CURIO WELLNESS

THE CASE FOR SAFE AFFORDABLE MEDICINAL CANNABIS IN THE US
De-Scheduling Cannabis is the Safe Route to Normalization

I. EXECUTIVE SUMMARY

Over the past year the Federal government has deliberated modifying the current regulation of the *Cannabis sativa* plant and derivative compounds (collectively, "*Cannabis*") as "Schedule 1" controlled substances, which effectively bans use of these products for any purpose. In response to formal inquiries by multiple US Senators an Governors, The DEA announced on August 11th, 2016 that *Cannabis* does not meet the criteria for removal from Schedule I. However, this finding is in stark contrast to the scientific data which supports the removal of *Cannabis* from the Schedule I. Even if *Cannabis* is taken out of Schedule 1, the question will remain whether and how *Cannabis* and *Cannabis*-containing products (collectively, "*Cannabis* products") should be regulated. Controlled substances are regulated by the Drug Enforcement Administration ("DEA"); however, assuming that *Cannabis* is de-scheduled, as it should be, an appropriate consumer product regulatory regime should be in place to enable consumer access, while ensuring safe and consistent manufacturing and distribution of products. With specific updates, the framework of the Federal Food, Drug, and Cosmetic Act ("FDCA") can be readily adapted for these purposes.

The States and Federal government must address both modern scientific knowledge and the political realities surrounding *Cannabis* products. It is timely for Congress to de-schedule Cannabis completely, and to establish an evidence-based regulatory paradigm that acknowledges: (1) *Cannabis* products are useful and in demand; (2) one size does not fit all products from a regulatory perspective; and (3) American consumers are very capable to choose whether individual products may be right for them. Moving *Cannabis* from a "Schedule 1" to a "Schedule 2" controlled substance is not appropriate or adequate, nor will it address the current legal conflict between the Federal and State governments. Instead, Congress should create an appropriate legal regime that incorporates the following elements:

1. **De-schedule *Cannabis* products so that they will no longer be regulated as controlled substances.** The collected scientific and medical evidence shows that *Cannabis* products have legitimate uses (including medical and consumer product uses) and do *not* present measurable risks of diversion and dependence that might properly subject products to continued regulation by DEA. Shifting *Cannabis* from "Schedule 1" to "Schedule 2" will not solve the problem. Rather, like similar products, *Cannabis* should be de-scheduled altogether (as it was prior to 1970), recognizing both scientific realities and State actions to date.

2. **Assign public health standards for *Cannabis* products that will align with existing standards and regimes for other consumer products.** Although Cannabis should be taken off of any DEA "schedule," it should not be de-regulated. Rather, Congress and the Administration can readily adapt the FDCA and the well-established agency regimes that govern drugs, foods, and dietary supplements to provide appropriate safety, efficacy, labeling, and quality requirements for *Cannabis* products that make drug, nutritional, or health supplement claims. The intended use and claims will define the classification for

each product. (Targeted statutory revision would be necessary to clarify the FDCA's applicability. See Sections III & IV.)

3. **Affirm the role of individual States to register or license the outlets through which *Cannabis* products may be sold in or into their jurisdictions.** The proposed *Cannabis* regulatory approach will provide consistent Federal standards for product manufacturing and labeling, but must still allow individual States to determine which outlets may sell to consumers.

II. CANNABIS PRODUCTS SHOULD BE DE-SCHEDULED

Cannabis has been used for health-related purposes for almost five millennia. As early as 2727 BC, the Chinese Emperor Shen Nung reported positive effects from *Cannabis* in relieving pain associated with rheumatism and gout. Only in recent history has Cannabis been villainized with respect to psychoactive effects of certain products on certain users. Alcohol similarly faced the Prohibition era; however, that product is now reasonably regulated and available for consumer choice.

Any consumer product may have negative effects, depending how it is used. Pharmaceutical products, for example, undergo rigorous testing to elucidate not only their positive health benefits, but also their risks. A key regulatory activity for all product developers under the FDCA (regardless of regulatory classification as a drug, food, or supplement) is to understand and to communicate potential uses *and* associated risks, in order to enable consumers (and, if applicable, their physicians) to make informed choices and to determine how to use individual products.

A. Medical and Health Acceptance

The scientific and medical understanding of *Cannabis* products has developed with time and experience. Federal regulation has not kept up, however. In 1970, *Cannabis* products were deemed to lack currently accepted medical use, and assigned to Schedule 1 under the Controlled Substances Act ("CSA"). Research since then has been stifled by the government in various ways. Nevertheless, current evidence shows that there is medical and other health-supportive demand for *Cannabis* products.

These products should not be without oversight, but they should be de-scheduled because current evidence shows they do not meet the criteria for extraordinary control under the CSA.

Regulatory determinations also need to be compound-specific. More than 100 compounds have been identified within the *Cannabis* plant, including numerous native terpenes and cannabinoids (collectively referred to as "Cannabinoids"). The most commonly known Cannabinoid is Δ9-tetrahydrocannabinol ("THC"). This is the compound within *Cannabis* that can have psychoactive effect. FDA has approved a synthetic form of THC (dronabinol; brand name Marinol® Capsules) for the treatment of nausea and vomiting associated with chemotherapy in certain patients.

In the August 11th 2016 press release, the DEA determined that there is currently "no accepted medical use" of *Cannabis.* Moreover, the DEA indicated *Cannabis* could not be used safely under medical supervision. According to the Marijuana Policy Project (MPP), there are over two million (2,000,000)

patients using *Cannabis* in states with medical programs. Additionally, the DEA has published that there have been no deaths caused by *Cannabis* Overdose.[1]

Medicinal or health supporting qualities exist in other Cannabinoids including, but not limited, to Cannabidiol ("CBD"), Cannabidiolic Acid ("CBDa"), Tetrahydrocannabivarin ("THCV"), Tetrahydrocannabivarinic Acid ("THCVa"), and Cannabichromene ("CBC"). For example, CBD may relieve pain and lower inflammation. CBD also may be used to support certain healthy functions (such as antioxidant properties supporting healthy cell function). Unlike THC, CBD and the other listed compounds do *not* have psychoactive effect.

In Addition, the US Department Veterans Affairs (VA) authorizes its care providers to recommend Cannabis through available channels where they exist. This action was achieved through H.R.4974 - Military Construction and Veterans Affairs and Related Agencies Appropriations Act, 2017 which passed in the House by a 295-129 vote.[2]

B. Physical and Psychological Dependence

Compared to the non-scheduled substances nicotine and alcohol, and Schedule I substance cocaine, the lifetime probability of physical dependence is lowest with *Cannabis*. As one example, the lifetime probability for nicotine dependence was reported at 67.5%; alcohol at 22.7%; cocaine at 20.9%; *Cannabis* at 8.9%.[3] In regard to psychological dependence, a 1968 study revealed "personality rather than pharmacological factors are the prime consideration" for abusers.[4] This finding is also represented in National Institute for Drug Abuse ("NIDA") executive Dr. Jack E. Henningfield's opinion that marijuana has less potential for psychological dependence than nicotine, alcohol, or cocaine.[5]

C. Toxicity

There have been no reported deaths from *Cannabis* according to the DEA[6]. It is estimated that the lethal dose for a 150 pound man is roughly nineteen pounds of *Cannabis*, an amount which is impossible to consume.[7]

D. Summary

A full and fair evaluation of Cannabis products under the standards set forth in the CSA demonstrate that de-scheduling is appropriate, and the current extraordinary controls are unnecessary

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[1] https://www.dea.gov/pr/multimedia-library/publications/drug_of_abuse.pdf#page=84

[2] https://www.congress.gov/bill/114th-congress/house-bill/4974

[3] Lopez-Quintero, Catalina et al. "Probability and Predictors of Transition from First Use to Dependence on Nicotine, Alcohol, Cannabis, and Cocaine: Results of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)." Drug and alcohol dependence 115.1-2 (2011): 120–130. PMC. Web. 28 Apr. 2016.

4 http://www.drugtext.org/Cannabis-marijuana-hashisch/acute-and-chronic-toxicity-of-marijuana.html

5 http://www.drugsense.org/tfy/addictvn.htm

[6] https://www.dea.gov/pr/multimedia-library/publications/drug_of_abuse.pdf#page=84

[7] http://www.health.gov.au/internet/main/publishing.nsf/Content/health-pubs-drug-cannab2-ch52.htm

for the protection of public health. This is not to say that *Cannabis* products should be unregulated. Rather, a fundamentally appropriate regime exists, as described in Section III below.

III. CANNABIS PRODUCTS SHOULD BE APPROPRIATELY REGULATED THROUGH THE FEDERAL FOOD, DRUG, & COSMETIC ACT

Cannabis products are being developed for a variety of different consumer purposes. These products are not all the same, and – like other botanical products – individual products should be regulated according to their intended uses and corresponding public health standards. The FDCA already provides a regulatory regime that has been adaptable over time to address a wide range of consumer products. With a few targeted modifications, that regime that can be easily adapted to apply appropriate standards to the range of *Cannabis* products that may be developed for present or future use.

More specifically, the FDCA regime currently enables the marketing of plant-derived compounds for different intended uses, ranging from those developed to treat disease ("drug" products such as Taxol (paclitaxel; derived from the Pacific Yew tree) to treat cancer and Fulyzaq (crofelemer; derived from the red sap of the Croton lechleri plant) to treat diarrhea in adults with HIV/AIDS); those developed to provide nutrition, aroma, or taste ("food" products such as garlic and herbs); and those to support healthy bodily function ("dietary supplement" products such as Garlique capsules or rosehip powder to support cardiovascular health, or Echinacea to support immune function). *Cannabis* products can, and do, fit within these various categories. Again, one regulatory classification does not fit all:

A. Some *Cannabis* products are intended to treat medical conditions. These products should be regulated as "drugs" by the FDA. For example, GW Pharmaceuticals is developing a product containing cannabidiol ("CBD") for the treatment of Lennox-Gastaut syndrome, a severe form of childhood-onset epilepsy. Such a product falls squarely within the FDCA definition of a "drug" (i.e., "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals" (21 U.S.C. § 321(g)), and GW Pharmaceuticals and the Food and Drug Administration ("FDA") are, in fact, applying that established pathway.

"Drug" products in the U.S. are generally subject to premarketing review and approval requirements, based on laboratory and animal studies, clinical trials in humans (including patients), and other evaluations. Data must demonstrate that a proposed drug product is both safe and effective for the intended use, and that quality standards (such as potency and purity levels) can be consistently achieved. Promotional claims must align with FDA-approved product labeling. If the circumstances warrant it, FDA may restrict drug products to prescription (Rx only) status due to potential toxicity of a product as it is intended to be used, or due to the inability of a patient to self-evaluate and treat a condition without professional oversight. If self-care is feasible, drug products may be approved for over-the-counter access.

Cannabis products bearing drug claims are similarly situated to other plant-derived medications. Claims to treat epilepsy, multiple sclerosis, or other specific diseases appropriately are considered "drugs" within the context of the existing regulatory regime.

B. Some *Cannabis* products are intended for use as food. For example, *Cannabis* products may be ingredients in baked products, or used to prepare herbal tea. Such a product should be presumptively a "food" (i.e., articles used for food or drink for man or other animals (21 U.S.C. § 321(f)) and subject to the safety requirements, health and nutritional claim regulations, and substantiation requirements that apply to food products.

Ingredients intended for food use must satisfy long-established FDA requirements for authorization. Some may be "generally recognized as safe" by qualified experts for their intended use; others must be affirmatively approved by FDA as "food additives" (a data-driven process that evaluates the composition and properties of a substance; the amount that typically would be consumed; immediate and long-term health effects; and various safety factors). Food ingredient evaluations consider appropriate levels of use, including built-in safety margins. In addition to compositional requirements, formulated food products are subject to requirements related to labeling disclosures, the types of health-related claims and nutrient content claims they may bear, and requirements for substantiation of claims. Manufacturers must apply good manufacturing practices in both food ingredient and finished product production to support consistency and quality.

Cannabis products used as food ingredients should be on a level playing field with other food ingredients and products that may be offered to consumers.

C. Some *Cannabis* products are intended as dietary supplements. For example, CBD oil is of interest for its antioxidant properties, or to support proper functioning of the human endocannabinoid system.[8] This type of product generally fits the FDCA definition of a "dietary supplement," which currently allows the marketing of botanical (and other) preparations[9] taken by mouth as tablets, capsules, powders, softgels, gelcaps, liquid or certain other forms intended to supplement the diet. Dietary supplements are authorized to describe documented mechanisms by which they help maintain the structure or a function of the body. These products may not, however, claim to diagnose, cure, mitigate, treat, or prevent disease (the latter products would be deemed "drugs").

Dietary supplements are subject to FDA regulation and oversight. The Dietary Supplement Health and Education Act of 1994 ("DSHEA") added specific supplement provisions to the FDCA. The statutory provisions distinguish certain historically-used ingredients from new dietary ingredients; for the latter, safety information must be submitted to FDA on a premarket basis. FDA has promulgated good manufacturing practice requirements specific to dietary

[8] http://www.prnewswire.com/news-releases/inergetics-nulief-the-first-branded-cannabinoid-cbd-based-nutritional-supplement-now-available-at-blum-dispensary-oakland-ca-300073165.html

[9] The current definition of "dietary ingredient" includes herbs or other botanicals and concentrates, metabolites, constituents, extracts, or combinations.

supplements. The FDCA, as amended, also requires reporting of serious adverse events that may be associated with marketed supplements.

Legislative Revision. To accommodate the unusual regulatory history of Cannabis as a Schedule 1 substance, a specific legislative revision will be needed to clarify the option to market appropriately qualified *Cannabis* products under the FDCA dietary supplement provisions. Specifically, the FDCA defines "dietary supplement" to *include* articles that were marketed as dietary supplements before the same article was approved in a "drug" form. Going the other direction, the statute *currently excludes* the possibility to market a compound in dietary supplement form if the compound was previously approved, or formally tested (even if not approved), for a pharmaceutical use. The FDCA defines "dietary supplement" to exclude:

> (i) an article that is approved as a drug under section 505 [of the FDCA, i.e., the new drug approval requirements] … or licensed as a biologic under section 351 of the Public Health Service Act …, or
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> (ii) an article authorized for investigation as a new drug … or biological for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public
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> which was not before such approval, certification, licensing, or authorization marketed as a dietary supplement or as a food unless the Secretary, in the Secretary's discretion, has issued a regulation, after notice and comment, finding that the article would be lawful under this Act.

Without any public process or elaboration of the evidence that it reportedly reviewed, FDA recently stated:

> *Based on available evidence, FDA has concluded that cannabidiol products are excluded from the dietary supplement definition under section 201(ff)(3)(B)(ii) of the FD&C Act*. Under that provision, if a substance (such as cannabidiol) has been authorized for investigation as a new drug for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public, then products containing that substance are outside the definition of a dietary supplement. FDA considers a substance to be "authorized for investigation as a new drug" if it is the subject of an Investigational New Drug application (IND) that has gone into effect. [FDA cited a 2007 press release about testing an investigational drug (Sativex®; composed of two cannabinoids: CBD (cannabidiol,) and THC (delta 9 tetrahydrocannabinol) being tested for cancer pain.]
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> There is an exception to section 201(ff)(3)(B)(ii) if the substance was "marketed as" a dietary supplement or as a conventional food before the new drug investigations were authorized. However, based on available evidence, FDA has concluded that this is not the case for cannabidiol…. FDA is not aware of any evidence that would call into question its current conclusion that cannabidiol products are excluded from the dietary supplement definition under section 201(ff)(3)(B)(ii) of the FD&C Act. Interested parties may present the agency with any evidence that they think has bearing on this issue.

The pertinent statutory provision should be revised for several reasons. First, because *Cannabis* products have been classified as Schedule 1 products, they were lawfully restricted from prior marketing under the dietary supplement rubric. Congress must tailor the time restriction for prior marketing to address this unique scenario. FDA also should be obligated to provide fair consideration to the historical restrictions and not simply be allowed to declare – without any public process -- that CBD is excluded from possible dietary supplement use. Congress can clarify the possibility for Cannabis products to be manufactured as dietary supplement by a specific statutory revision.

D. Some products are ingredients in cosmetics. For example, Aloe vera is a commonly extracted and used for its skin enhancing quality. It is often recommended by physicians for burn relief. Longstanding safety and labeling requirements apply to cosmetics (i.e., articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance (see 21 U.S.C. § 321(i)).

Core concepts underlying the existing FDCA regulatory regime include safety, substantiation of claims, and access. Time and again, it has been clear that American consumers can be trusted to understand information -- including truthful, non-misleading scientific information -- and to judge what products may be right for them.[10] There is legitimate industry striving to make and market useful, accurately represented products to the consuming public.

IV. STATES MUST MAINTAIN RESPONSIBILITY TO DETERMINE WHICH OUTLETS CAN SELL CANNABIS PRODUCTS IN THEIR JURISDICTION

Even when uniform safety and quality standards for *Cannabis* products apply under the FDCA, the States should retain clear authority to determine which providers or outlets are qualified to distribute and sell these products. Many states have established regulatory commissions to make medical *Cannabis* available to qualifying patients and otherwise regulated access to *Cannabis* products. In addition, states boards or pharmacy, state food and drug agencies, and local health departments routinely determine the qualifications and issue licenses to distributors of FDA-regulated consumer products (e.g., wholesale drug distributor permits; pharmacy permits; retail food permits). Preserving State and local oversight is further justified by the novelty of lawful *Cannabis* products and may provide added assurance of proper control, given the debate that has surrounded *Cannabis* products.

[10] See, for example, the Congressional findings underpinning the Dietary Supplement Health and Education Act of 1994 ("DSHEA"), which created the current rubric in the FDCA: "Consumers should be empowered to make choices about preventive health care programs based on data from scientific studies of health benefits related to particular dietary supplements." FDA has an oversight role (e.g., notification of marketing and safety information may be required to be submitted; the agency can take enforcement action against products that do not comply with applicable requirements).

Again, the FDCA already contains relevant precedent, shown in the 2009 amendment of that statute by the Family Smoking Prevention and Tobacco Control Act. When granting FDA various regulatory authority over cigarettes and other tobacco products, the Congress included Section 916, titled "Preservation of State and Local Authority." With minor revision to specifically address *Cannabis* products, similar language would achieve the Federal/State allocation appropriate here:

> SEC. 916. PRESERVATION OF STATE AND LOCAL AUTHORITY.
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> ''(a) IN GENERAL.—
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> ''(1) PRESERVATION.—Except as provided in paragraph (2)(A), nothing in this chapter, or rules promulgated under this chapter, shall be construed to limit the authority of a Federal agency (including the Armed Forces), a State or political subdivision of a State, or the government of an Indian tribe to enact, adopt, promulgate, and enforce any law, rule, regulation, or other measure with respect to Cannabis products that is in addition to, or more stringent than, requirements established under this chapter, including a law, rule, regulation, or other measure relating to or prohibiting the sale, distribution, possession, exposure to, access to, advertising and promotion of, or use of Cannabis products by individuals of any age, information reporting to the State, or measures relating to fire safety standards for Cannabis products. No provision of this chapter shall limit or otherwise affect any State, tribal, or local taxation of Cannabis products.
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> ''(2) PREEMPTION OF CERTAIN STATE AND LOCAL REQUIREMENTS.—
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> ''(A) IN GENERAL.—No State or political subdivision of a State may establish or continue in effect with respect to a Cannabis product any requirement which is different from, or in addition to, any requirement under the provisions of this chapter relating to Cannabis product standards, premarket review, adulteration, misbranding, labeling, registration, good manufacturing standards, or modified risk Cannabis products.
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> ''(B) EXCEPTION.—Subparagraph (A) does not apply to requirements relating to the sale, distribution, possession, information reporting to the State, exposure to, access to, the advertising and promotion of, or use of, Cannabis products by individuals of any age, or relating to fire safety standards for Cannabis products. Information disclosed to a State under subparagraph (A) that is exempt from disclosure under section 552(b)(4) of title 5, United States Code, shall be treated as a trade secret and confidential information by the State."

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Summary. *Cannabis* should no longer be "scheduled" by the DEA, and Congress should specifically act to de-schedule *Cannabis* products under the Controlled Substance Act. Yet, Congress should not leave cannabis products unregulated -- there is an existing regulatory rubric under the FDCA that already provides key framework (including regulatory oversight) for certain aspects of the production, marketing, and distribution of *Cannabis* products. In addition, express clarification is warranted that the States have an ongoing role to control the outlets through which *Cannabis* products may be sold

and distributed. Targeted modification of existing statutory language can achieve these purposes. Thus, at the same time Congress de-schedules cannabis products, Congress should subject them to appropriate regulation under the FDCA. By doing so, Congress can restore the balance between the Federal and State governments, and ensure appropriate regulation of Cannabis products consistent with all other foods, drugs and supplements.