CBD – Is it the new miracle drug or marketing hype?

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Disclaimer Statement

The views in this presentation are those of the Speaker and do not necessarily represent the views of Thermo Fisher Scientific. This presentation is sponsored by Thermo Fisher Scientific.

Who am I?

- In the field for 50 years.
- Original training and experience was with the FBI crime laboratory in WDC.
- Qualified as an expert in Forensic Toxicology in 26 states.
- Guest speaker on many radio talk shows and featured in newspapers and magazines.
- Authored and co-authored several articles that have appeared in the United States and abroad.
- Member of international Organization to establish Drug testing Policies for the Oil and Gas Industry Worldwide.
- Former Member of the Federal Drug Testing Advisory Board



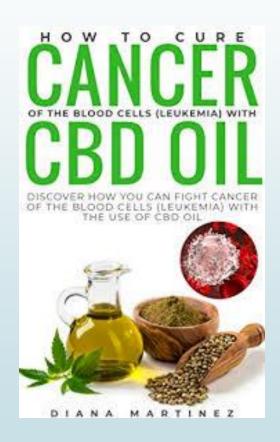
Pat Pizzo

What we will cover today

- 1. Information from government agencies on legality of CBD
- 2. Info on health issues incurred with CBD use.
- 3. What is CBD
- 4. Hemp
- 5. How does it impact urine drug screen testing.

Federal Agencies on CBD

FDA warns company marketing unapproved cannabidiol products with unsubstantiated claims to treat cancer, Alzheimer's, opioid withdrawal, pain and pet anxiety (FDA; 7/23/19)



Federal Agencies on CBD

Federal Trade Commission (FTC) sends warning letters to Companies advertising their CBD-infused products as treatment for serious diseases, including cancer, Alzheimer's and multiple

sclerosis (FTC: 9/10/19)

FDA July 2019



The U.S. Food and Drug Administration (FDA) recognizes the significant public interest in cannabis and cannabis-derived compounds, particularly CBD. However, there are many unanswered questions about the science, safety, and quality of products containing CBD.

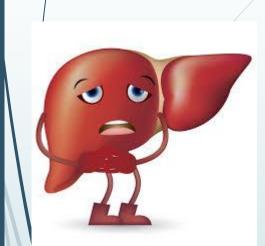
FDA July 2019

- Only one approved prescription drug (Epidiolex) to treat rare, severe forms of epilepsy.
- FDA has not approved any other CBD products, and there is very limited available information about CBD, including about its effects on the body.





- What are the effects CBD could cause in the body, such as toxicity to the liver, when someone ingests CBD regularly over a long period of time.
- During its review of the marketing application for <u>Epidiolex</u>, the FDA identified certain safety risks, including the <u>potential for liver injury</u>.
- These are serious risks that can be managed when an FDA-approved CBD drug product is taken under medical supervision, but it is less clear how these risks might be managed when CBD is used far more widely, without medical supervision and not in accordance with FDA-approved labeling.



FDA Medical Concerns with the use of CBD – Nov 25, 2019

- 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.

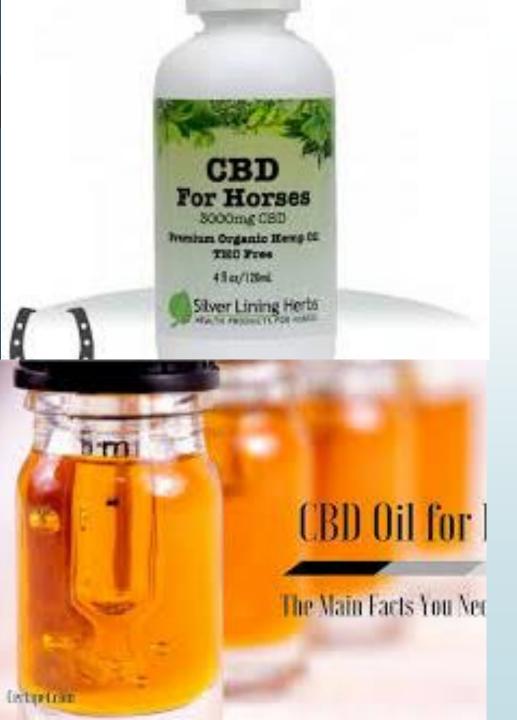
FDA Medical Concerns with the use of CBD – Nov 25, 2019

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

FDA Concerns July 2019

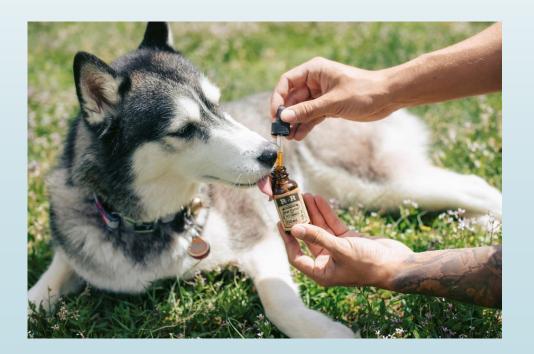
- Cumulative exposure to CBD if used in multiple products.
- What if you use these products daily for a week or a month?
- The effects of CBD on special populations.





FDA July 2019

The safety of CBD use in animals (e.g., species, breed, or class) including pets.



Risks of CBD Oil Use in Addiction Recovery

Lack of Regulation



Epidiolex is the only FDAapproved drug that contains CBD oil, and there is no guarantee that small businesses creating CBD oil products will be effective.

No Dose Management



Without regulation or a true understanding of how much is too much, it may be possible to abuse CBD oil for its sedative effects and sidestep the work of recovery.

Waste of Money



Products that purport to contain CBD oil may contain so small of an amount that it has no effect and wastes your money.

Vaste of Time



If you are struggling with anxiety, depression, PTSD, or chronic pain and these disorders are a threat to your recovery, choosing to mess around with CBD oil can postpone connection with research-based treatment.

Toxin Exposure



The lack of regulation of CBD oil products also means that you may be ingesting lead, pesticides, heavy metals or other toxic substances.

Negative Side Effects



Because there is little research into the effects of CBD oil, there is little documentation of side effects, but many report extreme sedation, diarrhea, and other negative effects.

Possible Drug Interactions



CBD oil may negatively interact with prescribed medications and over-the-counter medications. There is no research to determine potential conflicts.

Legal Consequences



Marijuana products containing more than 0.1 percent of THC are classified as Schedule I drugs and illegal to use, sell, or possess.

FDA Concerns July 2019

- Unapproved CBD drug products have not been subject to FDA review as part of the drug approval process.
- Are they safe and effective to treat a particular disease?
- What is the proper dosage?
- How do they interact with other drugs or foods?
- Do they have dangerous side effects or other safety concerns?

FDA Concerns July 2019

- Misleading and false claims associated with CBD products may lead consumers to put off getting important medical care.
- Talk to your doctor about the best way to treat diseases or conditions with existing, approved treatment options.

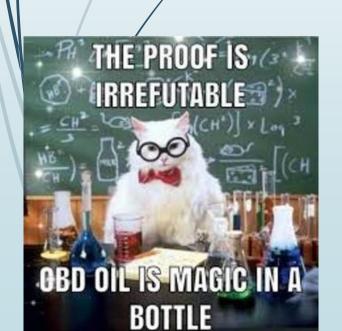




How is CBD produced

- Grind Flowers are ground to allow better extraction
- Extract Extractions are a way to separate CBD when it is mixed with compounds in hemp. The mixture is brought into contact with a solvent in which the substance of interest is soluble, but the other substances present are insoluble.
- Winterize -an alcohol wash of the cannabis plant. It extracts the cannabinoids and terpenes from each other, making a very pure and concentrated form of CBD. Winterizing the cannabis plant consists of soaking the CBD extract in alcohol and then freezing it.
- Solvent Recovery To separate crude cannabis and hemp oil from solvents used in the extraction process.
- Decarboxylation A process that removes the carboxyl group using heat and time. CBDA is converted to CBD
- **Distillation** a process used to concentrate cannabidiol from CBD oils or hemp extracts to produce a clear golden colored liquid.

What is really in your CBD





Pesticides

Solvents – Butane, Hexane, Pentane



Waxes



% THC

CBD - Miracle Drug or Marketing Hype?

Studies show that CBD oil helps with:

- + General well-being
- + Acne
- + ADD / ADHD
- + Addiction
- + AIDS
- + ALS
- + Alzheimer's
- + Anorexia
- + Antiboitic resistance
- + Anxiety
- + Asthma
- + Atherosclerosis
- + Arthritis
- + Autism
- + Bipolar
- + Cancer
- + Colitis / Chrons

- + Depression
- + Diabetes
- + Endocrine disorders
- + Epilepsy / seizure
- + Fibromyalgia
- + Glaucoma
- + Heart disease
- + Huntington's
- + Inflammation
- + Irritable bowel
- + Kidney disease
- + Liver disease
- + Mad Cow disease / Prion
- + Metabolic Syndrome
- + Migraine
- + Mood disorders
- + Motion sickness

- + Multiple Sclerosis
- + Nausea
- + Neuropathic pain
- + Obesity
- + OCD
- + Osteoporosis
- + Parkinsons
- + PTSD
- + Rheumatism
- + Skin conditions
- + Sleep disorders
- + Spinal cord injury
- + Stress
- + Stroke / TBI
- + Schizophrenia
- + Sickle cell animia

Source:





"Dude, we've struck cannabis oil! We're going to be rich!"

CartoonStock.com



What does Research Say

- → 72 adults presenting with primary concerns of anxiety (n = 47) or poor sleep (n = 25).
- Anxiety scores decreased within the first month in 57 patients (79.2%) and remained decreased during the study duration.
- Sleep scores improved within the first month in 48 patients (66.7%) but fluctuated over time.
- Cannabidiol may hold benefit for anxiety-related disorders. Controlled clinical studies are needed.





CBD and Psychosis

Psychological Effects- Subjects rated the effect of the drug for anxiety

Drug	Dose ml	0	1	2	3	4
Placebo	0.9	5	0	0	0	0
CBD	60	5	0	0	0	0
THC	30	0	0	1	0	4
THC + CBD	30 + 60	0	2	3	0	0



Karniol, European J of Pharmacol, 1974,p172

Does CBD work for Arthritis

Arthritis Foundation has commented on this issue



"I don't prescribe opioids, but feel free to grab a CBD-laced lollipop on your way out."

Arthritis Foundation Guidelines for CBD 10/12/19

- ► CBD may help with arthritis-related symptoms, such as pain, insomnia and anxiety, but there have been no rigorous clinical studies in people with arthritis to confirm this.
- While no major safety issues have been found with CBD when taken in moderate doses, potential drug interactions have been identified.
- CBD should never be used to replace diseasemodifying drugs that help prevent permanent joint damage in inflammatory types of arthritis.

Arthritis Foundation Guidelines for CBD 10/12/19

- ► CBD use should be discussed with your doctor in advance, with follow-up evaluations every three months or so, as would be done for any new treatment.
- There are no established clinical guidelines to inform usage. Experts recommend starting with a low dose, and if relief is inadequate, increase in small increments weekly.
- Buy from a reputable company that has each batch tested for purity, potency and safety by an independent laboratory and provides a certificate of analysis.

What Drugs Interact with Cannabis



Nearly 60 percent of the medications on the market are metabolized through a set of liver enzymes. CBD can interact with medications that are metabolized in the body by cytochrome p450, enzymes CYP3A4 and CYP2C19

Drugs. Com has indicated 24 major interactions and 309 moderate interactions with Cannabis

Common Drugs that interact with Cannabis

alprazolam	candesartan	cyclobenzaprine	furosemide
amitriptyline	captopril	desipramine	haloperidol
amlodipine	carbamazepine	dexbrompheniramine	hydrochlorothiazide
amobarbital	carisoprodol	dexchlorpheniramine	hydrocodone
amoxapine	carteolol	dextromethorphan	hydromorphone
atenolol	cetirizine	diazepam	hydroxyzine
aripiprazole	chlordiazepoxide	diphenhydramine	imipramine
baclofen	chlorothiazide	doxazosin	kava
benztropine	chlorpheniramine	doxepin	lisinopril
brompheniramine	chlorpromazine	duloxetine	lithium
buprenorphine	clonazepam	escitalopram	lorazepam
buspirone	clorazepate	etizolams	loxapine
butabarbital	clonidine	ethanol	meperidine
butalbital	codeine	flurazepam	mephenytoin

Common Drugs that interact with Cannabis

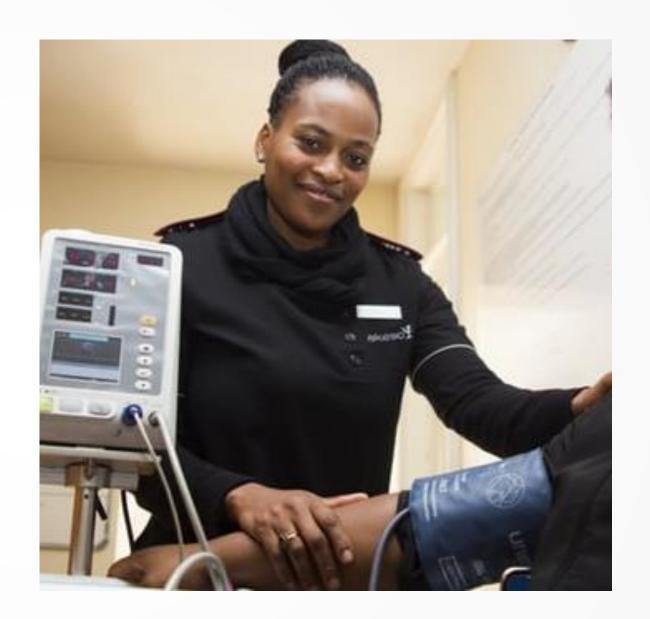
meprobamate	pentazocine	risperidone	valproic acid
methocarbamol	pentobarbital	secobarbital	venlafaxine
metolazone	phenacemide	sertraline	zaleplon
metoprolol	phenobarbital	St. John's wort	ziconotide
midazolam	phenytoin	tapentadol	ziprasidone
mirtazapine	prazosin	temazepam	zolpidem
morphine	primidone	theophylline	zonisamide
nabilone	promazine	thioridazine	
nitroglycerin	promethazine	topiramate	
nitroprusside	propranolol	torsemide	
olanzapine	protriptyline	tramadol	
oxazepam	quazepam	trazodone	
oxycodone	quetiapine	trimipramine	
oxymorphone	reserpine	valerian	



Using sertraline (Zoloft) together with cannabidiol may increase side effects such as dizziness, drowsiness, confusion, and difficulty concentrating. Some people, especially the elderly, may also experience impairment in thinking, judgment, and motor coordination.
www.Drugs.com

■ CBD has the potential to interact with SSRIs, and other antidepressants, resulting in increased amounts of antidepressant in the body and a higher risk of side effects. www.depressionalliance.org.

- CBD (cannabidiol) has been shown to cause a modest drop in blood pressure in people taking high doses. Nov 6, 2018 www.consumerlab.com.
- In the case of a blood thinner like warfarin (Coumadin), "other problems" could entail a traumatic bleed or a dangerous hemorrhage. Medication should be closely monitored by a physician.
 www.ncbi.nlm.nih.gov/pmc/articles/PMC5789126/





- The same goes for benzodiazepines (or benzos) like Xanax or Ativan. With CBD they could increase the side effects and potentially cause you to feel more sedated or drowsy. In some rare cases, the drug combo may become toxic or even interfere with your respiratory system. Michelle Henry.
- According to the District of Columbia Department of Health, CBD can also increase the amount of medication in your blood including antidepressants, antihistamines, antiretrovirals, calcium channel blockers and beta blockers.

https://medlineplus.gov/druginfo/natural/1439.html#DrugInteractions.

➤ You may have heard of the **grapefruit rule**, which suggests that the citrus fruit can impair how your body absorbs certain drugs — mainly cholesterol medications, blood pressure drugs and allergy pills. **The same is true for CBD**



https://medlineplus.gov/druginfo/natural/1439.html#DrugInteractions



Route of administration

- **■** Sublinguial
- Inhalation (Vaping)
- Eating or drinking
- Dermally

VAPING a popular method of CBD use

- As of 2/18/20 2807 hospitalized cases or deaths reported to CDC from the US and its territories.
- 68 deaths confirmed in 29 states and WDC as of 2/28/20

https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html



Questions to ask

- Have you discussed the use of CBD with your physician?
- Does it interact with any of your medications?
- Have you had your liver enzymes checked since you started using CBD?
- Does the product you use have a certificate of analysis?
- Has the product been checked for the presence of pesticides and solvents?
- What is the percentage THC in your product?
- Is the benefit from CBD or do you feel better because of the THC concentration in the product.

Why is CBD Important to the Criminal Justice System

Why are we even talking about CBD

Dec 2018 Farm Bill





"Remind me, is this medicinal or recreational weed?"

CartoonStock.com

What is the 2018 Farm Bill

It removed hemp, defined as cannabis (Cannabis sativa L.) and derivatives of cannabis with extremely low concentrations of the psychoactive compound delta-9-tetrahydrocannabinol (THC) (no more than 0.3 percent THC on a dry weight basis), from the definition of marijuana in the Controlled Substances Act (CSA).



Testimony of Amy Abernethy, Md, Phd., Principal Deputy Commissioner, Office of the Commissioner, Food and Drug Administration, Department of Health And Human Services before the Senate Committee on Agriculture, Nutrition, and Forestry, July 2019

2018 Farm Bill

- Specifies when the product must be tested (prior to and within 15 days of harvesting).
- Who can conduct the sampling.
- What part of the plant is tested (top 1/3)
- Actual sampling procedures
- Requirements for the testing lab
- Analytical procedures (total THC)
- Requirements for calculating and reporting percentages





So How much THC is actually allowed under the Farm Bill

- The FDA web site states the following: Laboratories shall use appropriate, validated methods and procedures for all testing activities and evaluate measurement of uncertainty.
- What does this mean:

Lab calculated value = 0.29%

Lab measurement of uncertainty =0.09%

Range of amount present = 0.20% – 0.38%

Structures of CBD and THC

What is CBD

Cannabidiol is a phytocannabinoid discovered in 1940. It is one of 113 identified cannabinoids in cannabis plants and accounts for up to 40% of the plant's extract.

What is CBD

receptors. This is probably why it does not make people high and is not mindaltering; in fact it may even blunt some of THC's psychotropic effects. NIDA July 2015

Bioavailability of CBD

Oral – Approximately 6% in humans

Inhalation – 11-45% mean 31%



Half-Life

Terminal half life – 18-36 hours

How long can CBD be detected: Plasma

	Researcher	Number	Route	Amount	Time tested	Concentration	Time detected
	Ohlsson	3	IV	20mg	1hr	37-61 ng/ml	72 hrs
	Ohlsson	3	Smoked	19.2 mg	1hr	3.0-17.8 ng/ml	
/	Agurell	2	oral	40 mg	1 hr	1.1-11 ng/ml	
	Nadulski		oral	5.4 mg	1 hr	0.3-2.57 ng/ml	3-4 hrs





Does CBD convert to THCA in the body

- The use of pure CBD oil will not result in the detection of THCA in the urine. CBD oil is cannabidiol and will not be detected in the confirmation method.
- In the paper "Conversion of Oral Cannabidiol to Delta9-Tetrahydrocannabinol Seems Not to Occur in Humans by Gerhard Nahler et. Al (Published in Cannabis and cannabinoid Research, Vol 2.1, 2017) the authors summarize with the following statement: Over 40 years of research on CBD does not suggest a conversion of CBD to delta9-THC and/or other cannabinoids in vivo after oral administration.

How long can CBD be detected: Urine 5 test subjects

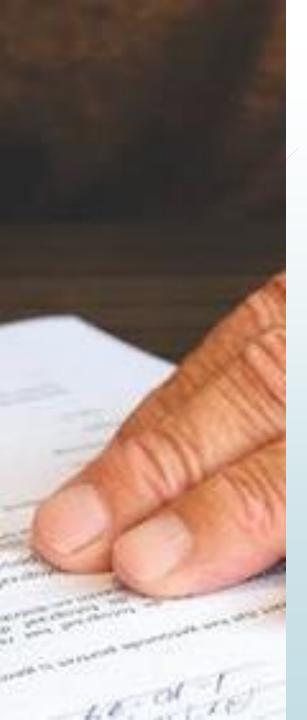
Dose mg	Route	Max CBD ng/ml	CBD Last Detected	Max THCA ng/ml	THCA Last Detected
100 CBD	oral	2941	103 hrs	2.9	103 hrs
100 CBD	Vaped	631.1	102 hrs	2.0	95 hrs
100 CBD/0.37% THC	Vaped	539.1	97 hrs	29.9	95 hrs

- 1. Peak THCA excretion 4-6 hrs
- 2. Same test subject had all of the highest levels
- 3. Federal Cut Off on confirmation is 15 ng/ml

Are you buying CBD or Hemp







SAMHSA Memo July 24, 2019

■ Studies have shown that some CBD products' labeling does not accurately reflect their content. Cannabis based products containing a THC level greater than 0.3% on a dry weight basis do not fall under the Farm Bill's definition of hemp even if they are labeled as such.

SAMHSA Memo July 24, 2019

In one study, the amount of CBD in 69% of the 84 tested CBD products was inconsistent with that on the label, and some products contained unlabeled cannabinoids, including THC in amounts up to 6.4 mg/mL.



- The paper Human Cannabinoid
 Pharmacokinetics in 2007. Huestis et al
- Oral administration of dronabinol and hemp oil. The study was performed on 4,381 specimens.
- The study concluded the low doses (7.7 mg/dl) cleared the urine in 2-3 days with half-life elimination of approximately 24 hrs.
- The high dose (14.8 mg/dl) test subjects cleared the drug in a maximum of 4.9 days (118 hrs) and had a half-life elimination rates of 44.2 -64 hours.



- Constantino, Schwartz and Kaplan published Hemp Oil Ingestion Causes Positive Urine Test for Delta-9tetrahydrocannabinol Carboxylic Acid (THCA) in The Journal of Analytical Toxicology in Oct 1997.
- In this study 7 test subjects were given 15 mls of hemp oil and urine collected at 8, 24 and 48 hours.
- The highest level detected, 78 ng/ml, was at 8 hours.
- At 48 hours the highest level detected was 18 ng/ml.

- Struempler, Nelson and Urry published A Positive Cannabinoids Workplace Drug Test Following the Ingestion of Commercially Available Hemp Seed Oil in Journal of Analytical Toxicology in Aug 1997.
- This was a case study on a single male that consumed 15 mls of cold-pressed hemp seed oil twice a day for 4 days.
- A total of 19 specimens were collected and analyzed beginning the 3 day of the study.
- The highest level of THCA, 68 ng/ml, detected was 108 hours into the study or approximately 3.5 days after the last dose.



- Dr. Marylin Huestis former Chief of Chemistry and Drug Metabolism at NIDA's Intramural Research Program (retired 2016) published the paper Human Cannabinoid Pharmacokinetics in 2007.
- Page 13 of this paper discusses excretion of THCA in urine after controlled oral administration of dronabinol and hemp oil. The study was performed on 4,381 specimens. Both low doses and high doses were used. The high doses were 7.5 and 14.8 mg/d.
- The study concluded the low doses cleared the urine in 2-3 days with half-life elimination in the range of 16-8 31.9 with means of 24.1 and 21.1 depending on the dose amount. The high dose test subjects cleared the drug in a maximum of 4.9 days (118 hrs) and had a half-life elimination rates of 44.2 -64 hours.



Can your screening reagent detect CBD?

Reagent/Device	CBD Detected/ Concentration Tested in Urine
CEDIA	Positive at <0.1% at 1000 ng/ml
DRI	Negative at 10,000 ng/ml
Rapid drug test cup	Positive 100,000ng/ml
EZ Screen	Negative at 100,000 ng/ml
Dip Stick Fastect II	Negative at 100,000 ng/ml
Siemens	Not listed
Immunalysis	Positive at <0.005% at 1,000,000 ng/ml

Distinguishing CBD/THC from Marijuana Use

- Light Cannabis sold in Europe: THC < 0.2% variable CBD concentrations</p>
- 1g cigarette 0.16% THC and 5.8% CBD
- Blood (B) and oral fluid (OF) specimens
- ► Mean OF/B ratio 0.6-1.2 after 1 cigarette
- Mean OF/B ratio 0.6-1.9 after 4 light Cannabis cigarettes
- Illegal marijuana OF/B ratio generally > 10



Questions to ask

- What is the stated % THC of the product being used?
- Does the user have a certificate of analysis to prove the concentration?
- Are they using more than one product?
- Route of administration?
- When was the last claimed use?

Thank You

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