US FDA Publishes Draft Guidance for Industry Regarding Cannabis and Cannabis-derived Compounds

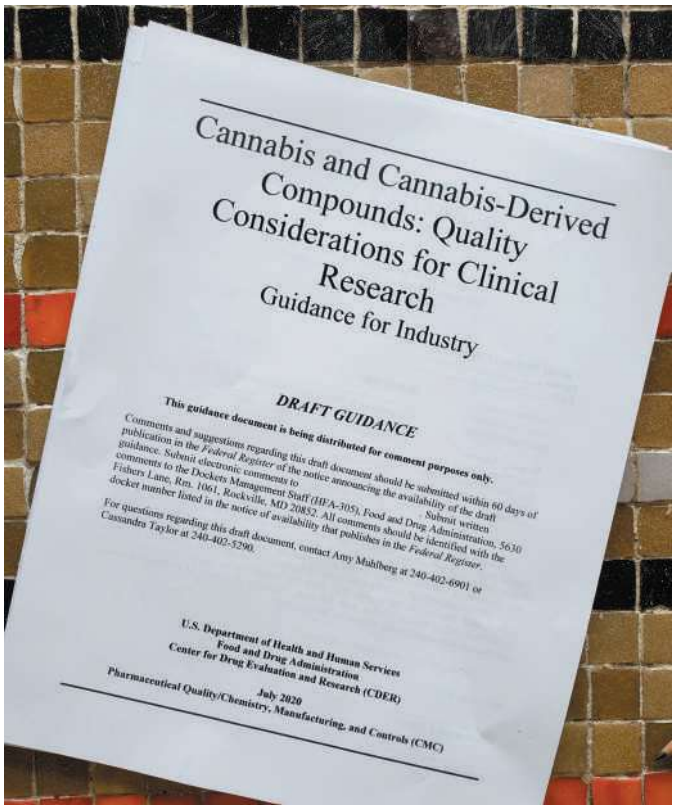
In July 2020, the US Food and Drug Administration (FDA) published the draft guidance entitled *Cannabis and Cannabis-Derived Compounds: Quality Considerations for Clinical Research Guidance for Industry*.[1] The 12-page draft contains non-binding recommendations and is not for implementation. Rather, FDA draft guidance is intended for public comment for the agency to consider as it compiles the final version of the guidance. The public comment period for this draft guidance ended on 21 September 2020.

This draft guidance outlines the FDA's current thinking on several topics relevant to the clinical research and development of drugs containing cannabis and cannabis-derived compounds: 1) The source of cannabis and cannabis-derived compounds for clinical research, 2) general quality considerations for developing drugs that contain cannabis and cannabis-derived compounds, and 3) calculation of percent delta-9 tetrahydrocannabinol (THC) in botanical raw materials, extracts, and finished products.

The legality of cannabis in the US has been changing over time at both the state and federal levels. Currently, 33 states, Puerto Rico, and Washington, DC, allow medical use of marijuana under state law, and 14 additional states have state law medical programmes that are limited to cannabidiol (CBD) products. Additionally, 11 states and Washington, DC, have legalised marijuana for recreational use under state law, and 16 other states have decriminalised recreational marijuana possession in some form under state law.

In the US, parts of the *Cannabis sativa* plant have been controlled under the Controlled Substances Act (CSA) since 1970 under the drug class "Marihuana." Cannabis contains more than 80 biologically active chemical compounds, including the two best-known compounds, THC and CBD. The Agriculture Improvement Act of 2018, or the Farm Bill, removed hemp from the CSA's definition of marijuana. The Farm Bill defined hemp as cannabis or derivatives of cannabis with a very low THC content (below 0.3% by dry weight). As a result, although marijuana remains a Schedule I drug (i.e., the most restrictive), hemp is no longer considered a controlled substance under federal law.

The Farm Bill explicitly preserved the FDA's authority to regulate products containing cannabis or cannabis-derived compounds under the Public Health Service Act. In doing so, the US Congress recognised the FDA's public health role with respect to the products it regulates, including products that are or contain cannabis ingredients. In general, drugs containing cannabis and cannabis-derived



compounds are subject to the same authorities and requirements as drugs containing any other substance.

Drugs intended for human use are evaluated by the FDA's Center for Drug Evaluation and Research (CDER) to ensure that drugs marketed in the US are safe and effective for their intended uses and will be manufactured in a manner that ensures quality. A CDER subunit called Small Business and Industry Assistance (SBIA) helps small pharmaceutical businesses and industry navigate FDA information about drug development and assists in understanding the regulation of human drug products.

As noted in the Federal Register announcement for the July draft guidance, the FDA encourages drug developers to meet with agency regulators early in their development programmes – ideally, before submitting an investigational new drug application (IND). Pre-IND meetings offer an opportunity to obtain FDA input on research plans and required content for an IND submission, complementing guidances and other information provided by the agency. Early interactions with FDA staff through a pre-IND meeting can answer sponsors' questions related to a specific drug development programme and provide information that will assist them in preparing complete IND applications. "Efficient use of FDA resources can lead to more efficient drug development."[2]

First CBD Product Approved by the FDA to Treat Rare Forms of Epilepsy

In June 2018, the FDA approved Epidiolex (cannabidiol), from GW Research Ltd – the first approved drug composed of an active ingredient derived from marijuana – to treat rare, severe forms of epilepsy (Dravet syndrome, Lennox-Gastaut syndrome). The FDA granted several incentives during the development of Epidiolex: priority review designation for the application, fast-track designation for the Dravet syndrome indication, and orphan drug designation for both the Dravet syndrome and Lennox-Gastaut syndrome indications. The FDA Press Release about the Epidiolex approval noted that CBD does not cause intoxication or euphoria (the "high") that comes from THC – the primary psychoactive component of marijuana.

Ahead of the Epidiolex approval, in April 2018, the FDA's Peripheral and Central Nervous System Drugs Advisory Committee (PCNSDAC) offered unanimous support for the benefit-risk profile of this CBD oral solution for the adjunctive treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients aged two years and older. The PCNSDAC based its support on data from three Phase III studies in patients with Lennox-Gastaut syndrome or Dravet syndrome, for which the primary endpoint was percentage change from baseline in seizure frequency (drop seizure frequency in two trials, convulsive seizure frequency in the third).

REFERENCES

1. Cannabis and Cannabis-Derived Compounds: Quality Considerations for Clinical Research; Draft Guidance for Industry; Availability, Federal Register 85 (141), 22 July 2020, 44305-7. https://www.govinfo.gov/content/pkg/FR-2020-07-22/pdf/2020-15907.pdf
2. Cannabis and Cannabis-Derived Compounds: Quality Considerations for Clinical Research Guidance for Industry Draft Guidance for Industry, July 2020 https://www.fda.gov/regulatory-information/search-fda-guidance-documents/cannabis-and-cannabis-derived-compounds-quality-considerations-clinical-research-guidance-industry

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