GREENWICH BIOSCIENCES
STATEMENT FOR THE RECORD

HOUSE ENERGY AND COMMERCE
HEALTH SUBCOMMITTEE HEARING:
"CANNABIS POLICIES FOR THE NEW DECADE"

JANUARY 15, 2020

Chairwoman Eshoo, Ranking Member Burgess, and Members of the Committee, we thank you for the opportunity to submit this statement regarding the importance of FDA regulation of cannabis-derived products.

Since our founding in 1998, GW Pharmaceuticals has been singularly focused on unlocking the potential of cannabinoids as medicines for development through the FDA pathway. Our drug, Epidiolex®, treats seizures associated with Dravet syndrome (DS) and Lennox Gastaut syndrome (LGS) in patients two years of age and older. DS and LGS are two rare, pediatric-onset, life-threatening and intractable epilepsies. With the approval of Epidiolex in 2018, we became the only company to have brought an FDA-approved cannabis-derived therapy to patients in need.

We have accumulated the most comprehensive body of scientific research on cannabinoids, including cannabidiol (CBD), and fully support FDA's thoughtful consideration of new regulatory pathways for consumer-focused CBD products. We will draw on our scientific research to assist this process.

FDA and Congress should take steps to encourage development of more FDA-approved cannabis drugs. As a result of GW's long-term involvement in cannabinoid research, we have a deep understanding of the promise that patients and their families see in cannabis-based products to treat intractable illnesses. The needs of patients motivated our efforts to research and bring Epidiolex through the FDA process.

In opening the door for consumer-market CBD products, FDA risks further diminishing the likelihood that more cannabis-derived products will be developed into proven medicines. The exclusionary rule embodied in the Dietary Supplement Health and Education Act (DSHEA)—which FDA would have to waive for the first time ever before authorizing CBD consumer goods—was intended by Congress to protect medical innovation. Jeopardizing innovation incentives is a serious concern in any circumstances, but it is particularly concerning for cannabis products.

Congress and FDA need to create a regulatory framework that encourages development of cannabis-derived drugs in a highly unique and saturated consumer market. Congress and FDA should support a comprehensive framework for cannabis-derived medicines that: (1) incentivizes the development of FDA-approved cannabis-derived medicines, (2) ensures the safety of consumer products containing cannabis derivatives, and (3) establishes a clear differentiation between FDA-approved cannabis-derived medicines and foods and dietary supplements containing CBD.

Implement New Policies that Encourage Development of More FDA-approved Cannabis-derived Therapies

Congress and FDA should incentivize the development of FDA-approved cannabis-derived medicines. Cannabis holds promise to treat intractable illnesses, but existing incentives are insufficient. Due to a variety of factors, including competition from unapproved products, incentives to develop and drive competition among FDA-approved cannabis medicines are weakened to begin with.

Patients are self-medicating serious diseases with unapproved cannabis products, and allowing CBD in supplements will further jeopardize innovation. It has been estimated that over 3,500,000 Americans use unapproved medical cannabis products.[1] And while for some, these products may offer symptom relief, there are risks to patients from self-directed treatment with unapproved products. A recent case study in Epilepsy and Behavior (2018) describes deaths in two patients who had discontinued conventional therapies in favor of self-directed care with unapproved cannabis-derived products.[2]

Quality deficiencies in unapproved cannabis products also pose safety risks for patients. Recent analyses show that unapproved CBD products frequently go to market containing either significantly higher or lower concentrations of CBD than indicated on the product label.[3] Because these manufacturers do not subject themselves to FDA oversight, there is no robust system in place to ensure product quality, identity, purity, or stability among unapproved cannabis preparations. A 2017 analysis found that after 14 days of storage, CBD content in commercial products is reduced by 15%–20% of initial concentrations, depending on method of oil preparation.[4]

---

[1] Pro Con, Number of Legal Medical Marijuana Patients, May 17, 2018 https://medicalmarijuana.procon.org/view.resource.php?resourceID=005889

[2] Kollmyer D.M., Wright K.E., Warner N.M., & Doherty M.J. (2019). Are There Mortality Risks for Patients with Epilepsy Who Use Cannabis Treatments as Monotherapy, *Epilepsy Behav Case Rep* 11: 52-53.

[3] Bonn-Miller M.O., et al. (2017). Labeling Accuracy of Cannabidiol Extracts Sold Online, *JAMA* 318(17): 1708-1709 (finding nearly 70 percent of artisanal CBD products tested were mislabeled with respect to CBD content); FDA, Warning Letters and Test Results for Cannabidiol-Related Products, https://www.fda.gov/news-events/public-health-focus/warning-letters-and-test-results-cannabidiol-related-products

[4] Pacifici R., Marchei E., Salvatore F., et al. (2017). Evaluation of Cannabinoids Concentration and Stability in Standardized Preparations of Cannabis Tea and Cannabis Oil by Ultra-High Performance Liquid Chromatography Tandem Mass Spectrometry, *Clin Chem Lab Med* 55(10): 1555-1563.

Gaps in quality assurance practices for unapproved cannabis preparations allow products to reach the market that are contaminated with a variety of harmful substances, including synthetic cannabinoids, molds, and bacteria.[5] In some cases, such quality deficiencies have serious consequences for patients. A recent case report described an eight-year-old boy who was admitted to the emergency room after consuming a commercial CBD product contaminated with synthetic cannabinoids. The child experienced heightened tonic-clonic episodes, intermittent agitation, delirium, depressed mental status, tachycardia, and mydriasis.[6]

The result is a public health challenge on a nation-wide scale. Not since before 1962 has there been such widespread, uncontrolled use of non-FDA approved products in vulnerable populations and for serious medical conditions. Families and patients see hope in cannabis-based products to treat intractable illnesses, but outside of Dravet and LGS, have no choice but to resort to unapproved drugs.

Ensure the Safety of Consumer Products Containing Cannabis Derivatives

FDA and Congress should work together to ensure consumer products containing CBD are safe. CBD is not a benign substance—it can present real safety risks, including liver toxicity if not used under the supervision and monitoring of a healthcare professional. The available data cannot provide complete assurance of safety in the environment of explosive demand for CBD-based consumer products.

FDA should seek to determine levels of CBD where there is sound data and benchmark safety margins. Liver injury occurs at the lowest dose systematically tested in clinical trials—5mg/kg—which presents an unacceptable safety signal for consumption outside a doctor-patient setting. Liver toxicity is unknown below that level, but benchmark safety margins can be applied to arrive at a dose with reasonable assurance of safety. Benchmarks suggest safety margins to account for: chronic use (10-fold), person-to-person variability (10-fold), and absence of data establishing levels with no-adverse effects (three- to 10-fold). A safe level should account for risk of cumulative exposure; demand is so explosive that consumers may ingest CBD from multiple sources per day. Rulemaking should also account for the potential presence of THC in finished products—it is a myth that CBD consumer products on the market today are free of THC.

---

[5] Horth R.Z., Crouch B., Horowitz B.Z., et al. (2018). Notes from the Field: Acute Poisoning from a Synthetic Cannabinoid Sold as Cannabidiol—Utah, 2017-2018. *Morb Mortal Weekly Rep* 67(20): 587-588; Thompson G.R., Tuscano J.M., et al. (2017). Letter to the Editor: A Microbiome Assessment of Medical Marijuana. *Clin Microbiol Infec* 23.

[6] Rianprakaisang, T., Gerona, R., & Hendrickson, R.G. (2019). Commercial Cannabidiol Oil Contaminated with the Synthetic Cannabinoid AB-FUBINACA Given to a Pediatric Patient. *Clin Toxicol* 24, DOI: 10.1080/15563650.2019.1619758

Ensure that Consumer-Market Products Containing Cannabis Derivatives are Clearly Differentiated from FDA-Approved Prescription Medications

FDA and Congress should take measures to differentiate between cannabis-derived medicines and CBD products. FDA should use its broad authority to ensure clear differentiation of medicines from consumer products, both for the sake of safety and to preserve the DSHEA principle that prescription drug ingredients should not later be introduced in consumer products. FDA should also close loopholes (e.g., "hemp extracts") that might allow circumvention of CBD rulemaking.

GW Envisions a Clear Path Forward for the Development and Regulation of Cannabis-derived Products

GW envisions a clear path forward for the development of cannabis-derived products through FDA's esteemed regulatory review pathway. Epidiolex has proven that cannabis-derived medicines can be successfully developed through the FDA pathway. For patients living with DS and LGS, their cannabis medicine meets the same "gold standard" applicable to every other approved prescription drug in the United States since 1962. As FDA undertakes rulemaking to create pathways for consumer-market CBD products, its focus should be directed equally toward other patient populations who could benefit from safe and effective cannabis-derived treatments that have yet to be developed.

GW supports a comprehensive approach to the regulation of cannabis-derived products because we believe that such an approach can create conditions that support development of new FDA-approved medicines from the cannabis plant while, in parallel, protecting consumers from unsafe products, bringing much-needed regulation to the existing marketplace, satisfying consumer demand, and creating new economic and agricultural opportunities.