The New Scooby Snacks?
Animal and Veterinary Products Containing CBD and Cannabinoids

Bill Bookout, President – NASC
Todd Harrison, Partner – Venable, LLP

QUALITY SEAL nasc NATIONAL ANIMAL SUPPLEMENT COUNCIL

VENABLE LLP

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Primary Topics for Today

- Very Briefly: What NASC Does and Why do we Exist
- The Animal “Supplement” Industry …
- Regulatory Differences vs. Human Products
- Available Pathways:
  - Food / Feed
  - Dosage Form Animal Health Product
- Actions to Address FDA Concerns for Cannabis / CBD
- Parallels with NAC for Enforcement Discretion

National Animal Supplement Council

- Founded in 2002, 501-c-6 Non-Profit Trade Association
- Represent 290 Brands (≈75% of the industry by $ spent)
  - Products similar to Human DS Products marketed for Dogs, Cats and Horses (non-human food chain animals)
  - Drop in Compliance Pathway:
    - Labeling, Claims, cGMPs, AERs, CE, Independent Quality Audit, Random Product Testing
    - Developed and Implemented with Input from Regulators (FDA, States)
- Supply Chain Vigilance / Qualification
  - RM Suppliers, CMOs, Testing Labs, Other Services
- Tip of the Cannabis Spear since 2015

The Animal “Supplement” Industry …

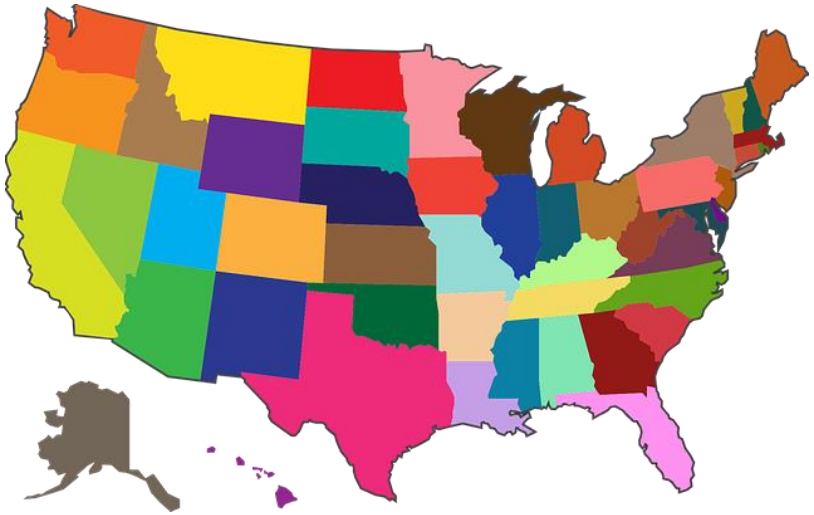
- Is a “fast follow” industry
- Growing market, 20% during Covid:
  - ≈ $1.7B consumer spending, Dogs, Cats
  - ≈ $800M Equine

Regulatory Differences vs. Human Products

- In the US, DSHEA Does NOT Apply to Animals (Federal Register Notice, 4/22/96) - https://www.govinfo.gov/content/pkg/FR-1996-04-22/pdf/96-9780.pdf
  - Legally we have 2 choices for Animal Products: Food / Feed or Drugs
    - Enforcement Discretion by FDA/CVM: The agency has exercised enforcement discretion with no safety concern, responsible conduct by marketers
- Who Regulates These Products?
  - Food & Drug Administration, Center for Veterinary Medicine (FDA-CVM)
  - State Regulatory Agencies (Animal Food or Animal Remedies)
    - Department of Agriculture
    - Other State Regulatory Agency: i.e. State Chemists Office
  - We do – NASC, self regulation does NOT mean unregulated

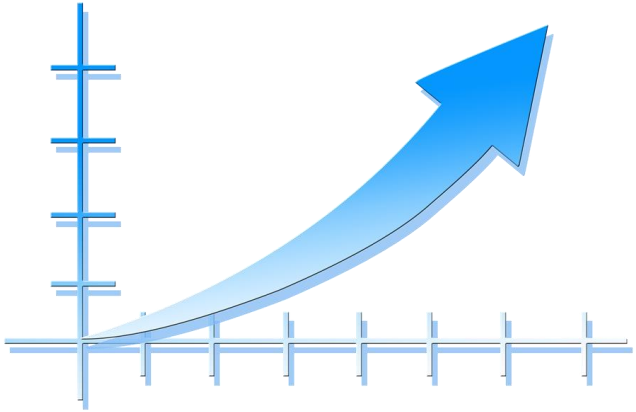
Who Regulates Hemp and CBD?

- Various state-level agencies
  - State Attorneys General
  - State Departments of Agriculture
  - State Departments of Health
  - State Boards of Pharmacy
- State-to-state differences on regulations, licensure processes, testing requirements, etc.



What Makes Hemp and CBD Important?

- Three competing forces
  - Increasing consumer interest in CBD products and CBD-related therapies
  - Wide-ranging and lucrative industry for CBD and CBD-containing products (e.g., cosmetics, edibles, etc.)
  - Continuing legal uncertainties at the state and federal levels about using CBD in consumer products



Hemp & CBD Animal Products

- FDA is aware that separate from human products, there is a growing market for CBD-containing products marketed for pets and other animals
- Currently, FDA has **not** approved CBD for **any use** in animals
  - The agency notes that its concerns regarding CBD products with unproved medical claims and unknown quality/composition for *human products* apply equally to *animal products*
- Regulated based on its intended use as established by labeling claims

Food Pathway: Hemp & CBD in Animal Feed

- Pathways to Approve Hemp for Use in Animal Feed?
  - Approved food additive
  - GRAS
  - AAFCO-defined
  - Common or usual
- What about CBD?
- If Hemp and CBD are not approved, why are there so many products available?

DFAHP Pathway (NASC): Hemp & Derivatives including CBD

- Dosage Form Animal Health Product (DFAHP)
- Non-Nutritional Structure Function Benefit
- Cannot be in a Food Delivery form or for Nutritional Benefit
  - E.g., Biscuit, treat, snack, cookie, jerky, peanut butter
- Full Spectrum / Broad Spectrum allowed
- Must meeting testing requirements
- What about CBD?
  - No synthetics
  - CBD is okay with testing verification

FDA Request for Information

1. The risk of liver injury from CBD **(SAFETY)**
2. Toxicities of some of the active metabolites of CBD
3. Impact of CBD on the male reproductive system
4. Effect of CBD co-administration
5. Impact on neurological development
6. Sedative effects of CBD
7. Transdermal penetration and pharmacokinetics of CBD
8. Effect of CBD on pets and food-producing animals

1. Clinical studies (including real-world data/evidence) to address safety questions related to long-term sustained or cumulative exposure to CBD, including in vulnerable populations such as children, the elderly, and women who are pregnant or breastfeeding
2. Long-term (chronic) repeated dose toxicity studies in appropriate animal models, evaluating the most relevant toxicological end points
3. Clinical studies on the effect of different routes of CBD administration on its safety profile
4. Studies to characterize the potential for bioaccumulation of CBD over long-term exposure
5. Effect of CBD on the eye

Actions to Address FDA Concerns

- Bill Bookout Testimony to FDA on May 31, 2019
  - 2-3 years is simply not acceptable, nor a realistic time frame given the rapidly increasing consumer demand
- NASC will define the pathway its member will follow until FDA released further guidance, including:
  - cGMPs (current Good Manufacturing Practices)
  - Ingredient Testing and Verification
    - ✓ THC below 0.3% - Raw Materials and Finished Products
    - ✓ CBD if stated is verified
    - ✓ Microbial Contamination
    - ✓ Heavy Metals
    - ✓ Pesticides
  - Claims Review – Limited to Structure / Function
  - Adverse Event Reporting System and Continuous Vigilance

Actions to Address FDA Concerns

- What is FDA's greatest Concern for any product?
  - Target Product Safety
- NASC Board of Directors authorized safety study for CBD in Dogs – SAFETY ONLY
  - 90-day study, began May 2022
  - 32 Dogs: 4 groups
    - ✓ CBD
    - ✓ CBD/CBA
    - ✓ CBD/CBG
    - ✓ Control Group
- Goal is NOT to identify a toxic level, rather to identify a safe level (e.g. – we will not euthanize animals demonstrating a substance is safe)

Enforcement Discretion

- Absent Safety Concerns: Regulators Can Exercise Enforcement Discretion –
  - Approval not economically viable
  - Consumers / Stakeholders negatively impacted
  - Animal Drugs Used Off-Label Animal Medical Devices
  - NAC - https://www.fda.gov/food/cfsan-constituent-updates/fda-releases-draft-guidance-enforcement-discretion-certain-nac-products
  - Products Similar to Human DS Products – we have worked with the agency and state regulators cooperatively and transparently for over 20 years

Summary

- We believe FDA/CVM has the ability to exercise Enforcement Discretion for CBD products
- Our objective to provide the data and standards that give the agency the confidence and willingness to do so for these products
- Removing Products from the Marketplace is not the answer
  - Would create a black market industry
  - May cause harm to animals as consumers may make poor choices
  - Would drive individual state legislation – potentially 50 different sets of statutory requirements, which would not be practical for a Multi-Billion $ National Industry

Thank You

Questions

&

Further Discussion following Dr. Rob Silver

VENABLE LLP

Food & Drug Law Institute

Legal and Practical Issues in Cannabis Regulation

Cannabis in Veterinary Medicine

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Today's Agenda

1. Cannabis and its Use in Pets

   Use of CBD or Cannabis by veterinarians
   - ***American Veterinary Medical Association (AVMA)***
   - ***State Veterinary Medical Associations***
   - ***State Veterinary Medical Boards***

   Unguided use of cannabinoids by pet owners for their own pets
   - ***Harm reduction*** with the help of veterinarians and their client education

2. Safety Studies
   - Product Quality Control and Safety
   - Dogs
   - Cats
   - Horses

3. Conclusion(s)
   - Supporting the Safe and Effective Use in our Veterinary Species


HELLO
My name is
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Shadow
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My name is
Rob Silver
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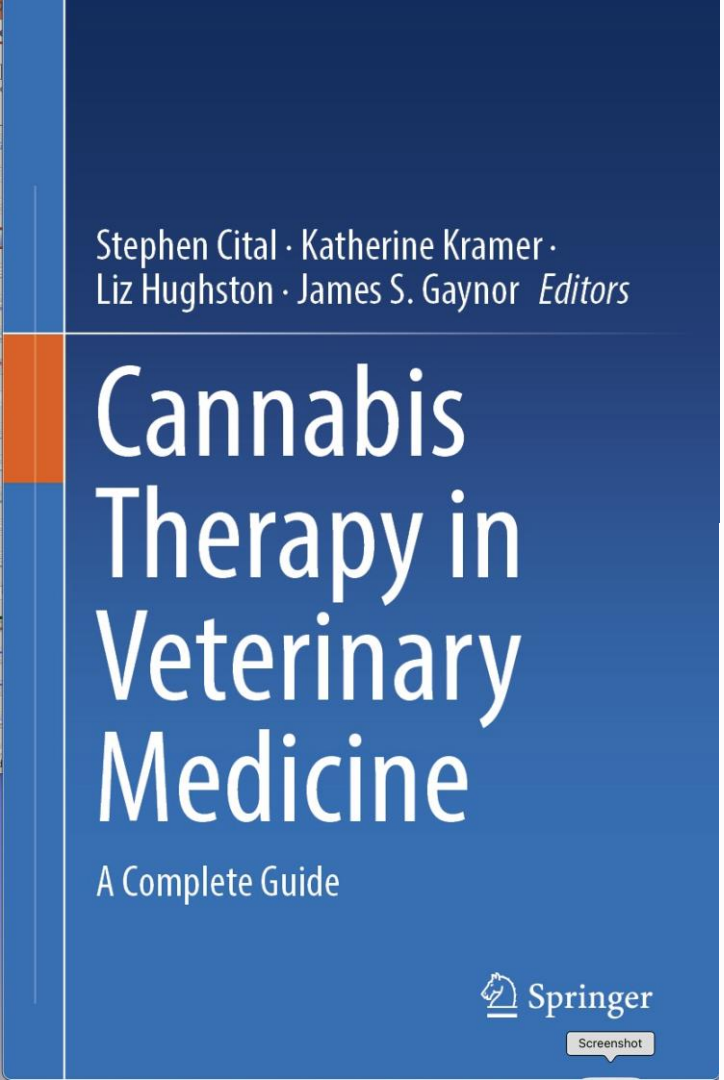
My name is
SPIKE
Reynolds



Contents

https://link.springer.com/book/10.1007%2F978-3-030-68317-7

animals

MDPI

Review

The Endocannabinoid System of Animals

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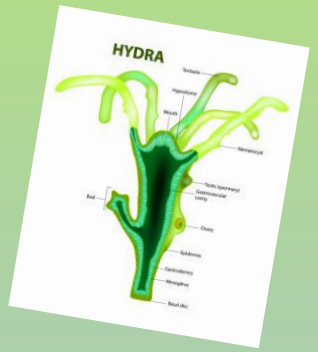
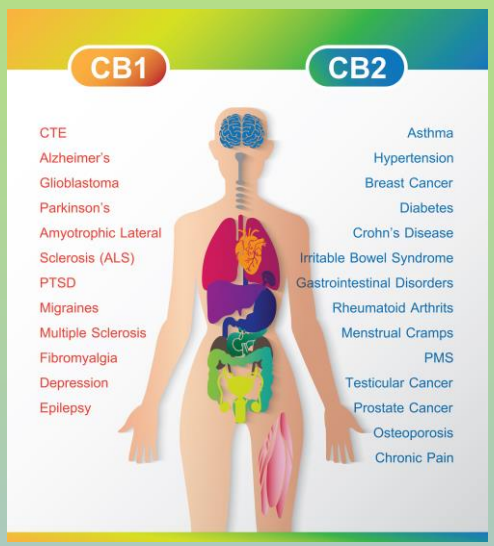
check for updates

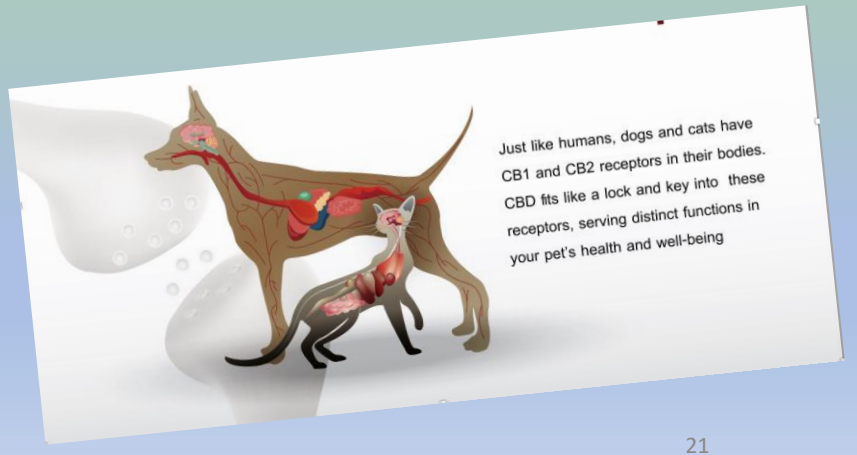
Simple Summary: Our understanding of the Endocannabinoid System of animals, and its ubiquitous presence in nearly all members of *Animalia*, has opened the door to novel approaches targeting pain management, cancer therapeutics, modulation of neurologic disorders, stress reduction, anxiety management, and inflammatory diseases. Both endogenous and exogenous endocannabinoid-related molecules are able to function as direct ligands or, otherwise, influence the EndoCannabinoid System (ECS). This review article introduces the reader to the ECS in animals, and documents its potential as a source for emerging therapeutics.

Abstract: The endocannabinoid system has been found to be pervasive in mammalian species. It has also been described in invertebrate species as primitive as the Hydra. Insects, apparently, are devoid of this, otherwise, ubiquitous system that provides homeostatic balance to the nervous and immune systems, as well as many other organ systems. The endocannabinoid system (ECS) has been defined to consist of three parts, which include (1) endogenous ligands, (2) G-protein coupled receptors (GPCRs), and (3) enzymes to degrade and recycle the ligands. Two endogenous molecules have been identified as ligands in the ECS to date. The endocannabinoids are anandamide (arachidonoyl ethanolamide) and 2-AG (2-arachidonoyl glycerol). Two G-coupled protein receptors (GPCR) have been described as part of this system, with other putative GPC being considered. Coincidentally, the phytochemicals produced in large quantities by the *Cannabis sativa* L plant, and in lesser amounts by other plants, can interact with this system as ligands. These plant-based cannabinoids are termed phytocannabinoids. The precise determination of the distribution of cannabinoid receptors in animal species is an ongoing project, with the canine cannabinoid receptor distribution currently receiving the most interest in non-human animals.

Keywords: endocannabinoid system; Anandamide; 2-AG; cannabis; cannabinoid receptor 1; cannabinoid receptor 2; G-coupled protein receptor; PPARS a; b; Ht1a; TRPV1; GPR55; cannabidiol; CBD; THC; CBG; CBC; tetrahydrocannabinol

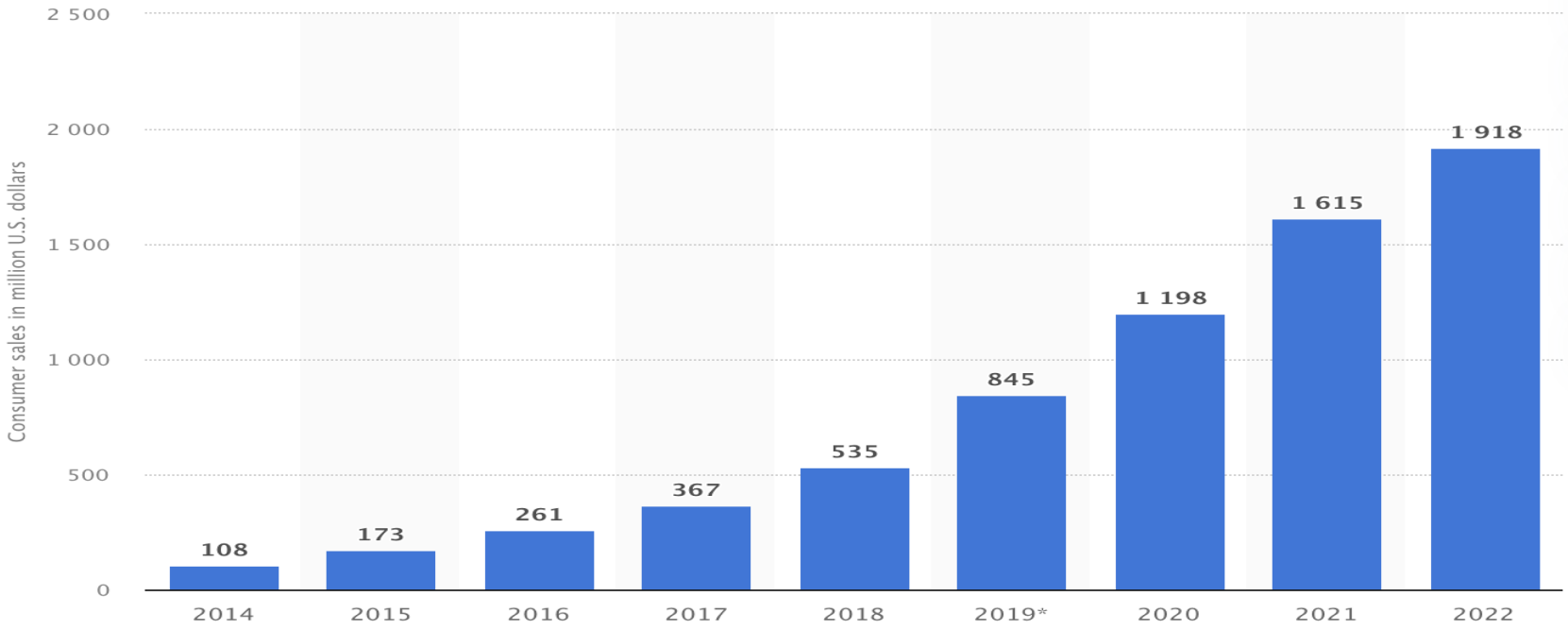






Total U.S. cannabidiol (CBD) product sales from 2014 to 2022

(in million U.S. dollars)



Additional Information

Show source

DON'T PUT THE CART BEFORE THE HORSE

WE CAN'T RETURN THE GENIE BACK INTO THE BOTTLE!!!!

Cannabis use and pets

What veterinarians need to know

Marijuana is federally designated as a schedule I controlled substance in the United States under the Controlled Substances Act – with the exception of "hemp" (Cannabis sativa L with tetrahydrocannabinol <0.3% dry weight), a type of cannabis that was recently descheduled through passage of the 2018 Farm Bill. How marijuana is handled under federal law contrasts with how it is handled under state law. More than half of U.S. states have passed legislation permitting medicinal use of marijuana in humans under strict guidelines. Additional states have passed laws permitting its recreational use. **State laws legalizing use in people do not apply to cannabis use in animals.**

As cannabis-derived products have become more available, veterinarians have seen increased interest among clients in using these products for their pets. These clients understandably are asking, "Are these products legal, safe, and effective for treating medical conditions in animals?" Our FAQs on the regulatory status of cannabis, cannabis-derived, and cannabis-related products can help you understand the legal landscape.

For a detailed guide to cannabis and its impact on veterinary medicine, view Cannabis in veterinary medicine.

RESOURCE

Cannabis in veterinary medicine

Compiled by veterinary experts, this report provides a firm base of knowledge for veterinary practitioners about cannabis in veterinary medicine.

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RESOURCE

Cannabis in veterinary medicine

Compiled by veterinary experts, this report provides a firm base of knowledge for veterinary practitioners about cannabis in veterinary medicine.

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CE webinars

Learn more about cannabis on AVMA Axon. Topics include cannabis' legal status, toxicity in patients, staff use of cannabis, and more.

Explore

CANNABIS FAQs

Q: IS IT LEGAL FOR VETERINARIANS TO SELL CBD PRODUCTS?

A: It depends on the intended use of the product and how it is marketed. Even if a CBD product meets the definition of 'hemp' under the 2018 Farm Bill, its use, marketing, and sale must comply with other applicable laws, including the FD&C Act and its regulations and those at the state level.

avma.org/Cannabis

AVMA

Best CBD Oil for Dogs 2021 — Isolates, Broad & Full-Spectrum Products

CANNABIS FAQs

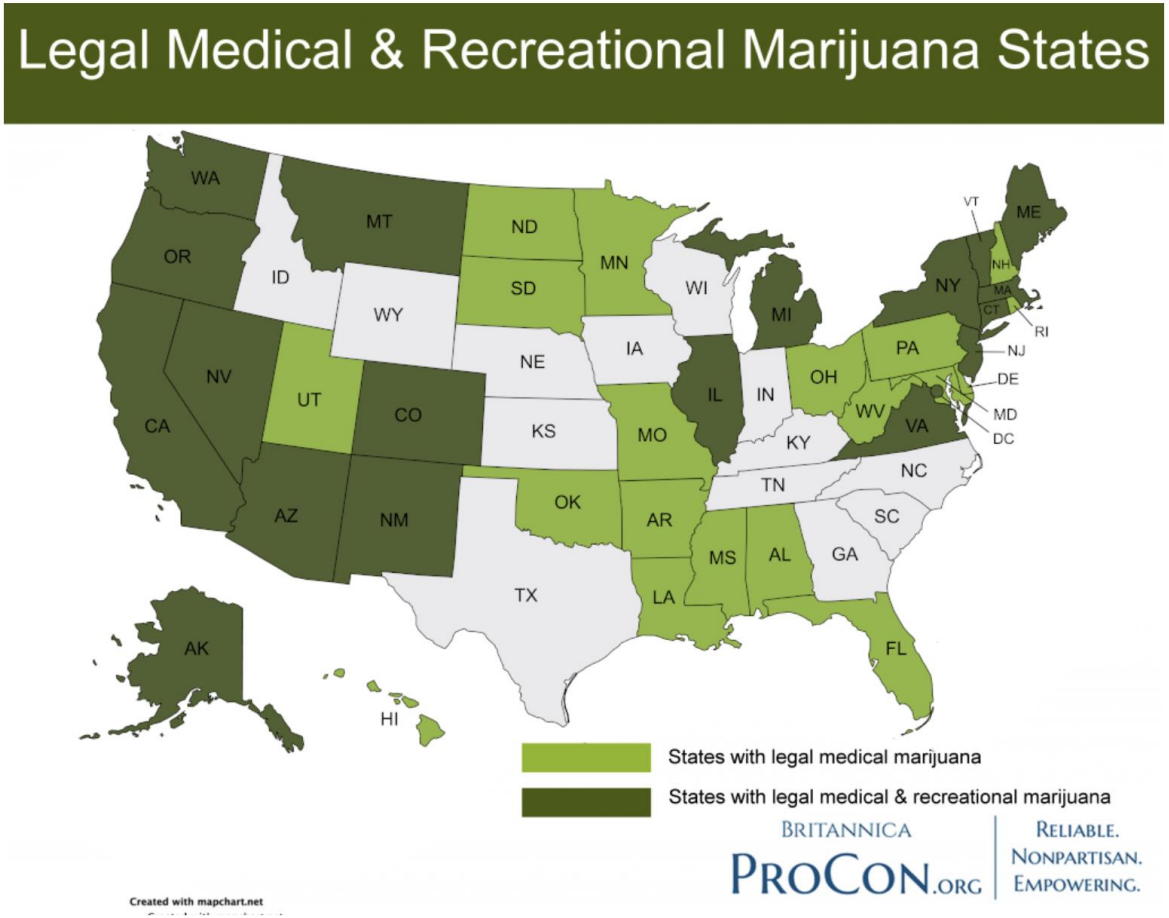
Q: MY STATE HAS LAWS THAT PERMIT MEDICAL USE IN PEOPLE WITHOUT FDA APPROVAL OF THE PRODUCT. DOES THAT MEAN, AS A VETERINARIAN, THAT I CAN LEGALLY USE AND/OR RECOMMEND CANNABIS FOR MY PATIENTS?

A: No. To date, laws that have been passed by states that remove state restrictions on the use of cannabis for medical or recreational use by people do not apply to their use in animals.

avma.org/Cannabis

AVMA

Medical Marijuana Legality by State



State Veterinary Medical **Associations**

- Provide state level guidance to vets
  - Business/Rabies licenses
  - Local disease guidance
    - Heartworm
    - Zoonoses

State Veterinary Medical **Boards**

- Consumer oriented; grant and remove professional licensure
- Bring action against the licenses of veterinarians based on consumer complaints

CBD for Pets – Top 3 Pros and Cons

Last updated on: 9/28/2021 | Author: ProCon.org | MORE HEADLINES

Source: Austin Community College Vet Tech Program, "Veterinary Tech Students from Austin Community College Are Involved in Helping with Heartworm, FeLV, FIV, and Socializing and Cleaning up the Animals at Bastrop Animal Control and Shelter," flickr.com, Nov. 10, 2014, creative commons license

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Is CBD Good for Pets?

Pro 1

A majority of veterinarians agree that CBD helps animals.

A Veterinary Information Network survey found that 79% of vets with clinical experience using cannabis products said CBD was somewhat or very helpful for chronic pain in animals; over 62% said it was helpful for managing anxiety. Over 80% of those vets said there were no reports of adverse effects aside from sedation. [11]

A study published in *Frontiers in Veterinary Science* found that 82.2% of veterinarians agreed or strongly agreed that there are medicinal uses of CBD products for dogs from a medical standpoint. [10]

Jeffrey Judkins, DVM, holistic veterinarian at Animalkind Veterinarian Clinic, said that CBD is "100% non-toxic. You can't overdose on CBD. It might make pets sleepy, but there's no toxicity." Judkins reported success in using CBD to alleviate pain and anxiety in animals, stating, "Recently I was able to significantly reduce the amount of a narcotic pain drug a dog was being given (with adverse side effects) by substituting a cannabis product." [12] [13]

Con 1

CBD pet products are unregulated.

The lack of regulation means pet owners could be buying CBD with unlisted ingredients that are potentially toxic to their pets, such as THC. Experts say these products are in need of testing for the presence of heavy metals, pesticides, and THC. "It's really the Wild West out there," said S. David Moche, MBA, CEO of a veterinary medicine company that sells CBD products. [14] [15] [16]

Researchers at the University of Pennsylvania found that 70% of the CBD products they analyzed didn't match the concentration listed on the label, and 21% of their samples contained THC despite it not being on the label. [17]

The US Food and Drug Administration (FDA) said in a statement, "We want to stress that FDA has not approved cannabis for any use in animals, and the agency cannot ensure the safety or effectiveness of these products." According to the FDA, animals who ingest cannabis could suffer negative side effects such as "lethargy, depression, heavy drooling, vomiting, agitation, tremors, and convulsions." [18]

Pro 2

Studies about CBD use in pets have had positive results.

A clinical trial found that 89% of dogs who were given CBD oil experienced fewer seizures. Researchers at Cornell University who performed a double-blind cross-over trial on dogs with osteoarthritis found "a significant decrease in pain and increase in activity" with CBD oil. There were no observed side effects from the CBD treatment. Studies on laboratory animals have shown benefits for cardiovascular health, the respiratory system, and cancer and pain treatment. [19] [20] [21]

While experts acknowledge that research in this area is preliminary, they speak positively about the results to date.

Stephanie McGrath, DVM, neurologist at Colorado State University's James L. Voss Veterinary Teaching Hospital, stated, "We saw a correlation between how high the levels of CBD were in these dogs with how great the seizure reduction was. It's really exciting that perhaps we can start looking at CBD in the future as an alternative to existing anticonvulsive drugs." [22]

Con 2

There isn't enough scientific evidence to support giving CBD to pets.

Research in this area is so new that no one knows the long-term impacts of CBD use in companion animals, or what an effective and safe dose would be. [23]

Sue Lowum, DVM, a veterinarian and associate professor at the University of Minnesota, said she wouldn't recommend CBD for pets because "We just don't have enough information at this point to draw any legitimate conclusions… there is no assurance the CBD oil they purchase is safe or effective." Veterinarians' knowledge about CBD use in pets is purely anecdotal at the moment because of the limited scientific evidence available. [16] [24]

Further, researchers found that some seller's websites contain "blatant lies" about CBD. [16] The American Veterinary Medical Association stated, "While both marijuana and industrial hemp products are available, no studies, doses, or uses in veterinary medicine have been determined… AVMA cautions pet owners against the use of such products." [25]

Q: What safety concerns may be associated with these products?

A: There are many cannabis-derived products being marketed and sold as animal health products, but—to-date—FDA has not approved cannabis for any use in animals. Accordingly, the agency has indicated that it cannot assure the safety or effectiveness of these products and cautions pet owners against their use.

In addition to lack of FDA-approval, the quality, purity, and strength of cannabinoid products matter and can be difficult to determine. Currently many of these products include insufficient labeling, and analyses by ConsumerLab[5] and a report[6] published in the *Journal of the American Medical Association (JAMA)* indicate that many of these products contained greater or lesser amounts of cannabinoids than indicated on their label. In addition, there is considerable inter-laboratory variability in analytical results, including when the same sample undergoes multiple evaluations.[7] There may also be large differences in potency between human and animal products (human products typically are more concentrated than those manufactured for pets) and, because of how some products are manufactured, contaminants are possible. Potential contaminants include chemicals intentionally added to increase yield, weight, or potency (e.g., pesticides, synthetic cannabinoids, metal particles); substances unintentionally incorporated during production (e.g., molds, bacteria); and solvents used as part of extraction processes (e.g., ethanol, petroleum-ether, butane).[8] All of this presents additional challenges to safe and effective use, as well as an increased risk of toxicosis.

Most reported cases of toxicosis from cannabis appear to be from unintentional exposures: getting into an owner's "stash," ingestion of edibles (e.g., candies, baked goods, chocolate bars and chips containing cannabis), consumption of vape cartridges, or the inhalation of second-hand smoke. Many of these accidental exposures have involved products high in THC and/or have been complicated by the presence of other toxic ingredients included in cannabis-containing products, such as chocolate, raisins, macadamia nuts, caffeine, xylitol, lead (vape cartridges), or the packaging itself.

With CBD oils and tinctures becoming increasingly popular for people and pets, however, the ASPCA Animal Poison Control Center (APCC) has reported[9] an increase in calls about cannabinoid treat and tincture ingestion, primarily by dogs. Many of these dogs who ate more treats or consumed more tincture than recommended exhibited clinical signs after ingestion and those signs were consistent with those in dogs suffering from THC overdoses. While the ASPCA APCC has shared information about these adverse events, we're told that FDA has not yet received similar reports associated with the intentional administration of cannabis products to animals. If you are aware of such incidents, we encourage you to report the adverse event to the FDA.

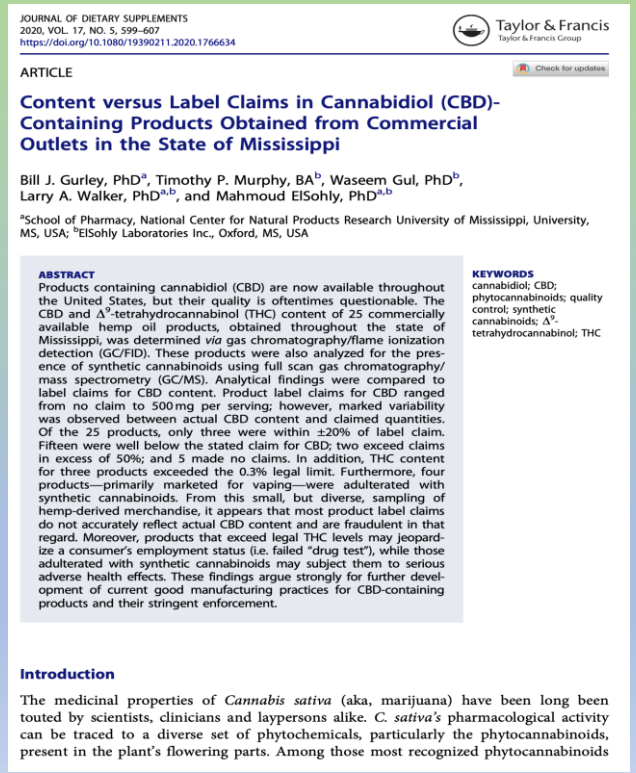
The Measurement of Safety Allows Us to Manage Risk

SAFETY of PRODUCT QUALITY

SAFETY of USE of CANNABINOIDS

CBD Content compared to Label Claims

- Survey of CBD-containing products for humans conducted by the National Center for Natural Products Research (U Miss) compared CBD & THC (and synthetic cannabinoids) analyzed content per label claim
- 25 products purchased from retail vendors in Mississippi and analyzed by the Mississippi DEA for CBD&THC
- RESULTS: 2 out of 25 products met label claim within 10%
  - 4 products had excessive amounts of THC above hemp levels (<0.3%)
  - 4 products contained synthetic cannabinoids



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ARTICLE

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Content versus Label Claims in Cannabidiol (CBD)-Containing Products Obtained from Commercial Outlets in the State of Mississippi

Bill J. Gurley, PhD[a], Timothy P. Murphy, BA[b], Waseem Gul, PhD[b], Larry A. Walker, PhD[a,b], and Mahmoud ElSohly, PhD[a,b]

[a]School of Pharmacy, National Center for Natural Products Research University of Mississippi, University, MS, USA; [b]ElSohly Laboratories Inc., Oxford, MS, USA

ABSTRACT

Products containing cannabidiol (CBD) are now available throughout the United States, but their quality is oftentimes questionable. The CBD and Δ^9-tetrahydrocannabinol (THC) content of 25 commercially available hemp oil products, obtained throughout the state of Mississippi, was determined *via* gas chromatography/flame ionization detection (GC/FID). These products were also analyzed for the presence of synthetic cannabinoids using full scan gas chromatography/mass spectrometry (GC/MS). Analytical findings were compared to label claims for CBD content. Product label claims for CBD ranged from no claim to 500 mg per serving; however, marked variability was observed between actual CBD content and claimed quantities. Of the 25 products, only three were within ±20% of label claim. Fifteen were well below the stated claim for CBD; two exceed claims in excess of 50%; and 5 made no claims. In addition, THC content for three products exceeded the 0.3% legal limit. Furthermore, four products—primarily marketed for vaping—were adulterated with synthetic cannabinoids. From this small, but diverse, sampling of hemp-derived merchandise, it appears that most product label claims do not accurately reflect actual CBD content and are fraudulent in that regard. Moreover, products that exceed legal THC levels may jeopardize a consumer's employment status (i.e. failed "drug test"), while those adulterated with synthetic cannabinoids may subject them to serious adverse health effects. These findings argue strongly for further development of current good manufacturing practices for CBD-containing products and their stringent enforcement.

KEYWORDS

cannabidiol; CBD; phytocannabinoids; quality control; synthetic cannabinoids; Δ^9-tetrahydrocannabinol; THC

Introduction

The medicinal properties of *Cannabis sativa* (aka, marijuana) have been long been touted by scientists, clinicians and laypersons alike. *C. sativa's* pharmacological activity can be traced to a diverse set of phytochemicals, particularly the phytocannabinoids, present in the plant's flowering parts. Among those most recognized phytocannabinoids

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ORIGINAL RESEARCH

Cannabinoid, Terpene, and Heavy Metal Analysis of 29 Over-the-Counter Commercial Veterinary Hemp Supplements

This article was published in the following Dove Press journal:
Veterinary Medicine: Research and Reports

Joseph J Wakshlag[1]
Stephen Cital[2]
Scott J Eaton[3]
Reece Prussin[2]
Christopher Hudalla[3]

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Purpose: The use of veterinary low tetrahydrocannabinol (THC) *Cannabis sativa* (ie, hemp) products has increased in popularity for a variety of pet ailments. Low-THC *Cannabis sativa* is federally legal for sale and distribution in the USA, and the rise in internet commerce has provided access to interested consumers, with minimal quality control.

Materials and Methods: We performed an internet word search of "hemp extract and dog" or "CBD product and dog" and analyzed 29 products that were using low-THC *Cannabis sativa* extracts in their production of supplements. All products were tested for major cannabinoids including cannabidiol (CBD), Δ9-tetrahydrocannabinol (THC), cannabigerol (CBG), and other minor cannabinoids, as well as their carboxylic acid derivatives (CBDA, THCA, CBGA) using an ISO/IEC 17025 certified laboratory. Products were also tested for major terpenes and heavy metals to understand constituents in the hemp plants being extracted and distributed.

Results: All products were below the federal limit of 0.3% THC with variable amounts of CBD (0–88 mg/mL or g). Only two products did not supply a CBD or total cannabinoid concentration on their packaging or website, while 22/29 could supply a certificate of analysis (COA) from a third-party laboratory. Ten of the 27 products were within 10% of the total cannabinoid concentrations of their label claim with a median concentration of 93% of claims (0–154%). Heavy metal contamination was found in 4/29 products, with lead being the most prevalent contaminant (3/29).

Conclusion: The products analyzed had highly variable concentrations of CBD or total cannabinoids with only 18 of 29 being appropriately labeled according to current FDA non-medication, non-dietary supplement or non-food guidelines. Owners and veterinarians wanting to utilize CBD-rich *Cannabis sativa* products should be aware of low-concentration products and should obtain a COA enabling them to fully discuss the implications of use and calculated dosing before administering to pets.

Keywords: cannabinoid, hemp, supplement, cannabidiol, pet, terpene, oral

Introduction

The recent federal legalization and deregulation of low-THC *Cannabis sativa*, otherwise known as hemp, as a commercial crop in the USA has created a new supplement market for humans and pets alike that is largely unregulated.[1] The de-scheduling of low-THC *Cannabis sativa* derived extracts forced any oversight of products containing hemp derived CBD, and other cannabinoids, to the Food and Drug Administration (FDA).[2] The lack of clear FDA regulations and inconsistent state regulations being

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29 Hemp Products for Dogs were Analyzed

All products were tested for

- CBD, THC, CBG, CBC, CBDA, CBDV, CBN, THCA, CBGA, major terpenes & Heavy Metals

Results:

- All products complied with <0.3% THC
- 75% of companies supplied a COA based on lot numbers
- "…presence of heavy metals or residual solvents does not disqualify a product as safe, but should comply with USP standards for orally consumed products"
- 10/29 products were within **90-110%** of label claims for cannabinoids
- 4/29 products contaminated with heavy metals primarily arsenic and lead
- ISO/IEC 17025 standards for the analytical laboratory are recommended and are a requirement for labs providing testing services in multiple states.

Safety Studies for CBD (& THC*) in 3 Veterinary Species

Canopy Animal Health Safety Studies for Health Canada

- **Dogs**
  - *Vaughn, 2020: Preliminary Investigation of the Safety. Of Escalating Cannabinoid Doses in Healthy Dogs: Front. Vet. Sci.; vol. 7(51)
  - Vaughn, 2021: Randomized Placebo controlled 28 day safety and pharmacokinetics evaluation of repeated oral cannabidiol administration in healthy dogs; AJVR; Vol.82(5): 405-416
- **Cats**
  - *Kulpa, 2021: Safety and Tolerability of escalating cannabinoid doses in healthy cats; J. Feline Med. Surg. Doi:10.1177/1098612X211004215.

Horse Studies that included safety evaluation:

- Ryan, 2021: Pharmacokinetics and effects on arachidonic acid metabolism of low doses of cannabidiol following oral administration to horses. Drug Test Anal. 1-13; doi:10.1002/dta.3028.
- Yocom, 2022: Pharmacokinetics, Safety, and Synovial fluid Concentrations of Single and Multiple-Dose Oral administration of 1 and 3 mg/kg Cannabidiol in Horses. J. Equine Sci. 113:103933.

- SUMMARY for Canopy Dog and Cat Safety Study
  - CBD alone had the lowest number of adverse events—lower than the carrier oils for the tinctures!
  - THC and CBD+THC had the highest number of adverse events

ADVERSE EVENTS RECORDED FOR EACH TINCTURE: CBD/THC/CBD&THC/SF/MCT

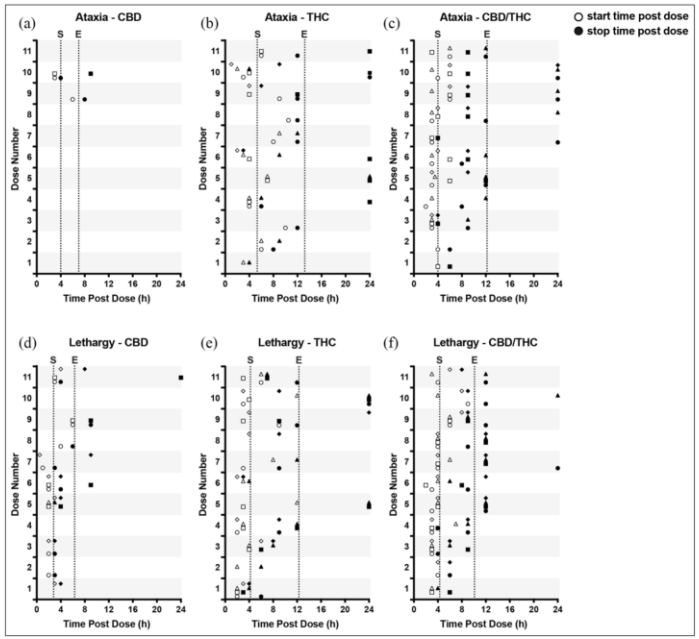

Figure 5 Start and end times (open and closed symbols, respectively) of (a–c) ataxia and (d–f) lethargy observed over 24 h following the administration of cannabinoid oil formulations. Within each plot, symbols (circle, square, triangle or diamond) are used to represent an individual cat across each dose when ataxia or lethargy were observed. Vertical dotted lines represent overall average start (S) and end (E) times across all observations during the study. CBD = cannabidiol; THC = tetrahydrocannabinol

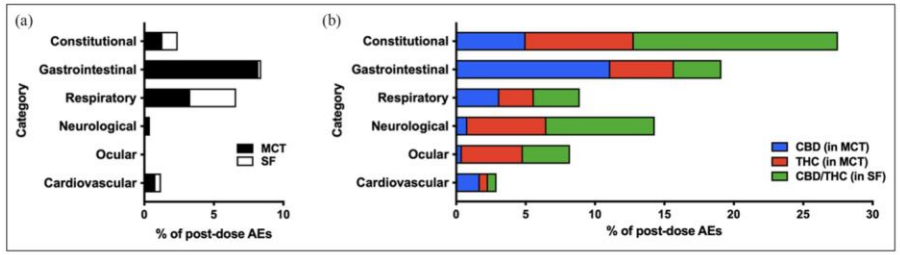

Figure 2 Proportion of post-dose adverse events (AEs) following dose escalation of cannabis or placebo oils (n = 4 per treatment). AEs were observed within 24 h of oil administration across 11 doses. (a) Medium-chain triglyceride (MCT) oil placebo and sunflower (SF) oil placebo; (b) cannabidiol (CBD) (in MCT oil), tetrahydrocannabinol (THC) (in MCT oil) or CBD/THC (in SF oil). A single occurrence of a musculoskeletal AE (muscle stiffness) in the CBD/THC group was not plotted

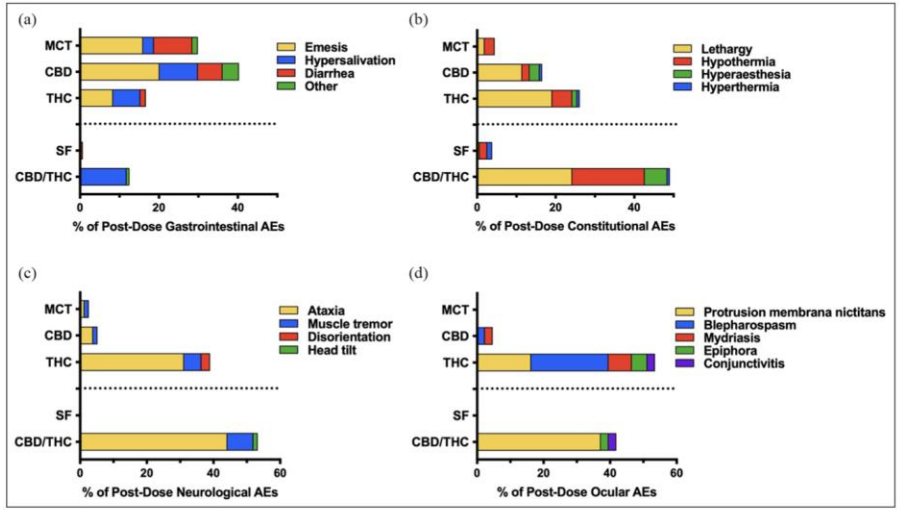

Figure 3 Proportion and profile of post-dose adverse events (AEs) attributed to dose escalation of each oil in up to 11 doses (n = 4 per treatment). (a) Gastrointestinal, (b) constitutional, (c) neurologic and (d) ocular AEs were observed within 24 h of oil administration. 'Other' gastrointestinal AEs include abnormal excreta, bloody stool, retching and dehydration. MCT = medium-chain triglyceride oil; CBD = cannabidiol; THC = tetrahydrocannabinol; SF = sunflower oil

NASC Adverse Event Reporting Database

- Records **AE** for hundreds of nutraceuticals and supplement ingredients
- Calculates **approximate** number of **doses administered** for a given nutraceutical
- Reports percentage of AE per ingredient by **species** and **year** as well as providing an **aggregate** value
- Information is **proprietary** but **FDA-CVM** has access to this website

NASC ADVERSE EVENT REPORTING WEBSITE DATA

National Animal Supplement Council
PO Box 5168
Sun City West, AZ 85376
T: 760-751-3360

NASC INGREDIENT RISK REPORT

INGREDIENT NAME: Hemp & Hemp-derived Compounds
REPORT DATA GENERATED ON: 05/19/2022 01:46 PM

AEs AND ADMINISTRATIONS

In Dogs:

Year	Adverse Events Reported	Report Rate Per Million Administrations Sold	Serious Adverse Events Reported	Report Rate Per Serious AE Per Million	Administrations Sold **
2010	0	0.00	0	0.00	25,016
2011	0	0.00	0	0.00	29,098
2012	0	0.00	0	0.00	104,421
2013	2	5.50	0	0.00	363,347
2014	0	0.00	0	0.00	802,026
2015	0	0.00	0	0.00	1,204,691
2016	0	0.00	0	0.00	2,117,161
2017	1	0.11	0	0.00	8,899,591
2018	20	0.50	0	0.00	40,159,328
2019	101	0.89	0	0.00	113,065,933
2020	432	2.46	0	0.00	175,614,355
2021	620	2.69	5	0.02	230,615,737
2022 †	170	6.70	1	0.04	25,379,652
Grand Total	1,346	2.25	6	0.01	598,380,356

† Usage data for 2022 is incomplete.

* The requirement for NASC members to enter AE reports began Q3 of 2003. Some companies were recording AEs prior to that time, and that data is displayed. NASC did not require reporting the number of administrations sold until Q3 2003, so data prior to that time is likely understated. Since we cannot be sure that the data prior to Q3 2003 is complete, we do not report AE Incidence prior to that time. Please direct questions about the NAERS system and the methodology to: Bill Bookout at NASC, 760-751-3360.

** Administrations sold is believed to be a close approximation to administrations consumed. Unlike human medicines, supplement bottles are generally consumed in their entirety, unless there is an adverse reaction, the animal starts refusing it, or the animal dies. The administrations sold data does include increased amounts of product carried in the distribution channel. However, with increasingly efficient supply chain management, it is believed that changes in the total product in the channel is a negligible factor over time.

Pet Poison Helpline
Retrospective Study: Cannabis Call Data

24/7 Animal Poison Control Center

- Ahna Brutlag DVM, MS, DABT, DABVT (Toxicology)
  - Director of Veterinary Services Animal Poison Control Center & Senior Veterinary Toxicologist
    - 24/7 hotline
    - *www.petpoisonhelpline.com*
    - 800.213.6680
  - Adjunct assistant professor
    - Department of Veterinary Biomedical Sciences
    - College of Veterinary Medicine
    - University of Minnesota
- Complied data from: **5 years of calls to PPHL (up 450%!!!)**
  - Presented safety data to FDA in discovery session in 2019

Summary of PPHL Retrospective Study

- Acute Exposure to CBD measured in these calls
- 49% of patients were symptomatic
  - **Found that CBD alone has good safety profile**
    - AEs generally are minimal
  - ***These AEs mainly are from poorly analyzed products with excessive amounts of THC or synthetic cannabinoids***
- Category with highest % AEs = vaping liquid 100%
- **Category with lowest % AEs = pet products (29%)**
  - Species differences in AEs (E.g.: UI in dogs, not cats)
  - **NO DEATHS !!!!!**

What Needs to be Done
(my wish list)

- **Veterinarians should be part of the conversation with pet owners about *reducing harm* with the safe use of CBD and Cannabis.**
  - State legislation including veterinarians as medical prescribers of THC-dominant cannabis ("marijuana")
  - State legislation allowing veterinarians to discuss, recommend and/or dispense CBD-dominant cannabis ("hemp")
- Improved guidance for the safe use of CBD products in pets and by veterinarians
- CBD and Cannabis ***product standards*** need to be established
- ***Federal legislation*** legalizing Cannabis that includes veterinarians same as human physicians in the legal language