material, botanical drug substance, or botanical drug product. This includes ensuring batch-to-batch consistency, conducting microbiological examinations and sterility tests, and testing for raw materials (among other specific requirements on p. 6 of the guidance).
- Quality tests, specific to dosage form, should be conducted.
- Impurities for naturally occurring compounds should be controlled.
- Researchers should not rely on published literature in place of data from a full toxicology program, as the particular botanical drug product under review may differ from that of the published study.
- Assess the metabolic profile of major cannabinoids in humans early for safety.

Impacts

This FDA guidance helps provides clarity to the cannabis industry on cannabis and cannabis-derived drug development in the wake of Congress passing the Medical Marijuana and Cannabidiol Research Expansion Act. Stakeholders have been eagerly awaiting updates from the FDA and other federal agencies regarding the sale and marketing of cannabis-derived products as well as a scientific review of cannabis to help reevaluate the substance's schedule under the Controlled Substances Act. As a high priority of the Biden Administration, we will likely see many key regulatory updates for cannabis in 2023.

Companies can submit online or written comments on this guidance at any time. The recommendations in this guidance are not mandatory or binding – researchers may use an alternative approach as long as it satisfies the requirements of the applicable statutes and regulations.

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