VERMONT MEDICAL SOCIETY RESOLUTION

Regulation of Cannabidiol (CBD)

Submitted by VMS Council for adoption at VMS Annual Meeting on November 2, 2019

WHEREAS, safety concerns exist for prescribed federally-regulated cannabidiol (Epidiolex) including: hepatocellular injury and necrosis,[i] hepatic toxicity and histologic evidence of necrosis,[ii] suicidal behavior and ideation,[iii] somnolence and sedation,[iv] hypersensitivity,[v] drug interactions,[vi] and possible risk of DNA damage and chromosomal aberrations;[vii] and

WHEREAS, more severe safety concerns exist for non-prescribed, non-federally regulated cannabidiol (CBD) as currently available and consumed by the public, and a number of side effects are documented including anxiety, confusion, nausea, vomiting,[viii] fatigue, somnolence, gastrointestinal symptoms and seizures,[ix]

WHEREAS, non-prescribed CBD consumer products may contain dangerous heavy metals, pesticides, rodenticides, molds; and

WHEREAS, CBD and THC (tetrahydrocannabinol) content in commercially available CBD products varies and is not easily determined by consumers: a 2017 analysis showed that only 31% of CBD-containing products were accurately labeled for CBD content, 42% were under-labeled and 26% were over-labeled, and moreover THC was detected in 21%;[x] and

WHEREAS, non-prescribed CBD consumer products sold can contain up to 24 mg of THC, more than that of a typical cannabis joint, which contains up to 17 mg of THC, putting the consumer at risk for intoxication, unintended cannabis addiction relapse, and unintended mental health harm;[xi] and

WHEREAS, the THC content of CBD products sold in Vermont is not routinely tested by the State so the public cannot reliably know the true content of THC or CBD of the non-prescription CBD products for sale in the state, though the Vermont Hemp Program is in the process of finalizing rules for the Vermont Hemp Program, which would include testing by certified labs for THC concentration as well as pesticides, heavy metals, mycotoxins and bacterial and fungal contaminants ;[xii]

WHEREAS, the public is subjected to pervasive false medical claims regarding non-prescribed CBD both online and in other media; and

WHEREAS, non-prescribed CBD is found in food for human consumption in Vermont, contrary to FDA regulations and law and there is confusion in Vermont as to the advisability and legality of placing CBD and/or hemp in animal feed destined for human consumption; [xiii] and

WHEREAS, the FDA has concluded that THC and CBD products are excluded from the dietary supplement definition[xiv] and therefore may not be added to foods;[xv] and

WHEREAS, the Secretary of Health and Human Services and the Commissioner of the U.S. Food and Drug Administration (FDA) have authority to regulate hemp and hemp products under applicable FDA laws in order to protect patients and the public health, foster innovation for safe and appropriate products, and promote consumer confidence;[xvi] and

WHEREAS, the FDA has stated: "We are aware that some firms are marketing CBD products to treat diseases or for other therapeutic uses, and we have issued several warning letters to such firms….Selling

unapproved products with unsubstantiated therapeutic claims is not only a violation of the law, but also can put patients at risk, as these products have not been proven to be safe or effective….;"[xvii] therefore be it

RESOLVED, that VMS support the distribution of evidence-based information to the public and clinicians regarding cannabidiol (CBD), including potential health risks of its use; and be it further

RESOLVED, that VMS oppose and work to increase enforcement against the false advertising of non-FDA approved CBD for therapeutic or medical purposes, and be it further

RESOLVED, the VMS oppose the sale or marketing of CBD without a prescription, as it is likewise illegal to market or sell any similarly classified FDA-approved drug without a prescription and under the care of medical professional; and be it further

RESOLVED, that VMS support regulation of the manufacture of CBD that protects human and environmental health including requirements that it be free of mold, heavy metals, pesticides, herbicides, insecticides; has reliable active drug concentration of cannabidiol; that it contain no more than trace amounts (ideally 0.15% or, at a maximum, 0.3%) of tetrahydrocannabinol (THC); that it be tested by independent third party laboratories for concentration and contamination; that it not be added to food, especially that attractive or appealing to children; that it not be fed to livestock or placed in livestock feed such that no food, including meat, milk and cheese containing CBD or THC be sold in Vermont; and that its cultivation not harm public health through excessive use of water, impaired water ways, smell or pesticide run off.

---

[i] 5 to 17% of patients in clinical trials developed elevated liver enzymes and some patients were withdrawn from the trials. Devinsky O., Nabbout R., Miller I., Laux L., Zolnowska M., Wright S., Roberts C. Long-term cannabidiol treatment in patients with Dravet syndrome: An open-label extension trial. Epilepsia. 2018 doi: 10.1111/epi.14628

[ii] Animal models using comparable CBD mouse equivalent dosages (20 mg/ kg / day) found hepatic toxicity and histologic evidence of necrosis and in a percentage of cases this led to animal death. Koturbash I et al. Hepatotoxicity of a Cannabidiol-Rich Cannabis Extract in the Mouse Model. Molecules 2019;24(9):1694. Doi: 10.3390/molecules24091694.

[iii] Patients taking purified CBD, Epidiolex (or other antiepileptic drugs) had twice the risk of suicidal thoughts or behavior and the risk did not decrease with time (monitoring stopped at 24 weeks). (Pooled analyses of 199 placebo-controlled clinical trials on antiepileptic drugs including purified CBD (epidiolex)

[iv] 32% of patients using purified CBD (Epidiolex 20 mg/kg/day) experienced somnolence and sedation, which could be potentiated by other CNS depressants such as alcohol, so that warnings regarding use with driving or with use of machinery are warranted (Greenwich Biosciences)

[v] Allergic reaction to purified CBD (Epidiolex) has been described (Greenwich Biociences); Anaphyphylaxis has also been described to hemp seed [containing negligible THC] ingestion. Bortolin, Kristen et al. Case series of 5 patients with anaphylaxis to hemp seed Ingestion. J Allergy Clin Immunol 2016;137(2):AB239.

[vi] CBD interacts with the metabolizing cytochrome P450 family complex enzymes and this gives rise to a number of drug interactions. Examples include: CBD potentiates the effects of Coumadin putting patients at risk for strokes and bleeds; CBD changes the effectiveness of immunosuppressants such as Tacrolimus, which is important for solid organ transplant survival.

[vii] Russo, Chiara, et al. Arch Toxicol (2019) 93: 179. https://doi.org/10.1007/s00204-018-2322-9 Low doses of widely consumed cannabinoids (cannabidiol and cannabidivarin) cause DNA damage and chromosomal aberrations in human-derived cells.

[viii] Hussain et al. (2015) Ep & Beh. 47: 138-141

[ix] Press & Knupp. (2015) Epi & Beh. 45:49-52; Treat et al. (2017) or Epilepsia; 58(1): 123-127.

[x] https://www.pennmedicine.org/news/news-releases/2017/november/penn-study-shows-nearly-70-percent-of-cannabidiol-extracts-sold-online-are-mislabeled

[xi] Greenwich Biosciences testimony to FDA 5/30/2019

[xii] See https://agriculture.vermont.gov/public-health-agricultural-resource-management-division/hemp-program/hemp-program-rulemaking.

[xiii] "Based on a study conducted by the FEEDAP Panel on the transfer of THC from whole hemp and hemp seed-fed cows' milk to humans, there would be small amounts of THC transferred from the product to the consumer…. The FEEDAP Panel concluded that given these safety concerns over THC exposure, there was no option for further use of whole hemp plant-feed materials for feeding dairy cattle." European Food Safety Authority, "Scientific Opinion on the safety of hemp (Cannabis genus) for use as animal feed," European Food Safety Authority Journal 9, no. 3 (2011), https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2011.2011. Several studies have demonstrated THC appearing in milk or other food products, including one in which 27% of children's urine contained THC due to ingesting milk from animals grazing on wild cannabis sativa plants comprising less than 10% of the animals total diet.

[xiv] See section 201(ff)(3)(B) of the FD&C Act, 21 U.S.C. § 321(ff)(3)(B); under this provision, substances cannot be deemed supplements if they have 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

[xv] https://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-questions-and-answers#othercbdapproved

[xvi] https://www.ams.usda.gov/sites/default/files/HempExecSumandLegalOpinion.pdf; see also July 25, 2019 remarks from Deputy Commissioner FDA Dr. A. Abernethy, https://www.agriculture.senate.gov/imo/media/doc/Testimony_Abernethy%2007.25.19.pdf

[xvii] https://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-questions-and-answers#othercbdapproved The FDA also states in this letter that under the FD&C Act, any product intended to have a therapeutic or medical use, and any product (other than a food) that is intended to affect the structure or function of the body of humans or animals, is a drug subject to FDA approval.