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Cannabis-Derived Ingredients in FDA-Regulated Products: More Questions than Answers at FDA's May 2019 Public Hearing

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As most folks with any interest in the burgeoning cannabidiol (CBD) industry likely know, on May 31, 2019, the Food and Drug Administration held a public hearing "to obtain scientific data and information about the safety, manufacturing, product quality, marketing, labeling, and sale of products containing cannabis or cannabis-derived compounds." Stakeholders who attended the hearing presented many diverse viewpoints and the FDA panelists – who were in listening mode – received extensive information from across that spectrum of perspective.

But if anyone expected clarity from the Agency on June 1st, they are probably feeling disappointed today. Almost every issue raised by presenters will require significant regulatory attention – from how to determine the proper dosing of CBD depending on whether it is intended to be used for therapeutic purposes or for "general wellness," as several commenters discussed, to how to set analytical standards for laboratories to follow when testing CBD or other cannabis derivatives for quality and potency – and the Agency will likely accomplish very little quickly given the dearth of data and the complex nature of the issues. All presenters urged FDA, however, to move deliberately and expeditiously in exercising its existing authorities to provide consumers, industry, health care professionals, and state regulators and law enforcement the certainty they need when it comes to how the Agency intends to handle cannabis-derived products.

Why Did FDA Hold This Hearing Now?

A few level-setting points before we share our takeaways from the FDA's public hearing.

First, it is important to understand that both marijuana (a Schedule I controlled substance) and industrial hemp (now de-scheduled following congressional enactment of the most recent Farm Bill in December 2018, and defined as having no more than 0.3% tetrahydrocannabinol (THC) on a dry weight basis) come from different strains of the Cannabis sativa plant. As a result, individual presenters spoke to the panel of 12 high-ranking FDA officials about either medical uses of marijuana or hemp-derived extracts like CBD. Although medical marijuana is legal at the State level in 33 states and the District of Columbia, its effectiveness as a therapeutic product still is not recognized at the Federal level. There are a variety of public health challenges resulting from this two-tier status of

medical marijuana, including the difficulties that arise if someone wants to do serious clinical research on its effects, but we will keep that topic for a different blog post and focus this one on the de-scheduled ingredients and their addition to FDA-regulated products like foods and personal care products.

Second, the commercial market for CBD products in particular has exploded since the 2018 Farm Bill removed industrial hemp from the Controlled Substances Act. Over the past six months, American consumers have seen CBD enter their coffee shops and restaurants, their drug stores and bodegas, and even their grocery stores. It is being sold as CBD oils, sprays and tinctures for ingestion, but also in creams and salves for topical use, in liquid form for "vaping" (using an electronic cigarette-like device), and in more traditional pills and capsules. One of the presentations during the hearing came from the independent non-profit organization Consumer Reports, which recently conducted a survey of over 4,300 adults and uncovered some striking trends, including that a quarter of Americans have tried CBD at least once in the past two years. (The Consumer Reports survey data is available for review here, and all of the presenters were asked to submit their reports and data to the FDA public docket, which can be accessed and searched here. As of now, this docket is set to close after July 2, 2019 although FDA has discretion to extend that comment period further, an action that at least a few people requested that the Agency take.)

Another recent study estimated that the CBD market will reach over $16 billion by 2026, so it was not surprising that many of the stakeholders who presented their views to FDA asked the Agency not to interfere with the growth of this industry. From many of the agricultural stakeholders as well, a major focus of the comments made to FDA was that American farmers need the economic boost that industrial hemp is providing to them and that this benefit should be top of mind for the Agency. One very interesting fact that emerged from one of the presentations was that, at least in North Carolina, nearly 100% of the hemp being grown there today is being harvested specifically for CBD extraction. However, as a public health agency with its mandate squarely on ensuring the safety of our foods, dietary supplements, personal care products/cosmetics, and medicines, it is unclear how much FDA will take those economic considerations into account when it is faced with such a lack of scientific evidence for either the safety or efficacy of CBD or other hemp-derived cannabinoids.

So, the short version is that FDA held this hearing because it could no longer ignore these issues – CBD and other cannabis-derived ingredients and products have become too mainstream, and consumers are using them even without an assurance of safety or effectiveness (when seeking a therapeutic effect). One parent of a child with a rare form of epilepsy who happened to be a doctor of pharmacy spoke of the sheer desperation that would drive someone like him to consider giving his preschooler an unregulated, untested, unproven form of CBD. In his case, he relayed, the timing was lucky for his family, and he did not have to resort to those options; his daughter is now taking the FDA-approved CBD medication Epidiolex® instead. He noted that her response to the drug has been incredible and he asked the Agency to keep rare disease patients in mind when deciding how to move forward with its regulation of cannabis-derived products, to ensure that legitimate drug development is not somehow disincentivized. This was one question that the FDA panelists asked often of certain presenters throughout the day – does or would the presence of dietary supplement forms of CBD and other cannabinoids in the market have an impact on your drug development programs or strategies? At least in the context of the public hearing, most speakers responded that it has not and it likely would not, but the written submissions made to the meeting docket will likely delve into this complex issue in much more detail.

Common Themes that Emerged During the FDA Hearing

We have previously written about the general enforcement position the Agency has taken to date with CBD products (see prior post here). Making drug claims about them is a high-risk proposition, and FDA has issued warning letters here and there over the past few years to marketers of such products. And even though FDA has clearly stated in several different forums that adding CBD as an ingredient to any food, beverage, or dietary supplement is prohibited (essentially because it's a known drug), the Agency has not taken any specific actions involving such consumer products that contain CBD but are not being sold with associated drug claims. This ambiguity has led to what several presenters on May 31st called a "Wild West" atmosphere in the country when it comes to CBD, with many marketers either unaware of the FDA's authorities over such products (i.e., they may presume that the fact hemp-derived CBD is no longer controlled means it can be added to everything) or accepting the regulatory uncertainty as a tolerable business risk in light of the massive consumer demand.

Consequently, probably the most consistent theme to come out of FDA's hearing was that everyone wants more certainty no matter where they stand in terms of CBD's benefits or what they think the Agency should do (or not do) with respect to this ingredient. A few speakers discussed lesser-known hemp derivatives, like other cannabinoids (CBC, CBG) and terpenes, and asked FDA to ensure that any regulatory framework(s) it establishes takes into account all of these derivatives, which we know less about than CBD but which also pose great promise for a variety of consumer and medical applications. They also noted that, unlike CBD, these other cannabis derivatives are not prohibited from the food supply because they have never been approved for use as a drug or tested in clinical trials for specific medical uses.

Acting FDA Commissioner Ned Sharpless delivered opening remarks at the hearing, during which he specifically addressed the prohibited-from-food problem faced by CBD in particular; he stated:

> "What that means is that, under current law, CBD and THC cannot lawfully be added to a food or marketed as a dietary supplement. Although the law says that FDA can issue regulations to create new exceptions to these statutory provisions, FDA has never issued a regulation like that for any substance. So, if we were thinking about doing that for a substance like CBD, it would be new terrain for the FDA."

Several of the presenters challenged the Agency on this interpretation of the law as well as its historical records, suggesting that on at least one occasion, such a regulation has been issued. Needless to say, it's possible FDA will be receiving Citizen Petitions asking it to take certain specific actions even though it has signaled its intent to do something in this area both with the public hearing and the announcement in early April 2019 of the creation of a "high-level agency working group to explore potential pathways for dietary supplements and/or conventional foods containing CBD to be lawfully marketed; including a consideration of what statutory or regulatory changes might be needed and what the impact of such marketing would be on the public health."

The FDA panelists, which included the co-chairs of the internal working group, asked many of the presenters a similar question, although it varied based on whether the speaker was an entrepreneur, a health care professional, or a consumer: "How do you determine dosing for the CBD that you add to your products/you give to your patients/you take at a given time?" Essentially no one had a good answer, and no one provided concrete information about how to take into consideration the risks associated with a cumulative dose of CBD, such as when a consumer uses a topical product but also

ingests and vapes the compound all in a single day. Because the prescription CBD drug Epidiolex has warnings in its label about liver toxicity, suicidal behavior/ideation, and hypersensitivity reactions, the safety risks cannot be ignored by FDA notwithstanding the many speakers who asserted to the Agency that “CBD is completely safe” and it should not be overregulated. Safety issues related to chronic use, as well as use by pregnant women, children, and vulnerable populations like the elderly were also addressed by multiple speakers. There also were requests for FDA to establish a zero-THC standard in all hemp-derived products, notwithstanding that the Farm Bill set a 0.3% threshold for purposes of de-scheduling the industrial hemp plant, because as commentators noted, the 0.3%-by-dry-weight standard still means that you can have a very high level of THC in a couple of CBD-containing gummy bears, thereby eviscerating the idea that all CBD products are non-psychoactive and “safer” than THC-containing products that are ingested or smoked precisely for their psychoactive properties.

Another major topic of discussion was the lack of standardization in the CBD industry, adherence to quality standards, and the lack of truthful labeling. For example, several stakeholders presented results of their own laboratory testing of commercially available CBD products that showed a large number of products containing much higher or much lower amounts of CBD than the label claims (and in some cases, zero CBD); in some cases containing high levels of THC; and even high levels of unsafe contaminants like lead. This type of survey data clearly demonstrates to the Agency and other regulatory and standards-setting bodies that there are both good and bad actors in this industry, and a certain level of regulation is definitely necessary to protect consumers from being defrauded, injured, or both. But perhaps the only clear message we can share coming out of the FDA public hearing is that what that regulation is going to look like remains to be seen!

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