



Cannabis Synthetics 101

An Introductory Webinar for Regulators



Lezli Engelking Founder & President

- Our Mission: To Protect Public Health, Consumer Safety, and Safeguard the Environment by Promoting Integrity in the Cannabis Industry



FARM BILL

SECURING OUR FUTURE





Legal Cannabis Markets After Passage
of the 2018 Farm Bill

2018 Farm Bill Wrecked Havoc on Supply & Demand

Within 45 days of passing, cbd prices dropped more than 30%

Total hemp planted WENT FROM 32,000 acres to 146,000 acres WITHIN MONTHS

2014 price of single kilo of refined cbd oil could go for up to \$70,000

2022 price of a same kilo average \$750



Hemp
Derived
Intoxicating
Cannabinoids
Are
Available
Everywhere

RARELY EQUAL
★★★★

THC RICH CANNABIS

PRODUCTS

NO MEDICAL CARD NEEDED

TINCTURES VAPES EDIBLES LOTIONS DEVICES

HHC
Δ9-THC
Δ8-THC

CBD
Δ10-THC
THCO

ELEVATE YOUR LIFE!
\$4.20 COUPON

TWO LOCATIONS TO SERVE YOU

SCAN TO SHOP NOW

VALLEY FAIR MALL
Center Court
Kiosk

THE SHOPS AT SOUTH TOWN
2nd Floor
East Entrance

CBD KRATOM

REACH
NEW
HEIGHTS
WITH
HHC-O

GUMMIES
15MG
15MG

NO MEDICAL CARD REQUIRED

amazon



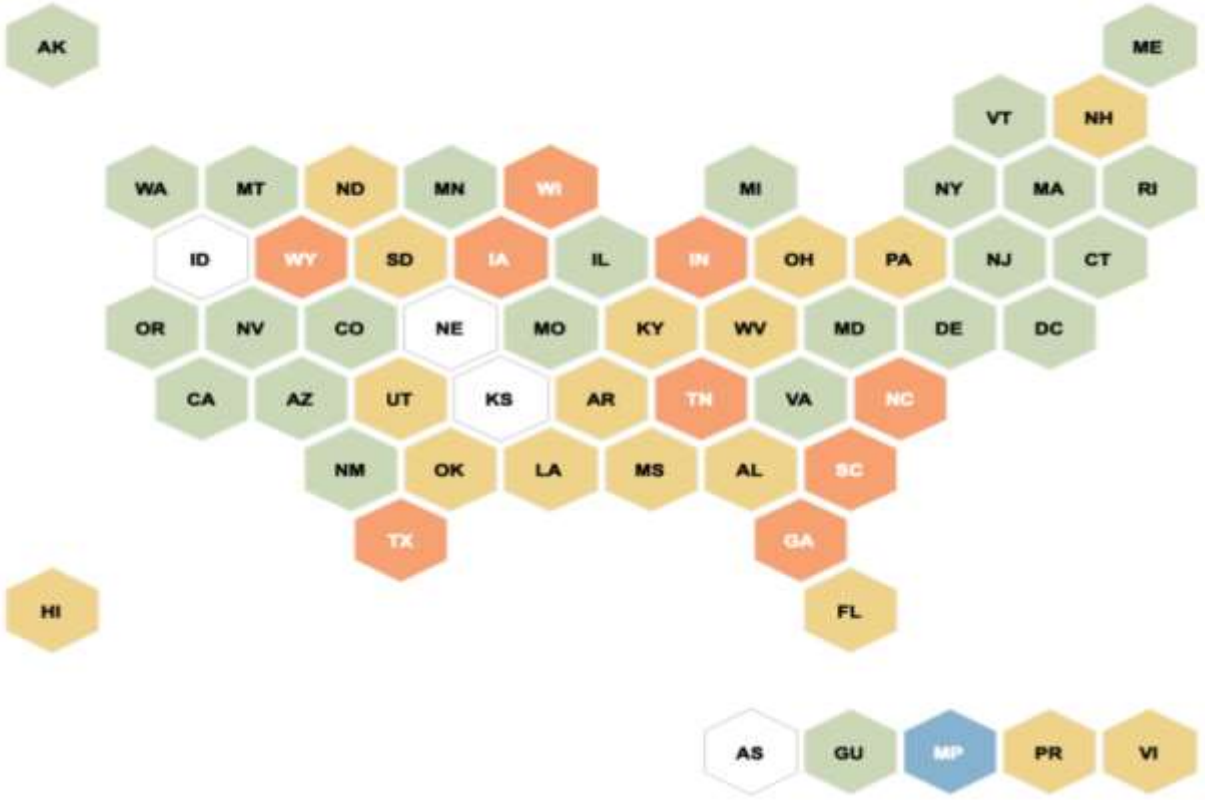
Vitamex Hemp Gummies -
Great for Peace & Relaxation -
2,500,000 - Natural Fruit
Flavors Tasty Relief - Made in
USA - Relaxing Gummies -
100ct



State Regulated Cannabis Programs

Switch View ▾

- No public cannabis access program
- Adult & medical use regulated program
- Adult use only, no medical regulated program
- Comprehensive medical cannabis program
- CBD/low THC program



NCSL June 2023



Identifying Hemp Derivatives

Recognizing Products of Concern

D8

D11

D9

HHC

HHCO

THCB

THCP

THCjd

THCX

THC-OH

THCO

THCO-
Acetate

THC-Hemp

High THCA
Hemp

Synthetic Cannabinoid Exposures

- First reported case in 2008
- Increased steadily since 2014
- All 50 states have reported adverse health effects
- Effects range from temporary changes in mental status to death



DEA Confirmation: delta-8-THC, if extracted from compliant hemp biomass, is exempt from the CSA

2021 email from DEA Section Chief clarified that arriving at delta-8-THC by a chemical reaction starting from CBD makes it synthetic and is not exempted by the Farm Bill

DEA has not addressed all THC isomers and synthetic byproducts, but has provided guidance that THC-O is a Schedule 1 drug because it is not naturally occurring

Many of the synthetic byproducts would also be deemed controlled substances because they do not exist naturally

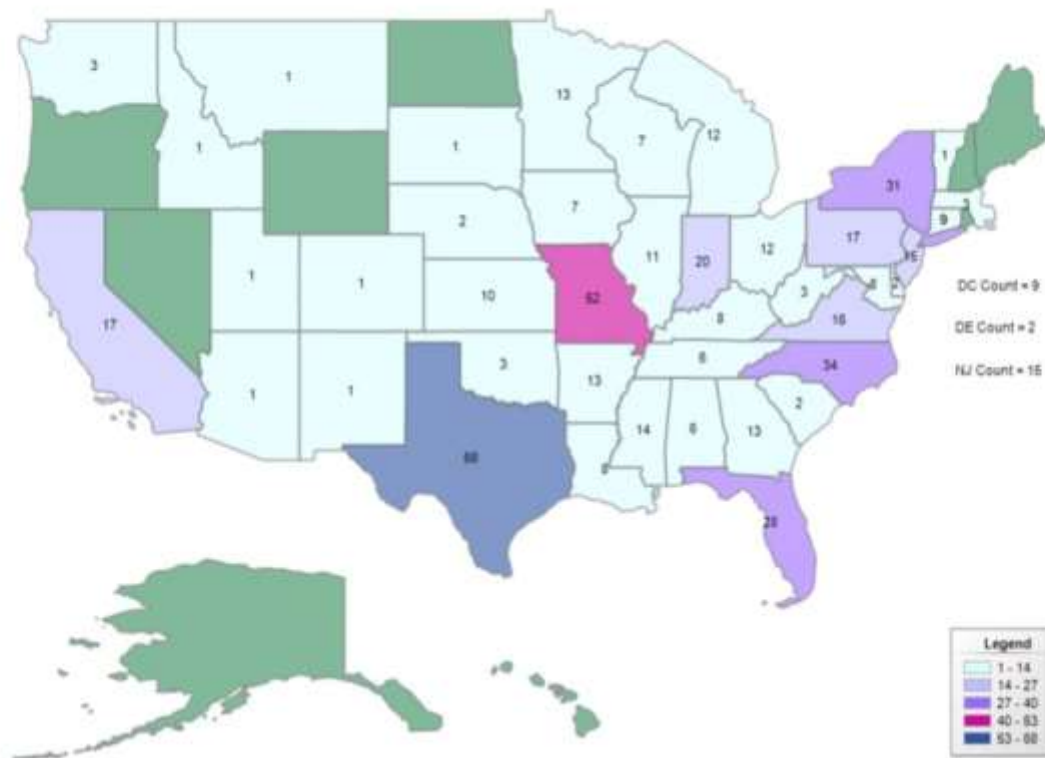


Cannabis and The Controlled Substances Act

- State laws specifically address natural and synthetic isomers of THC
- Often included under Schedule 1 in existing state code
- State codes often mirror the federal CSA



Synthetic Cannabinoid Calls to U.S. Poison Centers (1/1/2023 - 9/30/2023)



Hemp Derivatives and Isomers: Exploitation of an Unintended Loophole



October 12th, 2023
Webinar



Lezli Engelking⁽¹⁾ and Christopher Hudalla PhD⁽²⁾

(1) FOCUS • (2) ProVerde Laboratories

ProVerde Background

- Ph. D. in Analytical Chemistry
- > 35 years of academic and industrial research
 - 10 years focused specifically on Cannabis
- ISO 17025:2017 Accredited Analytical Testing Laboratory
- Providing Analytical Services for Cannabis and Hemp Industries
 - Growers, Extractors, Processors, Dispensaries, Care Givers, Patients and Adult-Users
 - Full Complement of Potency and Safety/Contamination Testing
- Serving Legal Cannabis Testing Clients in Massachusetts
- Serving CBD/Hemp-Based Testing Clients Worldwide
 - Clients across United States, Europe, Latin America and Asia



*“The public welfare outweighs the right to private gain . . .
No man may poison the people for his private profit.”*

— President Theodore Roosevelt.

President Theodore Roosevelt, Special Message to Congress, (Jan. 22, 1909)
available at <https://www.presidency.ucsb.edu/documents/special-message-368>

Delta-8-THC (D8-THC/ Δ 8-THC)



Industry thought process:

- Hemp is legal under farm bill
- CBD extracted from hemp is natural and legal
- Trace levels of Δ 8-THC has been observed in biomass and therefore is a natural product
- Since Δ 8-THC is naturally occurring, a derivative pathway from CBD for production is legal

Problem:

- Conversion of CBD to Δ 8-THC is not a natural process
- Many isomers formed are not naturally occurring
- There are both legal questions and consumer safety issues arising from these unknown contaminants

Natural $\Delta 8$ -THC

- $\Delta 8$ -THC is only found in trace amounts in natural cannabis biomass
- It would require 55,000 kilo of hemp to produce 1 kilo of natural Delta-8-THC
- At \$400 per kilo for biomass, raw plant material alone would be \$22,000,000
- Estimated market value for natural $\Delta 8$ extract would be somewhere between \$200,000,000 and \$500,000,000 per kilo
- Economically impractical

Rationale for Production/Distribution

Different rationales for positive positions on Delta-8

- High potential for therapeutic/recreational applications
 - Especially in markets where marijuana is not yet legal
- Scientifically interesting and relevant
 - Like many minor cannabinoids
- Relatively easy to produce, currently without regulatory oversight
 - Minimal capital investment for production equipment and supplies
- Oversupply of CBD isolate resulted in lower margins
 - Conversion to THC represents significant value add to products
 - Provides salvation for investors waiting for FDA approval of CBD

Delta-8-THC Concerns

Different rationales for negative positions on Delta-8

- Potential for intoxication with Delta-8 use
 - Much of hemp legislative success is based on absence of intoxicants
 - Could have negative consequences to future cannabis legislation
- Unregulated products cutting into regulated cannabis profits
- Consumer safety
 - Produced without regulatory oversight
 - Many unidentified contaminants observed in consumer products
 - No efficacy or toxicity information available for these contaminants

Regulatory and Consumer Safety Groups

Regulatory, Safety and Industry Groups Have Issued Statements

- US Food & Drug Administration (FDA)
- Centers for Disease Control and Prevention (CDC)
- FOCUS
- United States Pharmacopeia (USP)
- American Herbal Products Association (AHPA)
- US Hemp Authority
- Hemp Industry Association (HIA)

<https://www.fda.gov/consumers/consumer-updates/>

5-things-know-about-delta-8-tetrahydrocannabinol-delta-8-THC



Definition: Phyto-Cannabinoids

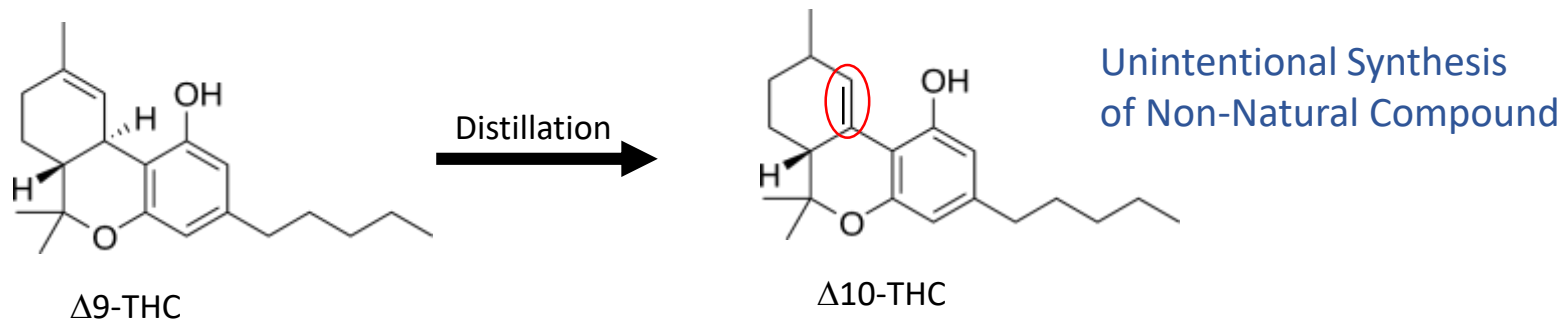
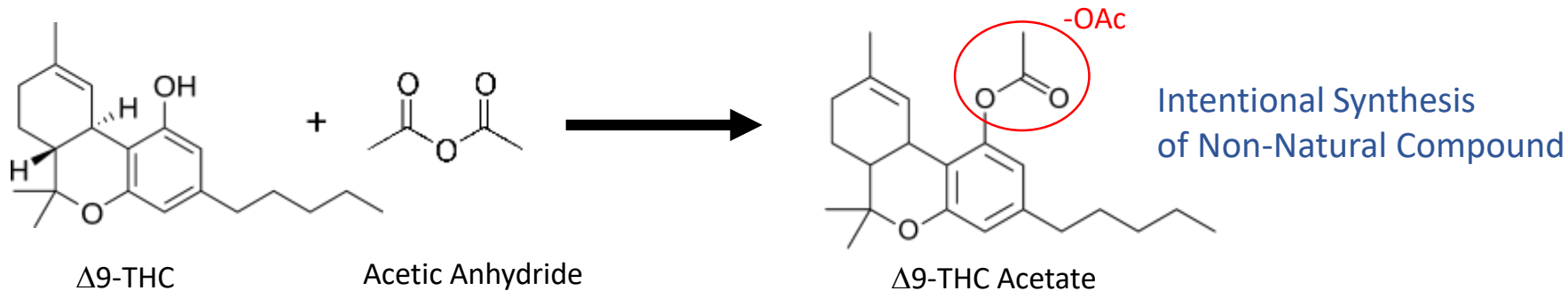
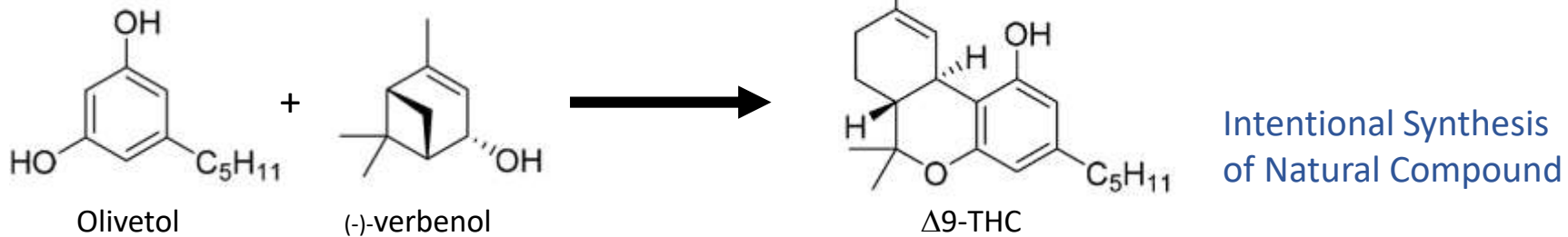
The term “phytocannabinoid” refers to cannabinoids produced by the cannabis plant.

- *Examples include: THCA, CBDA, CBGA*
- *While not produced directly by the plant, natural degradation occurs in the plant producing: Δ 9-THC, CBD, CBG, and CBN*
- *These cannabinoids are often extracted for production of consumer products: gummies, chocolates, vape devices*

Definition: Synthetic Cannabinoids

*The term “synthetic” refers to chemical compounds created through a chemical process by **human agency**, as opposed to those of natural origin.*

- *Synthetic compounds may imitate natural products (Marinol)*
- *Synthetic compounds may not found in nature (THC-O)*
- *Synthetic compounds can be intentional or accidental*

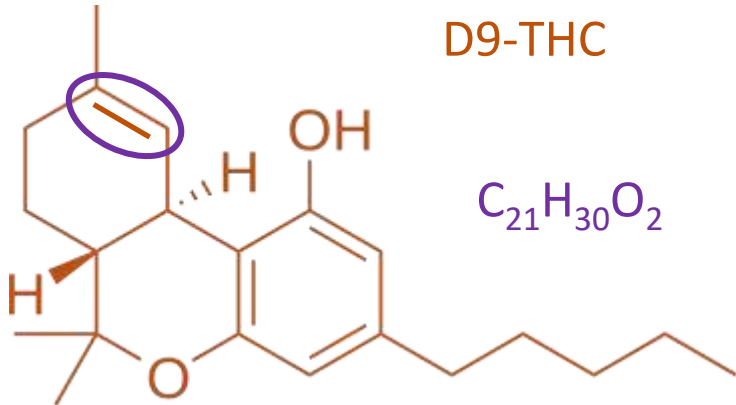


Definition: Isomers

The term “isomer” refers to compounds with the same chemical formula but a different arrangement or connectivity of atoms in the molecule.

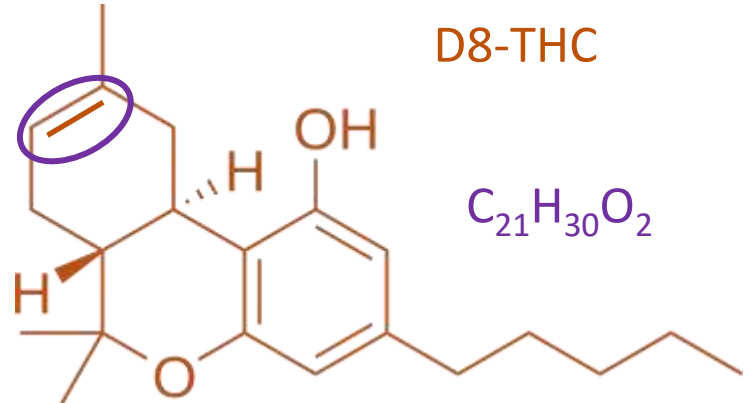
Δ^9 -Tetrahydrocannabinol

D9-THC



Δ^8 -Tetrahydrocannabinol

D8-THC



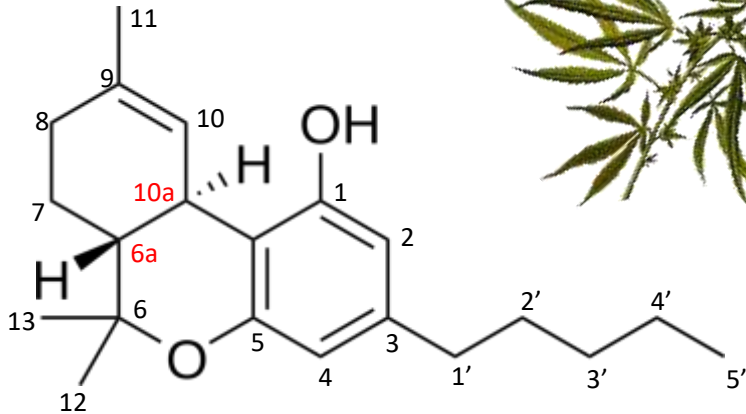
Isomers of THC

(6aR, 10aR)- Δ^9 -Tetrahydrocannabinol

(6aR, 10aR)- Δ^9 -THC

(-)-*trans*- Δ^9 -THC,

Δ^9 -THC, D9-THC

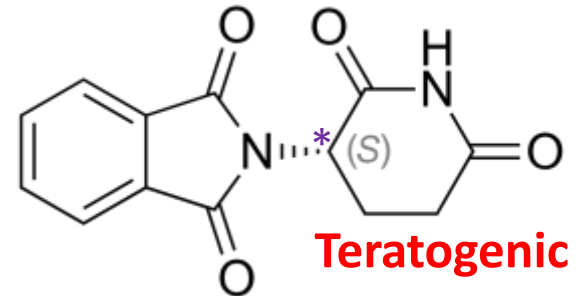
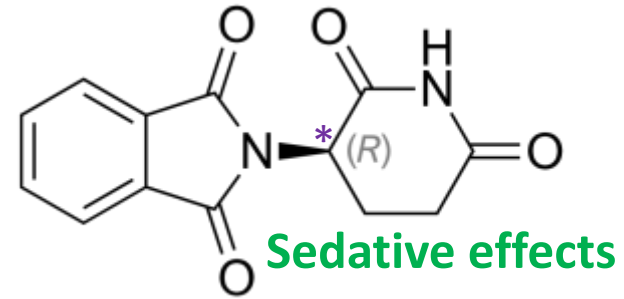


Isomers	Double Bond	Stereoisomers
$\Delta^{6a,10a}$ -THC	6a-10a	2
$\Delta^{6a,7}$ -THC	6a-7	4
Δ^7 -THC	7-8	8
Δ^8 -THC	8-9	4 (1)
Δ^9 -THC	9-10	4 (1)
Δ^{10} -THC	10-10a	4
$\Delta^{9,11}$ -THC	9-11	4

$\Delta = D$

Isomers Matters: Thalidomide

- First marketed in 1957 in West Germany
- Promoted for the treatment of anxiety, sleep disorders, tension and morning sickness
- Thalidomide is a “chiral” molecule
 - “right” and “left” handed isomers
- Use in pregnant women affected ~ 10,000 people
 - Approximately 40% died at time of birth
 - Survivors suffered from significant problems
 - Birth defects (limbs)
 - Eyes, heart, urinary tract



Isomers Matters: Thalidomide



Thalidomide
Birth
Defects



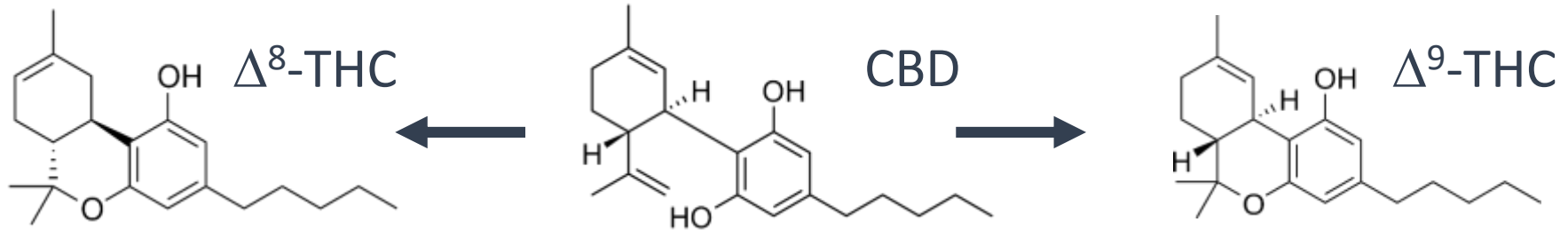
Isomers Matters: Thalidomide




- Used in Canada, Great Britain, West Germany and Australia
- Not approved by FDA for use in the US
- Frances Oldham Kelsey
 - Pharmacologist and Medical Reviewer with the FDA
 - Commented on the application:

“an interesting collection of meaningless pseudoscientific jargon apparently intended to impress chemically unsophisticated readers.”

Conversion of CBD into THC



First published by Roger Adams in 1941


US 20040143126A1

(19) **United States**
(12) **Patent Application Publication** (10) **Pub. No.: US 2004/0143126 A1**
Webster et al. (43) **Pub. Date: Jul. 22, 2004**

(54) **CONVERSION OF CBD TO DELTA8-THC AND DELTA9-THC** Related U.S. Application Data
(60) Provisional application No. 60/273,628, filed on Mar. 7, 2001.

(76) **Inventors:** G. R. Barrie Webster, Manitoba (CA);
Leonard P. Sarma, Manitoba (CA);
Raphael Mechoulam, Jerusalem (IL) Publication Classification

Most synthetic pathways employ acidic conditions with the addition of catalysts

Conversion of CBD into THC



Dissolve in solvent



Add Acid



Reflux

↑Temp



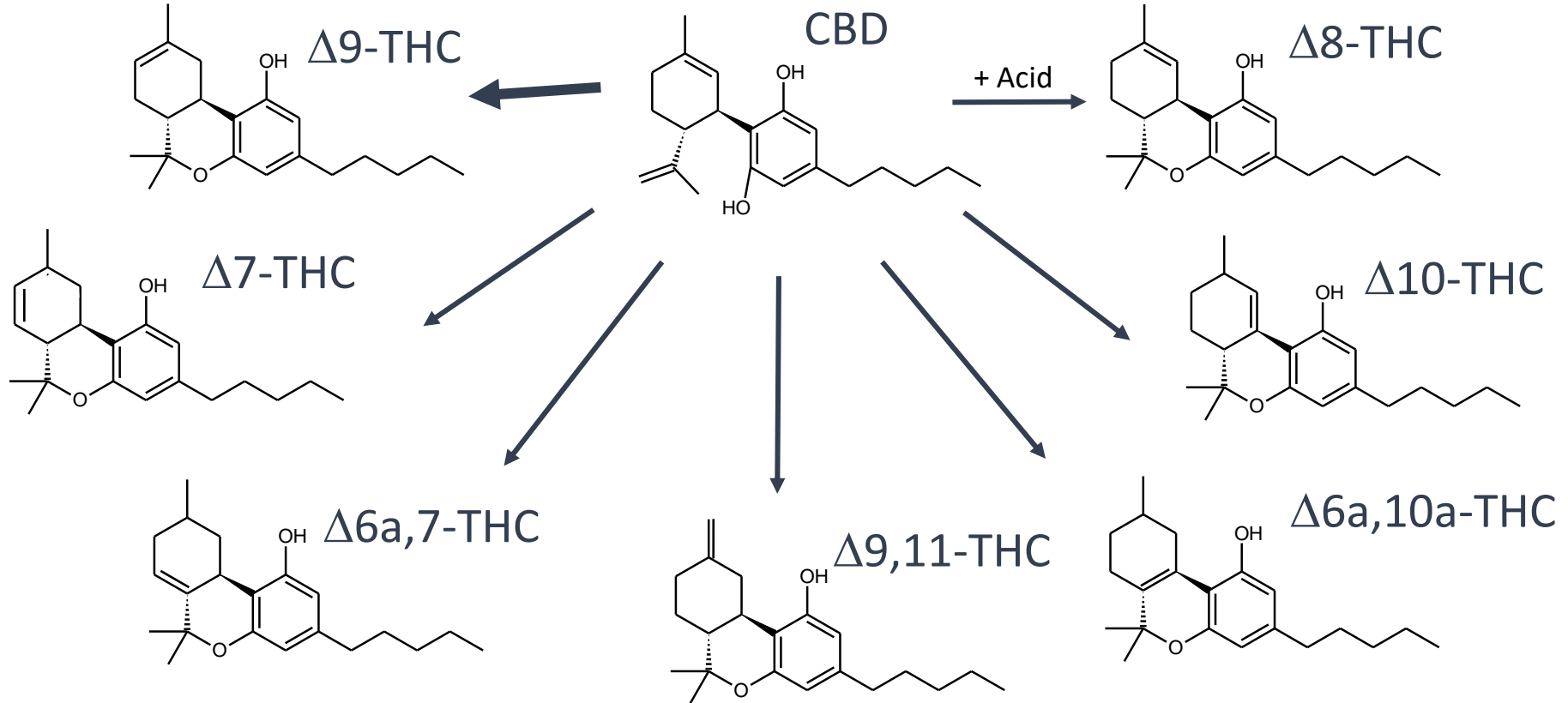
Neutralize Acid



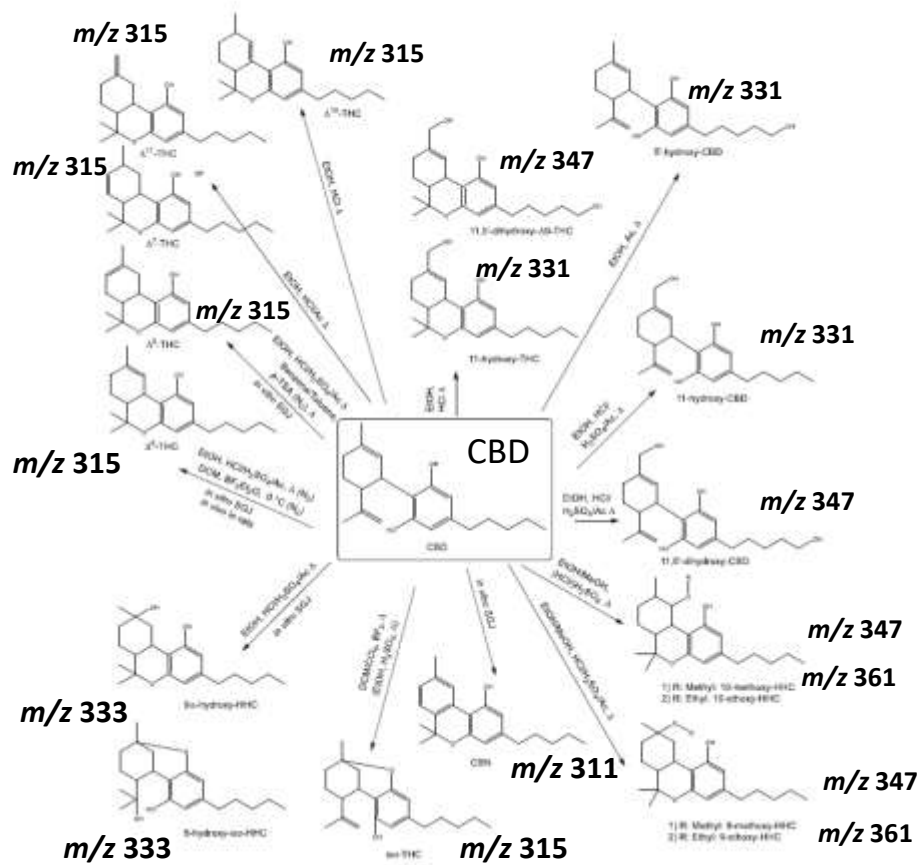
Remove Solvent



CBD + Acid \rightarrow THC



THC from CBD



Retention Time (min)	Structure	m/z	Fragments
1.96		347.244	329.203, 311.197, 287.215, 271.167, 231.137, 217.118, 193.116, 107.069
2.54		333.232	315.230, 259.160, 193.116, 135.104, 93.0541
2.87		329.211	311.204, 287.201, 271.160, 231.130, 193.116, 107.074
3.25		333.232	315.230, 259.160, 193.116, 135.104, 93.0541
3.56		347.325	315.230, 259.167, 193.116, 135.104, 93.0541
3.97		315.23	259.167, 193.116, 135.099, 123.024, 107.069, 93.0499

Golombek, P., et al. (2020). "Conversion of Cannabidiol (CBD) into Psychotropic Cannabinoids Including Tetrahydrocannabinol (THC): A Controversy in the Scientific Literature." *Toxics* **8(2)**.

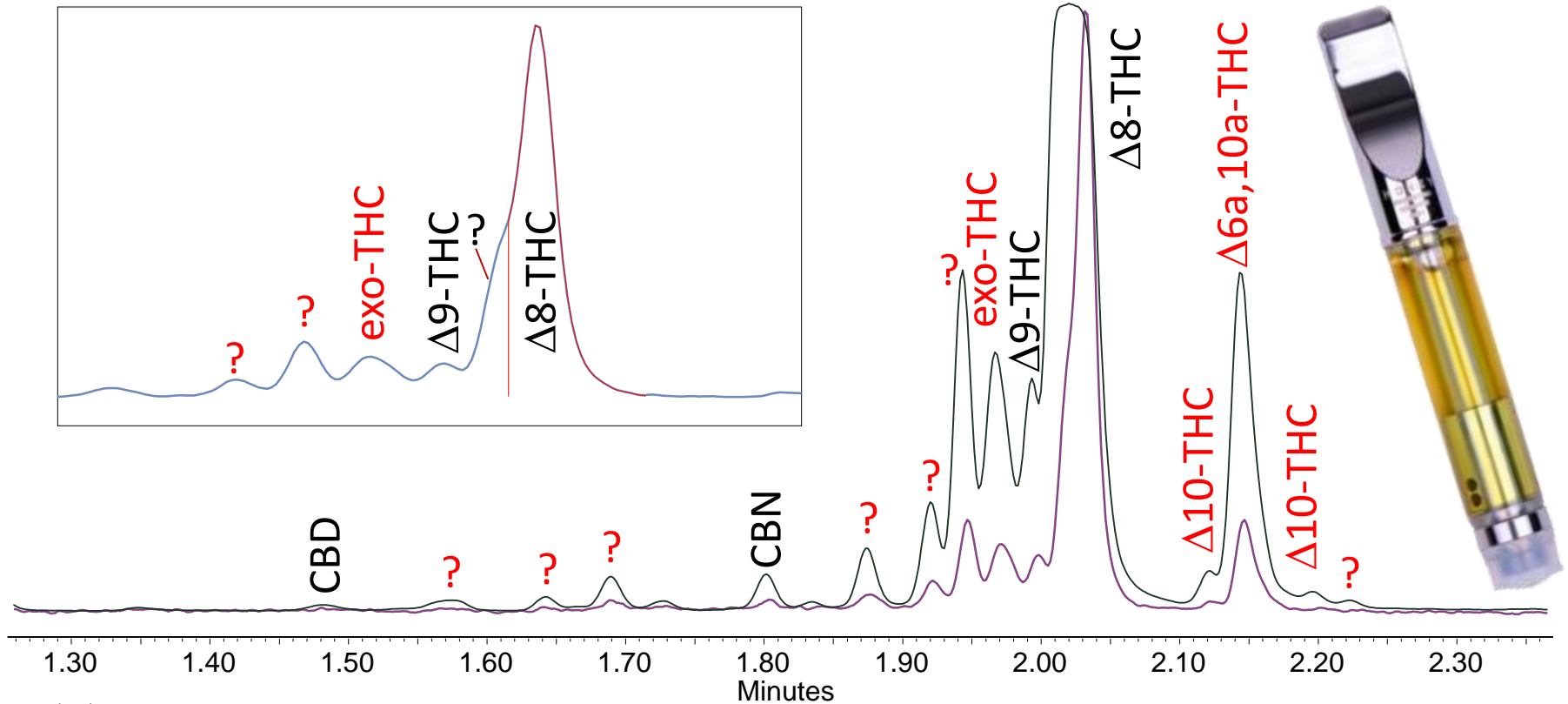
Kiselak, T. D., et al. (2020). "Synthetic route sourcing of illicit at home cannabidiol (CBD) isomerization to psychoactive cannabinoids using ion mobility-coupled-LC-MS/MS." *Forensic Sci Int* **308: 110173**.

Synthesis: Standard Operating Procedures

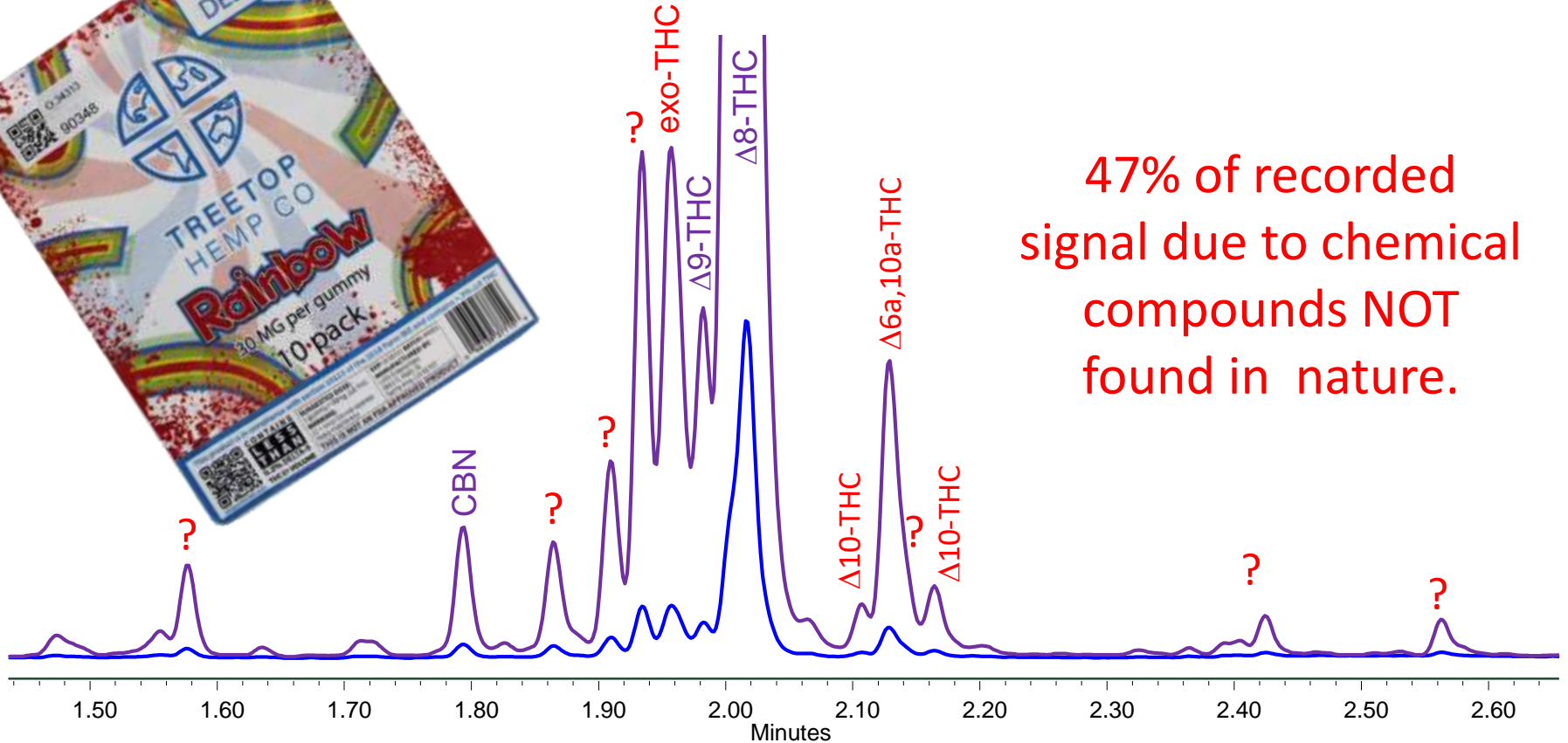


Beef Stew, Man-Style
2 lbs. lean beef, cut in 1-in. cubes
2 8-oz. cans Hunt's Tomato Sauce
1/4 t. pepper 1/2 bay leaf
2 t. salt 1 pt. thyme
1 c. onion, pure vegetable oil 1 c. sliced celery
6 each. sm. carrots, onions, potatoes, parsnips
1/2 qt. Drop in beef, a portion at a time
pot., brown beef over. low heat in hot
seasonings. Add vegetables to stew
simmer until vegetables are done
45 minutes. Makes 6 servings

Lemon Drop Vape Cartridge Oil



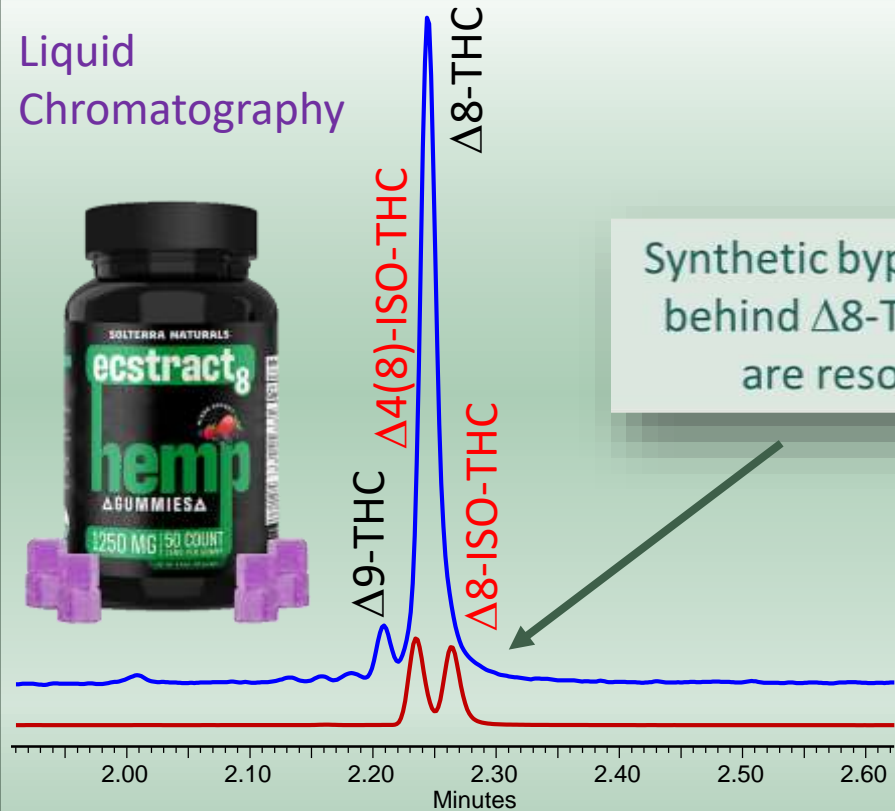
Tree Top Gummies



47% of recorded signal due to chemical compounds NOT found in nature.

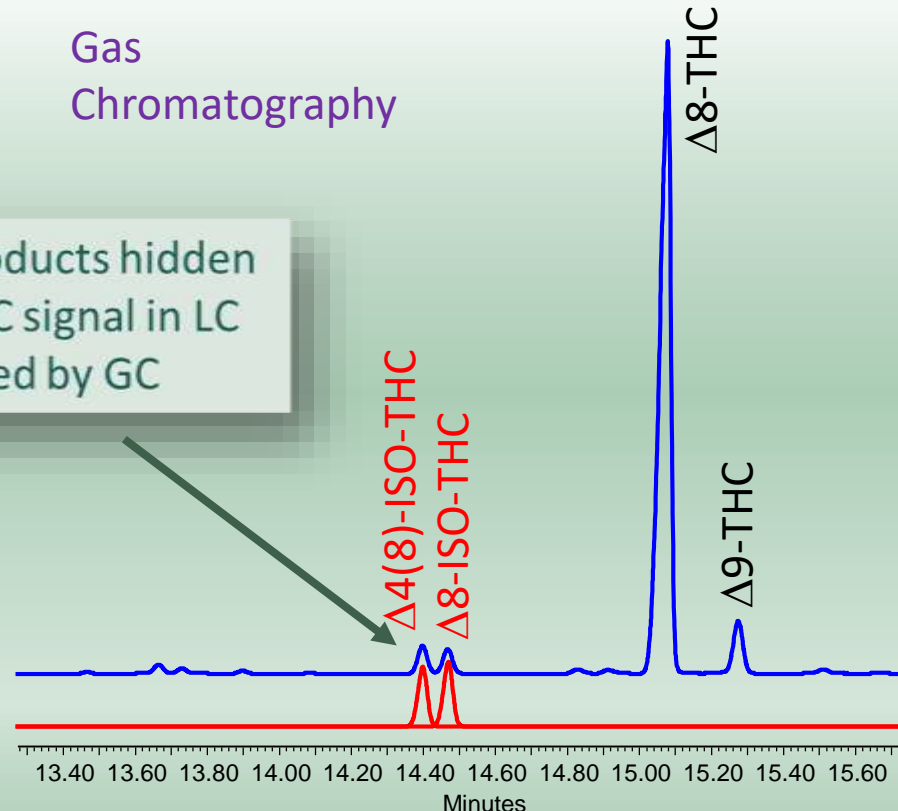
$\Delta 8$ -THC Analysis: LC vs GC

Liquid Chromatography



Synthetic byproducts hidden behind $\Delta 8$ -THC signal in LC are resolved by GC

Gas Chromatography



Δ^x – Wheel of Chance

- Commercially available Δ^8 -THC products represent complex synthetic mixtures
- Most laboratories are not reporting the unknown constituents
 - Certificates of Analysis are often unreliable
- Producers often do not know what they are producing and distributing
- Without regulatory oversight, consumers have no idea what they are consuming



Focus on Consumer Safety

- Isomers: Non-naturally occurring forms of THC
- Synthetic Byproducts: Chemicals not found in nature
- Synthetic Reagents: residual solvents, acids, catalysts
- Lack of Regulation: No labeling/distribution standards,
- Lack of Testing Methods: No appropriate methods
- Widespread Disinformation: Consumers are being misled
- Lack of Boundaries: Other synthetic analogs

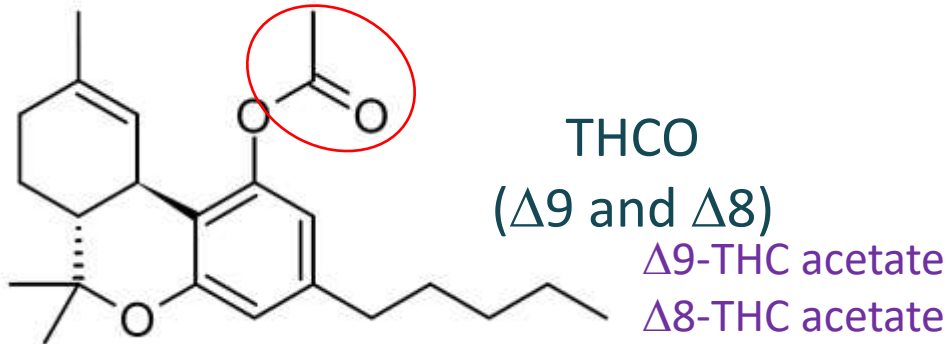
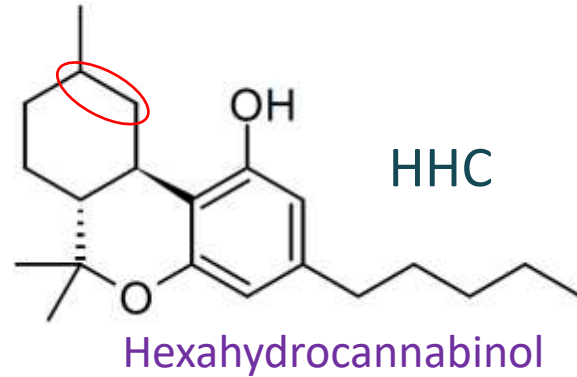
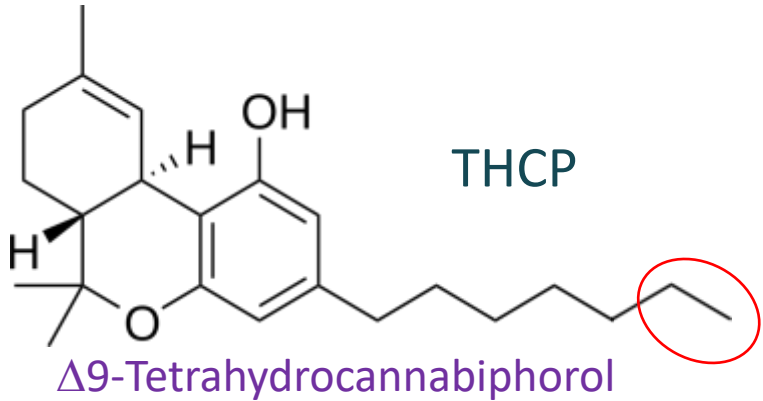
Points to Ponder

For these unknown synthetic contaminants in $\Delta 8$ -Samples:

- Are they doing liver damage because the body does not know how to metabolize these unknown compounds?
- Will they cause cancer with repeated long term exposure?
- Might some of these compounds cause birth defects or miscarriage if consumed during pregnancy?
- Will some of these compounds interact with other medications that a patient may be taking?
- Will use of these products trigger a positive drug test?

What's ~~Next?~~ Now?

- Other synthetic variants and analogs are already on the market:



($\Delta 9$ / $\Delta 8$)

THCb

THCh

THCp

THCO

THCPO

THC-X

PHC

CBNO

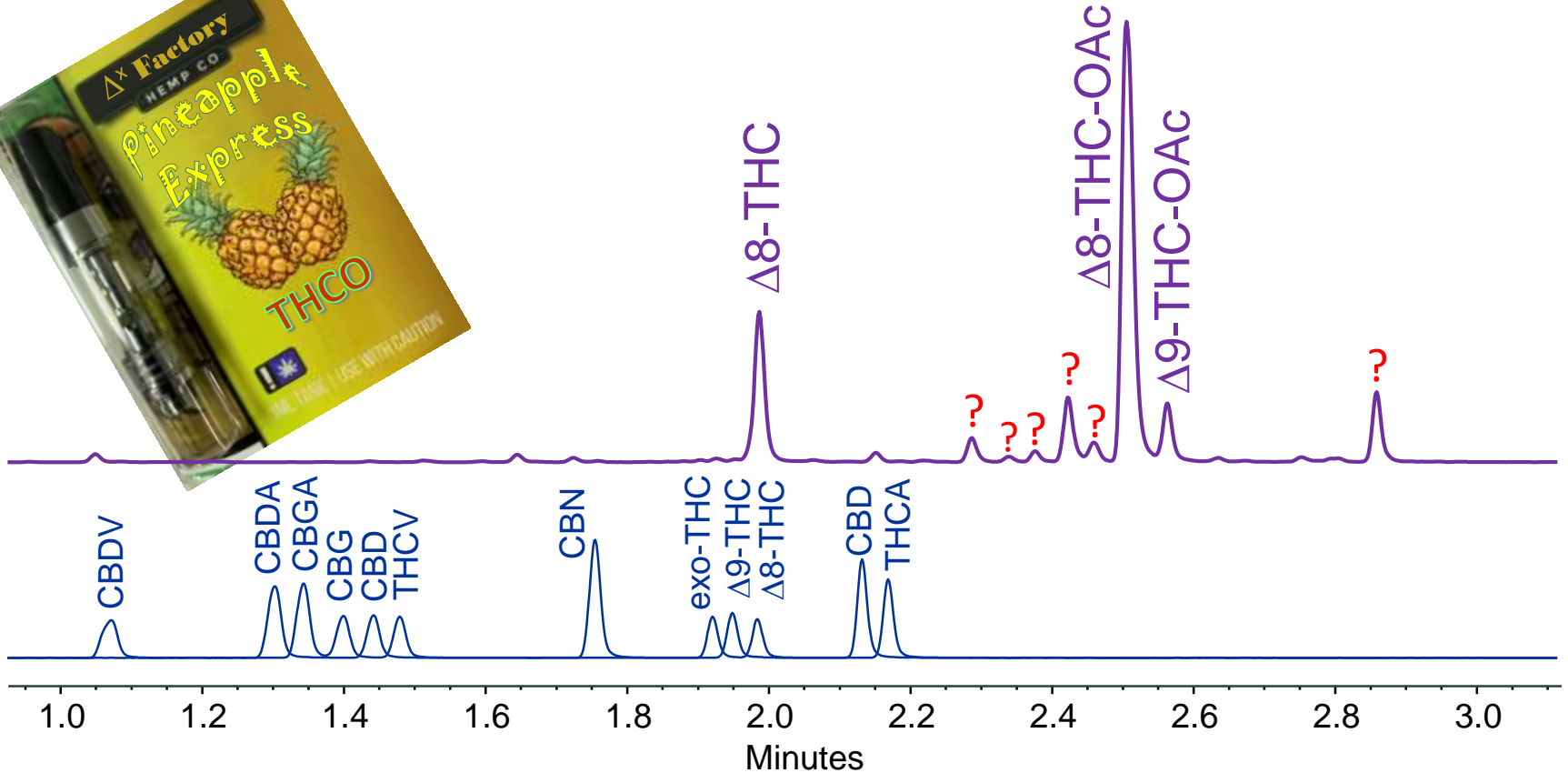
HCC

HHCP

HHCO

HHCPO

THC-O-Acetate Vape



Berry Gelato Vape Cartridge

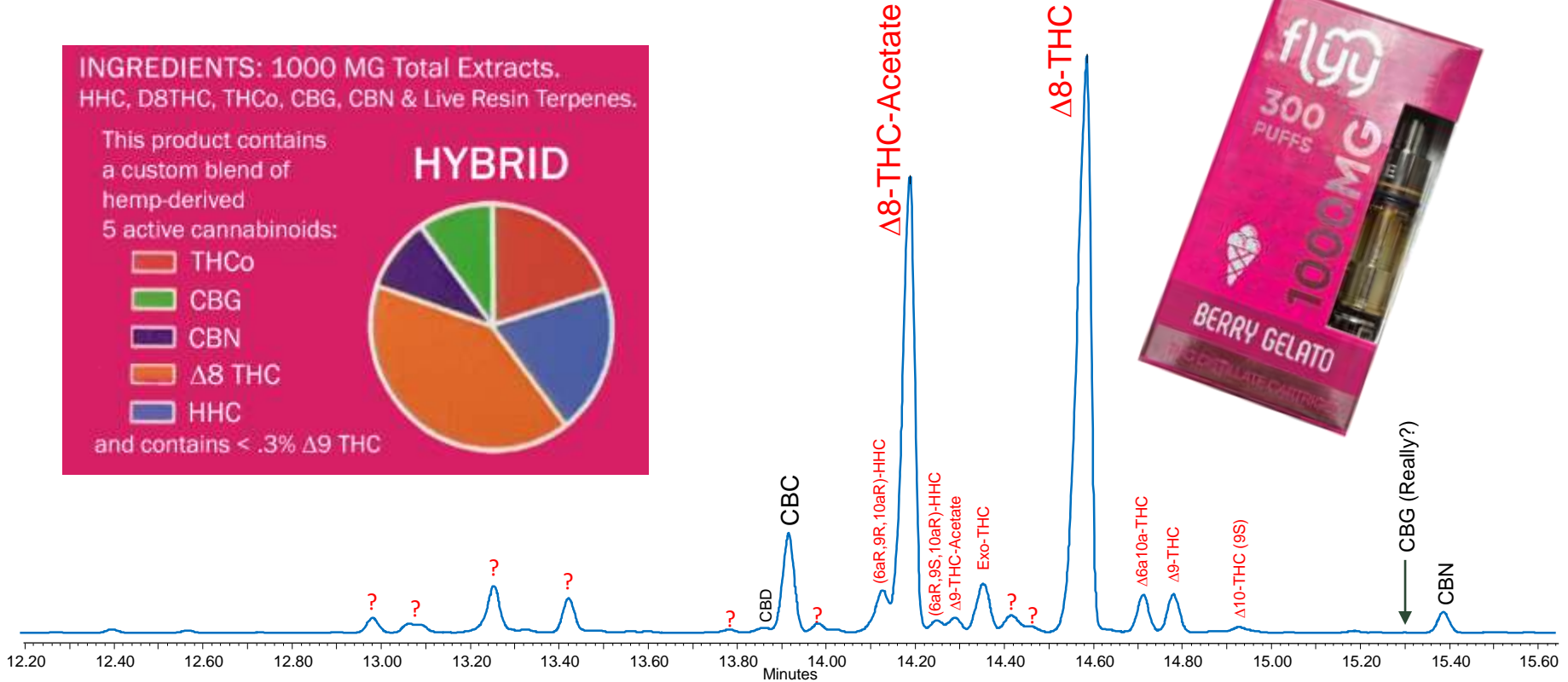
INGREDIENTS: 1000 MG Total Extracts.
HHC, D8THC, THCo, CBG, CBN & Live Resin Terpenes.

This product contains
a custom blend of
hemp-derived
5 active cannabinoids:

- THCo
- CBG
- CBN
- $\Delta 8$ THC
- HHC

and contains < .3% $\Delta 9$ THC

HYBRID



Science Summary

- Delta-8-THC has demonstrated potential for both therapeutic and recreational products
- While $\Delta 8$ -THC is found in nature, natural sources are impractical, making synthetic preparation the most economical source
- Currently, most $\Delta 8$ -THC products are synthesized in an unregulated environment, giving rise to multiple contaminants of concern
- Many of these contaminants have not yet been identified, and most laboratories ignore their presence, making COAs unreliable
- Post-synthesis isolation and purification may be used to produce a clean, uncontaminated $\Delta 8$ product

Mythinformation

- 1. (neologism) False information, when seen as having its own mythology or being believed in like a myth would be*
- 2. (neologism) Data or details not founded on factual evidence, intended to exploit the ignorance of others*

$\Delta 8\text{-THC} = \Delta 8\text{-THC}$

“we need to start classifying cannabinoids agnostic to source as the body processes them the same without cause or concern of source”

$\Delta 8\text{-THC}$ is $\Delta 8\text{-THC}$ regardless of whether it is natural or synthetic

WRONG!!!!!!

$\Delta 8$ -THC as an Agricultural Product

“Delta-8-THC, as a Hemp Derivative, under the US Farm Bill, is an agricultural product and should be regulated as such”

WRONG!!!!!!

With the addition of solvents, acids and other reagents, we leave the realm of agriculture and enter into the world of synthetic organic chemistry, no different from a pharmaceutical environment.

Organic Delta-8-THC? Not a Thing



Synthetic Products are Not Widely Available



Hemp Gummies Delta Premium 500 Milligram High Potency - 25 Per Fruity Gummy - Stress Relief, Inflammation, Pain, Restful Sleep

Brand: Generic

★★★★★ - 379 ratings | 17 answered questions

Price: **\$29.95** (\$1.50 / Count)

Coupon Save an extra 15% when you apply this coupon Terms

Get \$150 off. Pay **\$0.00** \$24.95 upon approval for the Amazon Business Card. Terms apply.

Brand	Generic
Item Form	Chewable
Flavor	Hemp
Product Benefits	Stress Relief
Unit Count	20.00 Count
Dosage Form	500-1000
Number of Items	1

About this item

- RELAX- Fight the stresses of the day naturally, and feel the calming and relaxing benefits.
- SLEEP- Fall asleep and stay asleep. No more tossing and turning.
- ANXIETY- Calm an overactive mind and stop the constant worrying
- NAUSEOUS- Prevent and combat the feelings of nauseous and stimulate a healthy appetite
- MADE IN USA- Proudly made and packaged in the USA

- Available on Amzon.com
- No mention of THC
- No mention of $\Delta 8$
- No waring on psychoactivity
- No Age restriction for purchase

Synthetic Products are Not Widely Available

business Deliver to Preferred Milford 01757

delta 8 thc gummies

Departments Get the app Amazon Business Card Prime Early Access Sale Amazon Commercial Vote for Grant Recipients Buy Again Add People Customer Service Savings Hub Gift Cards

EN

Hemp Gummies Delta Premium 500 Milligram High Potency - 25 Per Fruity Gummy - Stress Relief, Inflammation, Pain, Restful Sleep

Brand: Generic

★★★★★ 379 ratings | 17 answered questions

Price: \$29.95 (\$1.50 / count)

Coupon Save an extra 15% when you apply this coupon Terms

Get \$150 off. Pay \$0.00 \$29.95 upon approval for the Amazon Business Card. Terms apply.

Brand: Generic

Item Form: Chewable

- Available on Amzon.com
- No mention of THC
- No mention of $\Delta 8$
- No waring on psychoactivity
- No Age restriction for purchase

nikita paino

★★★★★ Intense

Reviewed in the United States on September 9, 2022

Verified Purchase

This stuff will definitely hit you hard! I thought since I am fairly overweight that one whole one wouldn't be too much but I was wrong! I'll be taking 1/8 of a gummy from now on lol.

Helpful

Report abuse

Consumer Safety

LACK OF EVIDENCE OF HARM



SAFETY

While these synthetic compounds have not yet been studied for safety, the CDC has recorded many adverse events associated with synthetic cannabinoid products

Synthetic Products Are Not Harmful



VIDEO

ADVERTISE

NEWSLETTER SIGNUP

PODCAST



Cultivation

Distribution

Extraction

Manufacturing

New Products

News

Packaging

Processing

VIDEO

Four Dead After Using Synthetic Cannabis Containing Rat Poison

There were a total of 52 cases of people affected with coagulopathy, a bleeding disorder.

By — Ben Munson, Editor, Cannabis Equipment News, Unit 202 Productions, Eric Sorensen

Oct 11, 2022

Four people in Florida died after using synthetic cannabinoids (SCBs) containing brodifacoum, which is typically used as rat poison.

Latest in Video

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Today in Manufacturing Podcast

August 4, 2022



Security Breach: Lessons Learned from DarkSide and the Solar Winds Hack

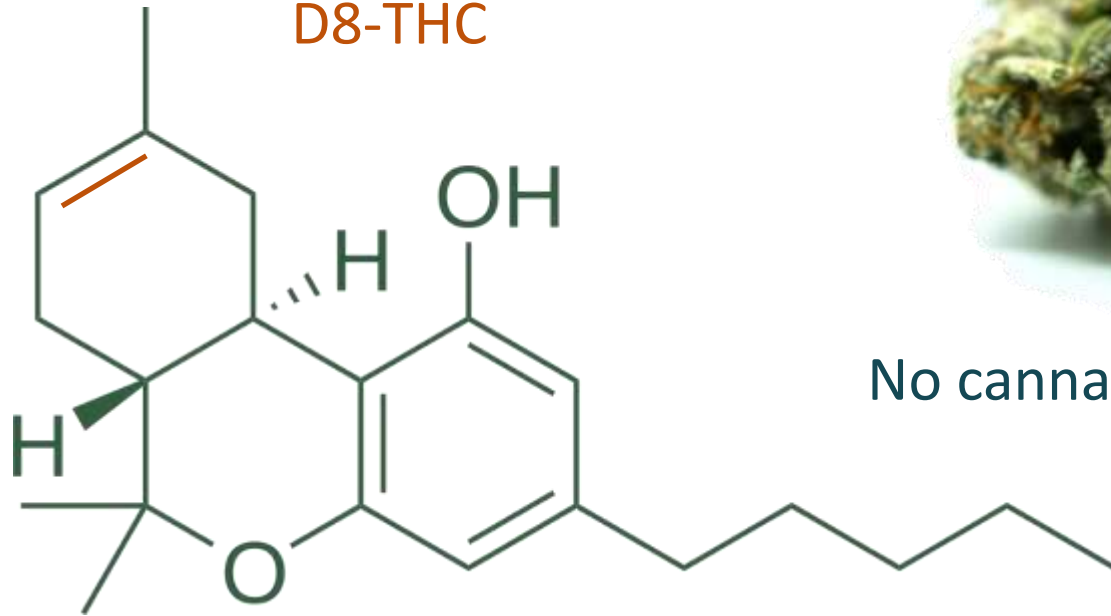
August 26, 2022



Natural Δ^8 -THC Flower

Δ^8 -Tetrahydrocannabinol

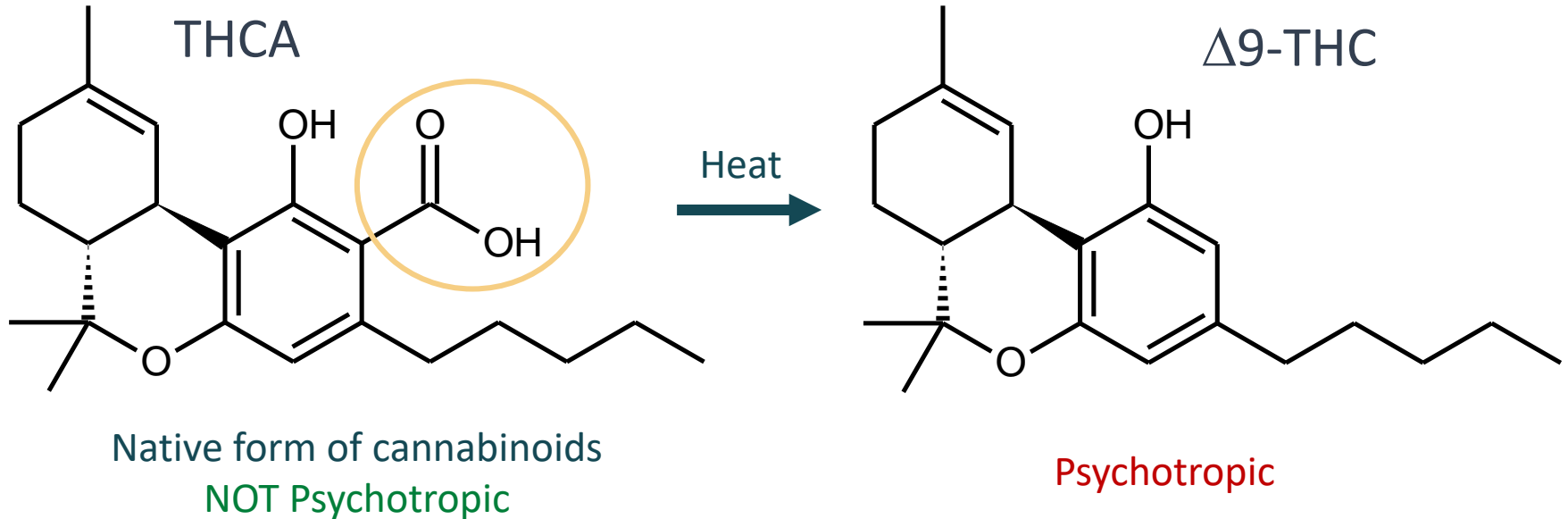
D8-THC



No cannabis genetics produce the Δ^8 -THC isomer

Definition of Hemp

What is decarboxylation?



Definition of Hemp



“Hemp” is defined by the 2018 Farm Bill as “the plant species *Cannabis sativa* L. and any part of that plant, including the seeds thereof and all **derivatives**, extracts, cannabinoids, **isomers**, acids, salts, and salts of isomers, whether growing or not, with a delta-9 tetrahydrocannabinol concentration of not more than 0.3 percent on a dry weight basis.”

Definition of Hemp



The 2018 Farm Bill mandates testing using **post-decarboxylation or other similarly reliable methods** where the total THC concentration level considers the potential to convert delta-9-tetrahydrocannabinolic acid (THC-A) into delta-9-THC, on a dry weight basis.

What does this mean?

Post-Decarboxylation Methods

(1) Analysis is performed using Gas Chromatography (GC)

- Injection of sample into hot GC inlet decarboxylates THCA to neutral $\Delta 9$ -THC prior to analysis, such that measured value represents total possible $\Delta 9$ -THC

(2) Sample is heated prior to analysis by Liquid Chromatography (LC)

- Heating sample decarboxylates THCA to neutral $\Delta 9$ -THC prior to analysis by LC, which is performed at moderate temperatures

(3) Analysis is performed using Liquid Chromatography (LC)

- Results provide separate quantitation of THCA and THC
- Total THC is calculated by a mathematical, theoretical decarboxylation

$$\text{Total THC} = (0.877 \times \text{THCA}) + \text{THC}$$

This last method is used most widely and is accepted by all Federal and State regulatory bodies

High THCA Hemp Flower



Δ 9-THC = 0.24% (by weight)

THCA = 32.8% (by weight)

**THCA HEMP
FLOWER
=
BLACK
MARKET
MARIJUANA**

Inclusion of Synthetics in Current Regulation

- Current State by State cannabis regulations pertain to agricultural products and processes.
- Synthetic organic chemistry utilizes a significantly different skill set – Not typically found in Cannabis Operations.
- Regulatory discussions on inclusion of synthetics in a regulatory program typically include the statement:

“We’ll just have laboratories test for the contaminants”



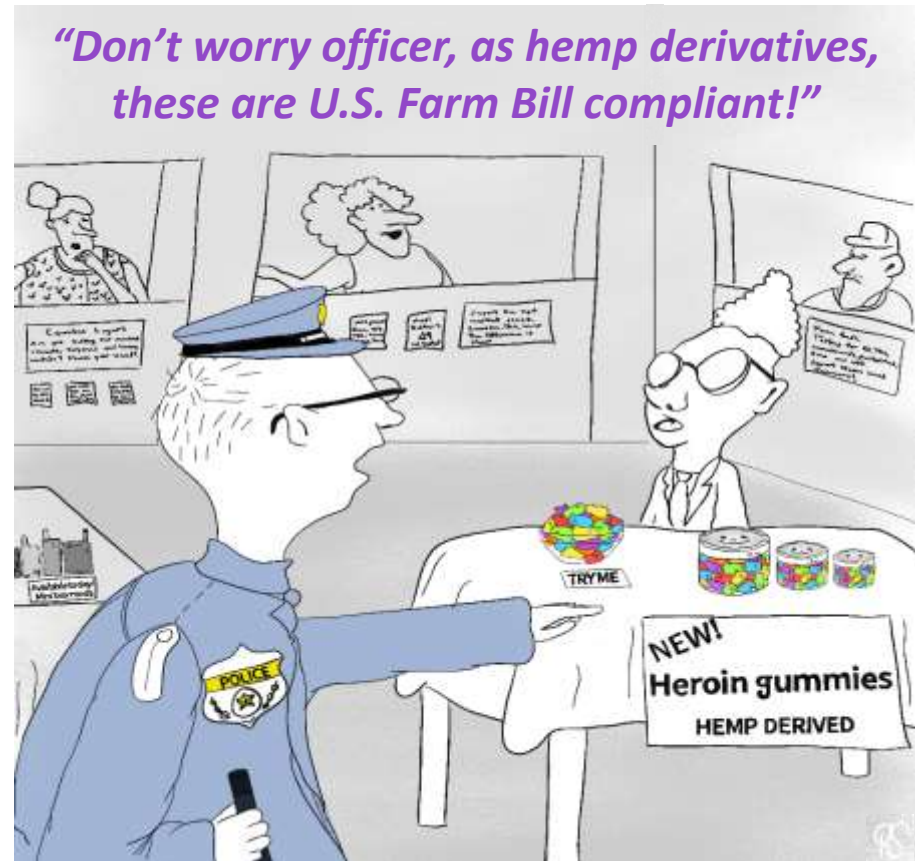
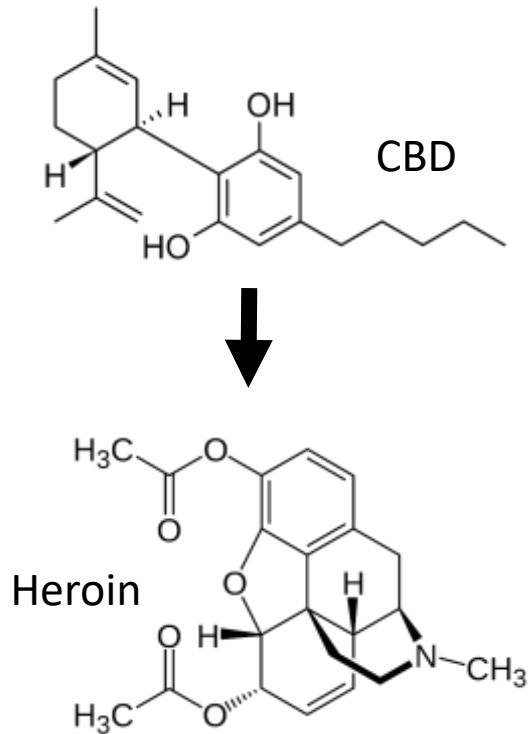
Inclusion of Synthetics in Current Regulation

Several problems with that statement:

- Many contaminants have not yet been identified
 - Their structures and toxicity are unknown
- Every recipe (SOP) will have a different contaminant profile
 - Which contaminants do the labs test for?
- Methods do not yet exist to test effectively for many of these contaminants
 - Typical lab instrumentation often cannot resolve contaminants
 - Specialized instrumentation is prohibitively expensive
- Certified reference standards do not exist for those standards



Legal Hemp Derivatives





FOCUS

Foundation of
Cannabis Unified Standards

Questions?

Chris.Hudalla@ProVerdeLabs.com

Lezli@FOCUSstandards.org

Conversion Supply Chain Metrics

- 1) Buy Winterized Hemp extract or CBD isolate at \$250/kg or less
- 2) Convert to D8, THCO, HHC, THCV, distillate at values ranging from \$500/kg to >\$2,000/kg wholesale
- 3) Add value by formulating into natural or flavored oils for manufacture into vape cartridges, gummies, softgels, edibles or smokables at significant lift
- 4) At retail, 1 kg of D8 Vape Oil cartridges retails for >\$4,000
- 5) One large D8 manufacturer has the capacity to make >400,000kg of Vape oil per year.....and they are just learning how to most efficiently run their equipment.