Council For Federal Cannabis Regulation

Mainstreaming CBD Infused Food and Beverages; FDA Regulation Needed

Part 2

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Food and beverages containing cannabidiol ("CBD") seem to be everywhere. But is any of this legal? You would think so given the number of products in the market and the 2018 Farm Bill that legalized hemp at the federal level. However, from the perspective of the Food and Drug Administration ("FDA") and other federal agencies the answer is no, with a few limited exceptions. The lack of clear regulations from the FDA makes it difficult for major consumer packaged goods companies to enter this market and meet the surging demand by the public for CBD infused food and beverages. The previous article provided an overview of cannabis (the plant from which CBD is derived), including its physical properties and purported health benefits. This article discusses the FDA and federal regulatory framework relevant to CBD infused products going mainstream.

Legality of Marijuana and Hemp at the State and Federal Level

Pre-2018; Marijuana and Hemp Illegal at the Federal Level

As discussed earlier, cannabis was widely used until the 1930s. Things changed dramatically following the passage (over the opposition of the American Medical Association) of the Marihuana Tax Act of 1937. While this law did not expressly prohibit the sale of cannabis it nonetheless made it illegal in effect by imposing a host of onerous tax reporting requirements and restrictions.

Then in 1970 under the Controlled Substances Act all types of cannabis (including hemp, which does not get users high) were formally made illegal as a result of being classified as a Schedule 1 narcotic- the most dangerous class of narcotics that by statute are classified as having no accepted medical use, having a high potential for abuse, and not safe for use even under medical supervision. Other drugs listed as Schedule 1 substances are heroin, LSD and ecstasy. Many observers have questioned why marijuana is a Schedule 1 narcotic while seemingly more potent drugs like cocaine are a Schedule 2 narcotic.

Growing Legality of Cannabis at the State Level

Notwithstanding the federal prohibition of cannabis, in 1996 California became the first state to legalize the use of medical cannabis. Interest in cannabis, and in particular CBD, increased greatly in 2013 following the publicity surrounding a young girl named Charlotte Figi, suffering from a rare seizure disorder called Dravet syndrome. Desperate to help their daughter, Charlotte's parents heard through the grapevine that

a low-THC, high-CBD strain of cannabis might help their daughter and they received medical approval to try. The results were dramatic and years later Charlotte was doing much better until she passed in 2020, possibly due to Covid 19.

Currently, 36 states and the District of Columbia have approved cannabis for medicinal use, and in 17 states and the District of Columbia recreational or adult use is also permissible. The state laws approving cannabis vary dramatically, so there in nothing resembling any type of standardization. In states with just medical marijuana laws a recommendation from a health care professional is required to obtain cannabis, and in most states "prescribed" cannabis can only be used to treat certain specified conditions identified in the enabling statute.

Post 2018; Hemp Legal at the Federal Level

This situation of treating hemp like marijuana under federal law was corrected in 2018 under the Agriculture Improvement Act of 2018 (the "2018 Farm Bill"), which provided that hemp containing 0.3 percent or less of THC on a dry weight basis was no longer classified as a controlled substance under federal law, effectively making it legal throughout the United States. Importantly though, all other types of non-hemp cannabis (that is, marijuana), including CBD that is derived from these types of cannabis, are still Schedule 1 controlled substances under the Controlled Substances Act, but permissible under the laws of those states that have legalized cannabis. As a result of the 2018 Farm Bill, under federal law products containing hemp derived CBD can be sold nationally and across state lines; however, products containing marijuana derived CBD (with or without THC) can only be grown,

processed and sold with in the boundaries of those states that have legalized such products (and not sold or transported across state lines).

The 2018 Farm Bill includes two key limitations. First, it allows states to be the primary regulators of hemp in their states and potentially take a more restrictive approach to the sale of hemp and hemp-derived products than the federal government, which several states have done. In that regard, most states have their own schedules of controlled substances that did not automatically change when the Controlled Substances Act changed; a minority of states have incorporated federal controlled substance schedules by reference from the Controlled Substances Act. So, notwithstanding that the 2018 Farm Bill legalized hemp at the federal level, a careful review of state law is still needed to determine how hemp is regulated in any given state. Second, the legislation expressly reserves the right of the U.S. Food and Drug Administration ("FDA") to regulate products containing cannabis, or cannabis-derived compounds, under the Federal Food, Drug and Cosmetic Act in the same way that it regulates other products (more on this below).

Federal Food, Drug and Cosmetic Act & the FDA

As an agency within the U.S. Department of Health and Human Services, the FDA's mission is to protect the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, biological products and medical devices; and by ensuring the safety of our nation's food supply, cosmetics and products that emit radiation (which at high levels results in cell damage). The FDA's stated position is that it will regulate products containing CBD-hemp in the same way it regulates other products.

FDA Regulation of Drugs

The Food, Drug and Cosmetic Act ("FD&C Act") prohibits the introduction into interstate commerce (that is, moving something across state lines) any drug, medical device, food, tobacco product or cosmetic without the required FDA approval, permit or registration. It also prohibits the introduction of any food or drug product that is "adulterated" (which includes products containing unacceptable levels of contaminants or products that were not manufactured in compliance with Good Manufacturing Practices) or mislabeled. Good Manufacturing Practices refers to regulations established by the FDA that require manufacturers, processors and packagers of drugs, medical devices and some foods to take certain actions, on an ongoing basis, to ensure that their products are safe, pure and effective.

The FD&C Act generally defines a "drug" as (a) any article intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in humans or animals, or (b) any article (other than food) intended to affect the structure or function of any human or animal body. The FD&C Act generally prohibits a company from introducing a drug into interstate commerce without the FDA having first approved the drug as being both safe and effective for treating a specified medical condition.

FDA approval of drugs for human consumption generally involves a long and expensive process. First, the drug manufacturer performs laboratory and animal tests to determine how the drug works and whether it is safe enough to test on humans. Second, if the manufacturer determines that a drug is safe enough to test on humans, it submits for FDA review what is called an Investigational New Drug. Third, following review of such application, if the FDA determines a drug is sufficiently safe to test on humans the FDA will permit the manufacturer to proceed with human clinical trials. Finally, if the FDA determines after its review of the clinical trials that the drug's benefits outweigh its known risks and the drug can be manufactured in a way that ensures a quality product, the drug will be approved as safe and effective for treating the specified medical condition. A drug generally may not be marketed for treating a condition other than a condition for which the FDA has found the drug to be a safe and effective treatment; however, most FDA approved drugs can be prescribed by doctors to treat other conditions. Over-the-counter drugs can be marketed after receiving FDA approval through the above process or by conforming the drug to an existing over the counter "monograph" (a "recipe book" indicating acceptable ingredients, doses, formulations and labeling) established by the FDA.

Cannabis Based Drugs Approved by the FDA

Cannabinoid-based pharmaceuticals are drugs containing cannabinoids, or cannabinoid-like compounds, that are either derived from natural cannabis or chemically synthesized. The FDA has approved several of these types of drugs. In 1985 Marinol, a drug comprised of dronabinol (a synthetic THC) encapsulated with sesame oil in a soft gelatin capsule, and Cesamet, a drug comprised of encapsulated nabilone (a synthetic cannabinoid similar to THC) were approved for treatment of nausea and vomiting associated with chemotherapy in patients who have failed to respond to conventional treatments. Marinol was later approved, in 1992, for treatment of anorexia associated with weight loss in patients with AIDS. Syndros, a drug comprised of dronabinol in a liquid solution, was approved by the FDA in 2016 for treatment of the same symptoms for which Marinol was approved. The FDA also approved the drug Epidiolex, which contains a purified form of CBD from the cannabis plant, for the treatment of seizures associated with Lennox-Gastaut syndrome and Dravet syndrome.

The FDA is aware that some firms have and are marketing (without FDA approval) CBD products (foods, gummies, cosmetics and more traditional drug delivery dosage forms such as tablets and capsules) as drugs in order to treat diseases or for other therapeutic uses, and under FDA rules such products are unapproved drugs. Consequently, the FDA has issued several warning letters to such firms. The FDA has also received reports of adverse effects on patients using cannabis or cannabis-derived products to treat medical conditions, and it is monitoring such reports.

FDA Regulation of Food Additives and Dietary Supplements

Under the Food Additives Amendment of 1958, which amended the FD&C Act, the FDA was given regulatory oversight over food additives. A food additive generally means any substance that is deliberately added to food or beverages. The Dietary Supplement Health and Education Act of 1994 further amended the FD&C Act to give the FDA regulatory oversight over dietary supplements. A dietary supplement is a product taken by mouth that contains a "dietary ingredient", which includes vitamins, minerals, herbs, botanicals, amino acids or other dietary substances used by humans to supplement their diet. The terms food additive and dietary supplements overlap somewhat, and it is possible that a particular substance may be both such items at the same time.

The FD&C Act requires most foods and dietary supplements to have labels that specify nutrient content claims and contain certain health messages. Dietary supplements must be manufactured in compliance with Good Manufacturing Practices for Dietary Supplements. The FDA is authorized to enforce safety and labeling regulations by conducting inspections, sampling, recalls and seizures, and by pursuing injunctions and criminal prosecutions. The only active ingredients that may lawfully be included in dietary supplements are "old dietary ingredients" ("ODIs"; dietary ingredients that were marketed before October 1994, the date that the Dietary Supplement Health and Education Act became effective), "new dietary ingredients" ("NDIs", which require FDA "premarket" approval before marketing an NDI), or NDIs that have been included in food on the basis of being "generally recognized as safe" (NDIs that are generally regarded as safe in the scientific community do not require premarket approval from the FDA before marketing them).

The current view of the FDA is that CBD is not an ODI, so its approval as a dietary supplement is subject to the NDI premarket approval.

The regulatory authority of the FDA over food (including food additives) and dietary supplements is not nearly as expansive as its regulatory oversight over drugs, where it exercises tight control over which drugs enter the market. Rather, in the case of food and dietary supplements the producers are largely responsible for ensuring that their products are safe, effective, manufactured in compliance with Good Manufacturing Practices and properly labeled. The FDA will generally step in only if a manufacturer is making false or misleading claims (for example, that a dietary supplement cures a particular disease), or in response to complaints. Consequently, while there is some FDA oversight of food and dietary supplements, for the most part consumers are putting their trust in the hands of the manufacturers when they purchase their products.

The process of obtaining FDA approval to market food additives and dietary supplements are described in greater detail below.

FDA Announces CBD is not a Permissible Ingredient in a Dietary Supplement or Food Product

When CBD (even derived from federally legal hemp) or other cannabinoids are included in a food or beverage they would appear to be a "dietary supplement" or "food" based upon the defined meaning of those terms and a common sense understanding of those terms.

However, the FDA's current position is that cannabinoids that are included in food or beverages are not a dietary supplement or food ingredient under the FD&C Act because of the so-called "Drug Exclusion Rule". This rule states that an article (including hemp- CBD) cannot be sold as a food or dietary supplement unless that article was marketed as such before it was used an active ingredient in an approved FDA drug or the active ingredient of a new drug in clinical trials that have been made public (technically called an "Investigational New Drug"). The thinking behind this rule is that if a particular product has already been approved as a drug it cannot, at the same time, also be a food ingredient or dietary supplement. The FDA's current view is that since CBD had been approved by the FDA as a new drug, namely Epidiolex, before it was sold as a dietary supplement or food, it cannot now be sold as such. Of note, the CBD in Epidiolex was derived from the cannabis plant; had it been synthetically produced the Drug Exclusion Rule might not apply.

Notwithstanding the FDA's current position that CBD is not a food ingredient or dietary supplement because of the Drug Exclusion Rule, there are several paths around this.

First, the FDA has the authority to issue a regulation, after a notice and hearing, to waive the Drug Exclusion Rule as it relates to hemp-CBD. To date, the FDA has declined to exercise that authority.

Second, bi-partisan bills H.R. 841 and S.1698 have been introduced in Congress that would expressly amend the FD&C Act to exempt hemp-CBD from the Drug Exclusion Rule.

Third, the FDA has indicated an openness to hearing evidence that hemp-CBD was marketed as a dietary supplement prior to Epidiolex being approved as a drug.

While the issues and law related to establishing prior marketing are complex, the possible argument boils down to the following. Hemp-CBD contains many cannabinoids, among them CBD, and those compounds can be processed in a variety of ways. In some cases, particular

compounds can be isolated from the other compounds (so-called “isolates”); this was the case for Epidiolex, which uses isolated CBD. However, hemp can be processed to extract not just CBD, but also other compounds found in the hemp plant (so-called “full spectrum” extracts). It could therefore be argued that full spectrum hemp-CBD, which has been consumed for thousands of years as food and medicine, is different than the CBD isolate used in Epidiolex and should not be barred by the Drug Exclusion Rule. Any such claim would face the further hurdle that, until the passage of the 2018 Farm Bill, the marketing of hemp was illegal.

Of note, the Drug Exclusion Rule may not prevent cannabinoids, other than CBD, which are included in food or beverages from being a food ingredient or dietary supplement. This is because, as the FDA has stated, only CBD (and not other cannabinoids) was included in Epidiolex.

Also of note, the Drug Exclusion Rule does not impact the sale of cosmetic products containing CBD. Under the FD&C Act a product is a cosmetic or a drug depending on its intended use; a cosmetic is a product “...applied to the human body... for cleansing, beautifying, promoting attractiveness, or altering the appearance" and drugs are described above. Intent is determined in several ways; claims made by the seller of the product, consumer perception and the use of ingredients that have a drug like therapeutic use.

Warning Letters and Safety Concerns from the FDA

FDA Warning Letters

In July 2019 the FDA issued a warning letter to the cannabis producer Curaleaf, who was planning on selling in interstate commerce its hemp-CBD lotions, pain-relief patches, tinctures and vape pens in 800 CVS Health stores. On its web site and in various social media platforms Curaleaf claimed that these products treated medical conditions such as cancer, Alzheimer’s disease, chronic pain and anxiety. Since these products had not been approved by the FDA as a drug they were being sold in violation of the FD&C Act, and Curaleaf was required to pull them from the market. About two dozen similar warning letters were previously issued by the FDA to other companies for marketing their CBD products as a dietary supplement or drug that claimed to prevent, diagnose, mitigate, treat, or cure various diseases despite these products not meeting the definitions of such.

Later in 2019 and in 2020 the FDA issued additional warning letters to three dozen companies for illegally selling products in interstate commerce containing CBD (oil drops, capsules, syrups, food products such as chocolate bars and teas, and topical lotions and creams) in violation of the FD&C Act. The marketing of these products, on various product webpages, online stores and social media platforms, as drugs (including as treatment for Covid-19) or dietary supplements violated the FD&C Act because prior FDA approval was not received. The FDA also noted that some of the products were foods to which CBD had been added and the inclusion of CBD would constitute an unapproved food additive under the FD&C Act.

FDA Concerns About CBD

While the FDA recognizes the potential therapeutic benefits of cannabis and acknowledges the significant interest from

the public in these possibilities, it nevertheless has serious concerns as to whether the products being sold work, what dosages are appropriate, how these products interact with other drugs and whether these products have dangerous side effects. The FDA is concerned about the public attitude that trying CBD "can't hurt" and that consumers may delay or forego entirely getting conventional medical attention while relying on unsubstantiated claims associated with CBD products. The FDA has also received reports of cannabis products containing contaminants, such as pesticides and heavy metals, further complicating this issue. In a Consumer Update issued by the FDA in November 2019 they specifically noted the following health concerns:

"CBD has the potential to harm you, and harm can happen even before you become aware of it.

- *CBD can cause liver injury.*
- *CBD can affect the metabolism of other drugs, causing serious side effects.*
- *Use of CBD with alcohol or other Central Nervous System depressants increases the risk of sedation and drowsiness, which can lead to injuries.*

CBD can cause side effects that you might notice. These side effects should improve when CBD is stopped or when the amount ingested is reduced.

- *Changes in alertness, most commonly experienced as somnolence (drowsiness or sleepiness).*
- *Gastrointestinal distress, most commonly experienced as diarrhea and/or decreased appetite.*
- *Changes in mood, most commonly experienced as irritability and agitation.*

There are many important aspects about CBD that we just don't know, such as:

- *What happens if you take CBD daily for sustained periods of time?*
- *What is the effect of CBD on the developing brain (such as children who take CBD)?*
- *What are the effects of CBD on the developing fetus or breastfed newborn?*
- *How does CBD interact with herbs and botanicals?*
- *Does CBD cause male reproductive toxicity in humans, as has been reported in studies of animals?"*

The FDA noted that, based on the lack of scientific information supporting the safety of CBD in food, there is currently no basis to find that CBD is generally recognized as safe among qualified experts for use in human or animal food (more on this below). Further, the FDA said that they do not know of any other regulation that would permit the use of CBD as an ingredient in human food or animal food.

Making CBD an Approved FDA New Dietary Ingredient or Food Additive

As discussed above, CBD cannot be used in foods as a food additive or a dietary supplement as long as its characterization as such is blocked by the Drug Exclusion Rule. However, if the Drug Exclusion Rule no longer applies CBD might be included:

1. In dietary supplements under the FDA New Dietary Ingredients rules.
2. In foods as a food additive under the FDA Food Additive Petition Rules.
3. In both foods as a food additive and in dietary supplements under Generally Regarded as Safe rules.

NDI Process for Approving CBD as an Approved FDA Dietary Supplement

A "dietary supplement", as discussed above, is a product that is intended to supplement a diet (and is not represented as a conventional food) that contains one or more "dietary ingredients", a term that is defined to include vitamins, minerals, herbs, botanicals, amino acids and other substances such as extracts and concentrates. A "new dietary ingredient" or "NDI" is a dietary ingredient that was not sold in the U.S. in a dietary supplement before October 15, 1994 (the date the law governing dietary supplements, the Dietary Supplement Health and Education Act ("DSHEA"), became effective). The FDA does not maintain a definitive list of substances that were marketed as dietary ingredients before October 15, 1994. Before that time dietary supplements were regulated the same way as other foods. FDA approval is required to market dietary supplements containing NDIs either from an NDI Notification process or, as described later in this article, a Generally Recognized as Safe process.

Under DSHEA, the manufacturer or distributor of an NDI or a dietary supplement that contains an NDI must submit a premarket notification (an "NDI Notification") to the FDA at least 75 days before introducing the product into interstate commerce unless the NDI and other ingredients in the dietary supplement have been part of the food supply and did not alter the chemical composition of food. If a particular NDI does alter the chemical composition of a food, then the manufacturer or distributor must file with the FDA an NDI Notification in which it provides evidence that the NDI will reasonably be expected to be safe under the conditions of suggested use as specified in its labeling. The FDA must respond to the NDI Notification within 75 days after the filing has been accepted with: a letter of acknowledgement, without objection; a letter listing deficiencies that make the NDI Notification incomplete; an objection letter raising safety concerns based upon the information contained in the NDI Notification or identifying deficiencies in the safety evidence provided; or a letter raising other regulatory issues with respect to the NDI Notification or dietary supplement. The existence and terms of an NDI Notification are kept confidential for 90 days after the NDI Notification is accepted for filing by the FDA; after that, the NDI Notification is made public, except for proprietary or trade secret information.

The NDI Notification to the FDA requires, among other things, a detailed description of the dietary supplement and constituent NDIs, levels of the NDIs, conditions of use of the product recommended in the labeling, manufacturing and processing methods, terms of usage and evidence that the NDIs, when used under the conditions recommended in the labeling, will reasonably be expected to be safe. For botanicals such as CBD, the FDA requires further detailed disclosure as to the conditions in which the plants were propagated and cultivated, and how the NDIs were extracted.

Safety of NDIs can be established a number of ways, including a history of safe usage (at least at the levels of intended use), and from scientific and other literature (including published and unpublished peer-reviewed scientific literature, reports from authoritative bodies, survey data, promotional material and cookbooks). Evidence of the foregoing from other countries is acceptable to the FDA. When the historical uses of an NDI differs significantly from the proposed use of the NDI in a dietary supplement, the FDA typically requires additional evidence as to safety in the form of toxicity and other studies conducted by the applicant.

Manufacturers can only make three types of claims with respect to their dietary supplements: health claims (the link between the dietary supplement and a disease or health related condition), structure/function claims (the intended benefit of using the dietary supplement),

and nutrient content claims (the amount of the nutrient in the dietary supplement). A dietary supplement cannot, however, be marketed as a treatment or cure for a specific disease, as it would then be considered an unapproved drug.

FAP Process for Approving CBD as an Approved FDA Food Additive

Any substance that is intentionally added to food is a food additive; adding such a substance requires approval from the FDA from a Food Additive Petition ("FAP") process or as described in the next section, a Generally Recognized as Safe process. The FAP contains information identifying the food additive, its proposed use (as specified in its labeling), estimated daily intake, and data concerning its effect on food and safety studies (toxicological and other studies). In addition, the FDA may request details of production methods and facilities, as well as samples of the food additive for testing. Designated confidential information and trade secrets provided to the FDA are exempt from public disclosure.

Within 30 days of accepting a FAP the FDA publishes a notice of filing in the Federal Register (the official journal of the federal government, published every weekday, that contains government agency rules, proposed rules and public notices). Within 90 days of filing, the FDA then issues a regulation or denies the petition, in either case notifying the petitioner of the reasons for such action. A final order is issued by the FDA within 180 days of the filing date; however, this date is often extended. Unlike a new drug application, which gives the petitioner an exclusive private license to sell a drug product, a food additive petition results in a non-exclusive public regulation that permits anyone who complies with the terms of that regulation to use the approved food additive.

The FDA will not approve a food additive unless the data establishes that the additive is safe for its intended use. Unlike drugs, which are consumed often only for discrete periods, the FDA reviews the safety of food additives assuming that they may be consumed by various segments of the population over their entire lifetimes. In determining the safety of food additives, the FDA considers, among other things, the following: (A) the probable consumption of the food additive and of any substance formed in or on food because of its use; (B) the cumulative effect of such food additive in a diet, taking into account any chemically or pharmacologically related substances; and; (C) safety factors which in the opinion of experts, qualified by scientific training and experience to evaluate the safety of food additives, are generally recognized as appropriate.

GRAS Process for Approving CBD as an Approved FDA Food Additive or Dietary Supplement

A food additive may also be approved by the FDA if the FDA determines it to be Generally Recognized as Safe ("GRAS"). For CBD to be added to food as a food ingredient under GRAS it must be "common knowledge," throughout the expert scientific community that is knowledgeable about CBD, that there is a reasonable certainty CBD is not harmful under the conditions of its intended use. The GRAS process is the preferred way for companies to obtain approval for food additives since it is quicker and less expensive than going through a FAP process described previously. A substance included in a dietary supplement is not directly approved under the GRAS process in the same way as a food ingredient. Rather, FDA rules

provide that if a substance has been approved as a food additive under GRAS food additive rules, that same substance, if not chemically altered, may be included in a food supplement without the need to go through the NDI Notification process described above.

GRAS Process for Food Additives

The GRAS process permits companies, rather than the FDA, to determine whether a food ingredient meets the definition of GRAS in one of two ways. If an ingredient was used in food before 1958 it is GRAS, if there is a substantial history of consumption of the substance in food by a significant number of consumers. If the ingredient was not used in food before 1958, then the FDA requires evidence of "common knowledge" of the safety of an ingredient to the same extent as required to obtain approval of a food additive. GRAS does not require that the safety of food ingredients be established with absolute certainty; rather it must only be established with a degree of reasonable certainty that no harm will result from the intended use of such food additive.

Evidence as to the "common knowledge" of a food additive's safety must in all critical respects be based on scientific information that is public. This can include publications in peer-reviewed and other scientific journals, together with reports from recognized organizations such as the World Health Organization. Companies will typically undertake a "self-affirmation" GRAS study by hiring an outside firm to conduct safety studies regarding the substance, including its intended uses and anticipated consumption levels. This study is then reviewed by an independent panel of qualified experts who rule on whether the substance is safe for its intended use. The results of these self-affirmation safety studies then become part of the public record.

Each GRAS notice contains seven parts:

1. ***Signed Statements and Certification:*** Describes the intended conditions of use and the basis for the conclusion of GRAS status.

2. ***Identity, Method of Manufacture, Specifications and Physical or Technical Effect:*** Describes the information necessary to characterize the substance and to understand the method of manufacture.

3. ***Dietary Exposure:*** Describes the amount of the relevant substance that consumers are likely to eat or drink as part of a total diet.

4. ***Self-Limiting Levels of Use:*** Describes the circumstances where the amount of the substance that can be added to food is limited because above a particular level the food would become unpalatable or technologically impractical.

5. ***Common Use in Food Before 1958:*** For common use in food before 1958 to be the basis for the GRAS conclusion, the pre-1958 consumption must be by a significant number of consumers.

6. ***Narrative:*** Describes the basis for the conclusion of GRAS status.

7. ***Supporting Data and Information:*** Describes the supporting data, including the extent to which it is publicly available.

The FDA generally responds to a GRAS notice within 180 days of submission, but the FDA can extend this period for another 90 days as needed. The FDA will respond to GRAS notices in one of three ways: with a "no questions letter", which means that the FDA does not have concerns about the safety of a substance; with an "insufficient basis letter", which means that the GRAS notice did not provide the FDA with sufficient grounds to conclude that the relevant

substance is safe for its intended use; or with a "cease to evaluate letter", which means the FDA will cease (at the request of the submitting company) evaluating the GRAS notice. The "no question letter" is not an official approval, as is the case of a drug, for example, but more akin to the FDA not objecting to a GRAS determination made by a company. The FDA can de-GRAS a substance, in which case the substance may be marketed only if it receives premarket FAP approval by, or a later GRAS no questions letter from, the FDA.

It should be noted that the GRAS notice process is a voluntary mechanism. Before 1997 companies were required to have the FDA affirm GRAS status, but this was changed to the current voluntary method in order to lighten the FDA's administrative burden. Companies are free to "self-affirm" GRAS status for a food ingredient and go straight to market, however this is rarely done given the potential liability of putting an unsafe substance in the food stream and the requirements of manufacturers.

The FDA has not approved CBD as GRAS generally because of, as noted above, the lack of scientific studies. However, in December 2018 the FDA did not question the GRAS determination for (and hence the safety of) the following hemp seed-derived food ingredients, which were then permitted to be legally marketed in human foods: hulled hemp seed, hemp seed protein powder and hemp seed oil. The FDA noted that the seeds of the hemp plant do not naturally contain THC or CBD and, to the extent that they do contain trace amounts of these compounds, they are picked up during harvesting and processing when the seeds come in contact with other parts of the hemp plant. Some of the intended uses for these hemp-seed derived ingredients include adding them as source of protein, carbohydrates, oil and other nutrients to beverages, soups, dips, spreads, sauces, dressings, plant-based alternatives to meat products, desserts, baked goods, cereals, snacks and nutrition bars.

There are still many questions as to the purported health benefits and safety of consuming food and beverages containing CBD. There is also a significant lack of consumer knowledge about CBD notwithstanding the countless anecdotal stories about its effects. Having said all this, there is a huge demand for these products that is not being met because of the lack of regulatory guidance from the FDA and other federal agencies. This situation needs to change. This article provides the background and basis for informed discussions, among relevant private industry and regulatory stakeholders, to agree on a framework for CBD to be included in food and beverages.

This article was prepared by Jeffrey L. Dunetz and Sheri L. Orlowitz, co-founders of the Council for Federal Cannabis Regulation ("CFCR"). CFCR, an Internal Revenue Code 501(c)(3) and 501(c)(4), serves as a forum in which stakeholders - both from the federal government and industry - can analyze and support the creation of informed federal regulations to govern the cannabis industry. CFCR is currently focused on working with the FDA to mainstream the use of CBD and other hemp constituents in food and beverages.