

# MEDICAL MARIJUANA: WHAT DOES THE EVIDENCE SAY?

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# A Brief History of Marijuana in the United States

1600's to present



**1619, the Virginia Assembly passed  
legislation requiring every farmer to grow  
hemp that could be exchanged for legal  
tender in Pennsylvania, Virginia and  
Maryland**

**`1600's-1890's Domestic Hemp Production  
Mandate**





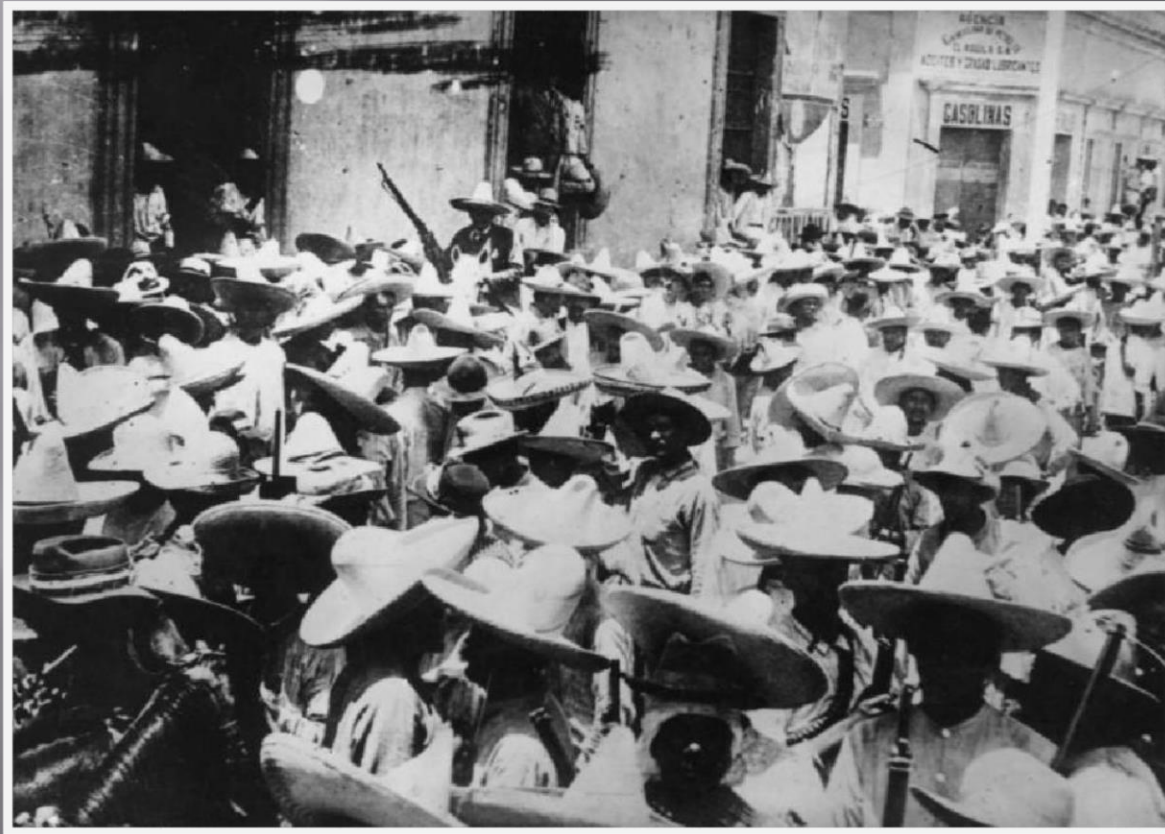
**1906: The Federal Pure Food and Drug Act  
Required labeling for any Cannabis  
Contained in Over-the-counter Remedies**





## 1910-1911: The Mexican Revolution

Mexican Immigrants introduced recreational marijuana to Americans



## 1930: Creation of the Federal Bureau of Narcotics (predecessor to DEA)

Harry Aslinger was the first commissioner.  
Undertook multiple efforts to make marijuana illegal  
in all states.



## 1936: Reefer Madness

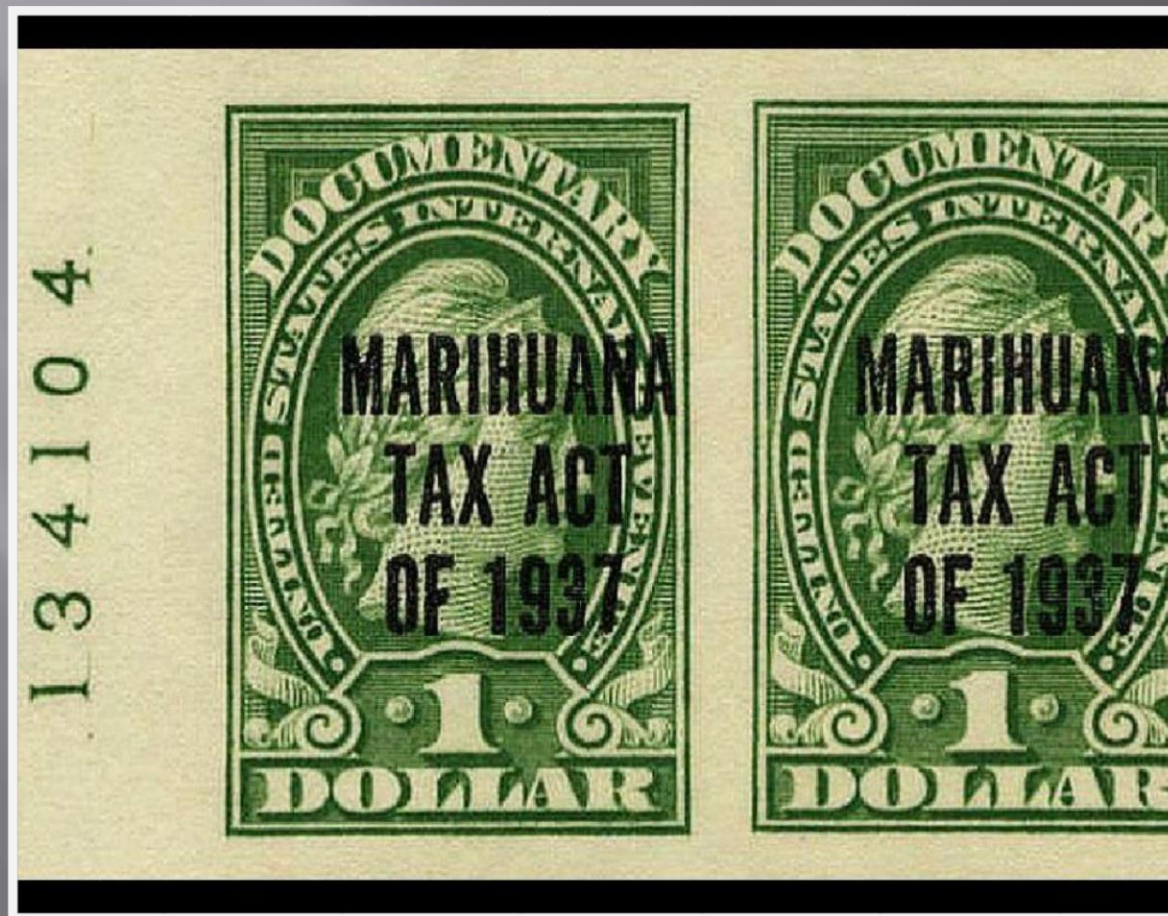
Infamous anti-marijuana propaganda film was released





## 1937: Marijuana Tax Act

MTA adopted the “prohibition through taxation” method of de facto prohibition.



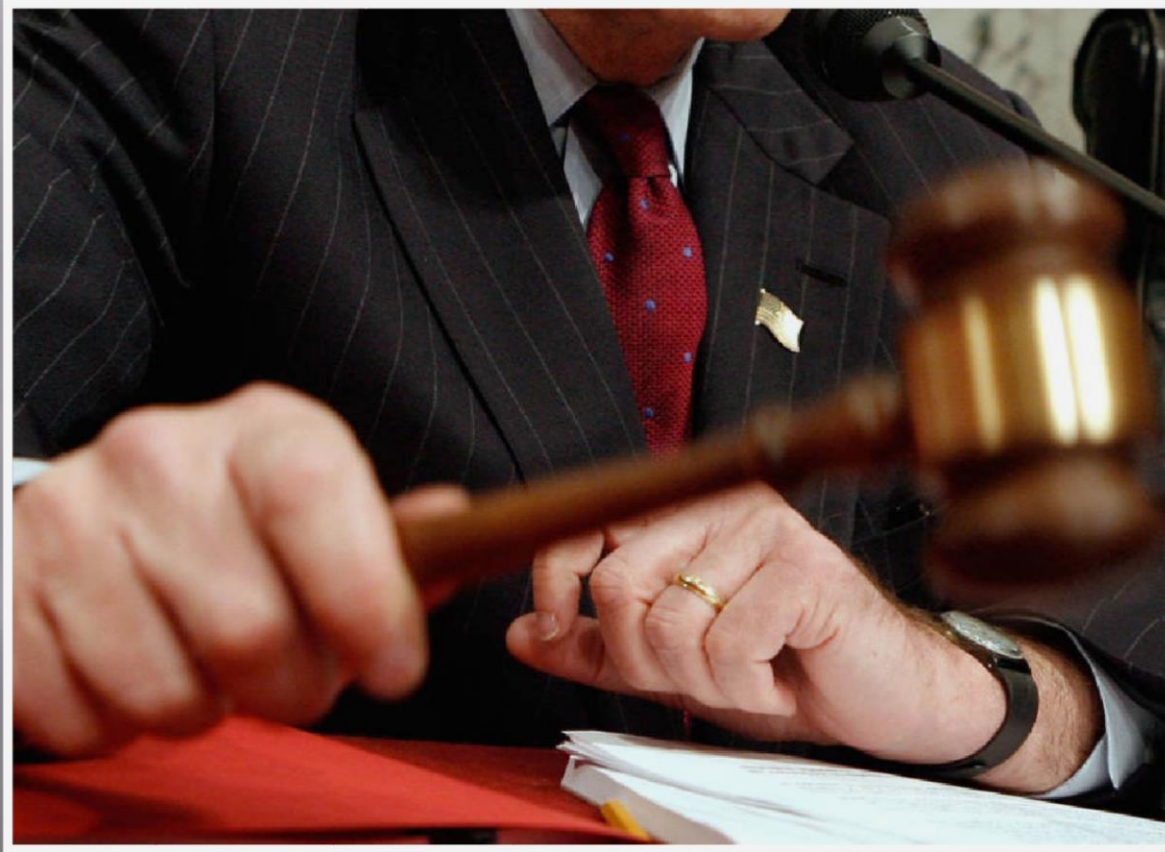
**Even after congress cracked down on  
marijuana in 1937, farmers were encouraged  
to grow the crop for rope, sails and  
parachutes during WWII**

A film released in 1942 by the U.S. Dept. of  
Agriculture



**1956: The Boggs Act and Narcotics Control Act set mandatory minimum penalties for illegal drugs including marijuana.**

1<sup>st</sup> offense marijuana possession—minimum sentence of 2–10 years with fine up to \$20,000





## 1960's Counter culture marijuana comeback

“Hippie, free spirit” culture. Attitudes began to change at policy level as well



## **1970: Mandatory minimum sentencing repealed for drug offenses**

Comprehensive Drug Abuse Prevention and control  
Act of 1970 repealed almost all mandatory penalties



**1970: NORML is formed by Keith Stroup with  
a \$5,000 grant from Playboy**

National Organization for the Reform of Marijuana  
Laws (NORML)





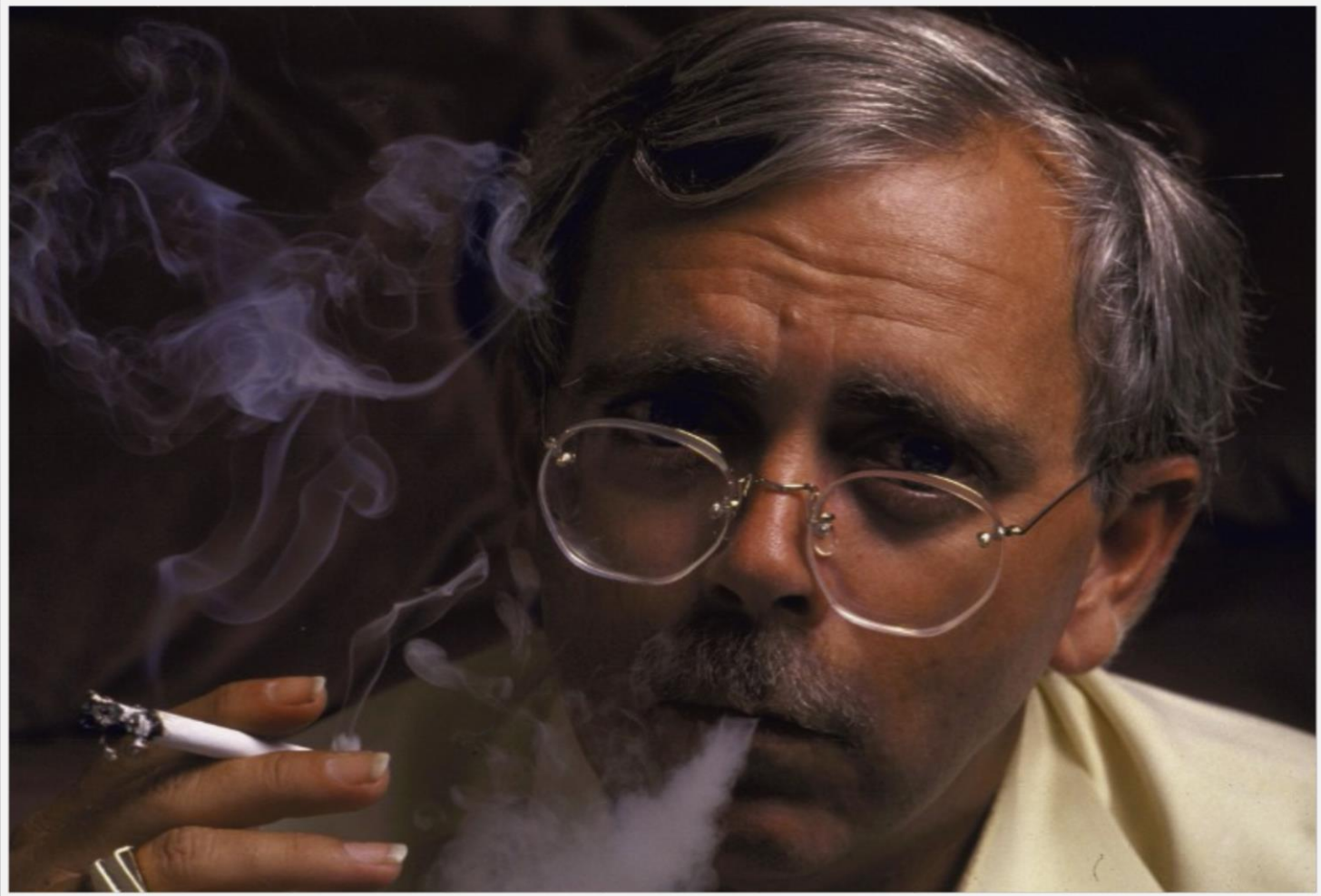
## **1973: Drug enforcement Agency is created**

President Nixon created the DEA by an Executive Order to “combat an all-out global war on the drug menace”.



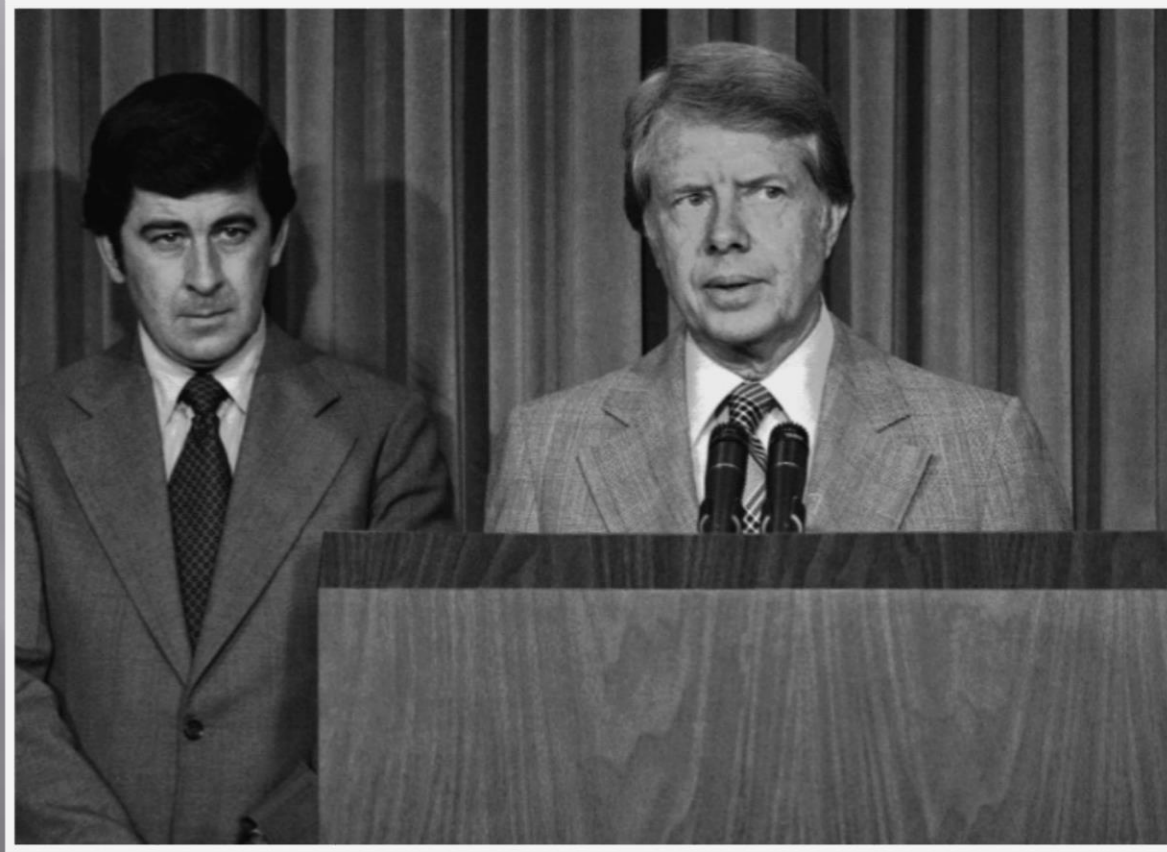
**1976: Robert Randall , first legal medical  
marijuana patient in modern America after  
winning landmark case**

Sued government after all known glaucoma drugs failed to halt the  
loss of eyesight.



## 1977: Decriminalization catches on

1977, President Carter pushed for marijuana decriminalization. The Senate voted to decriminalize





## 1980-1990” Zero tolerance .

Nancy Reagan “Just Say No” anti drug campaign.

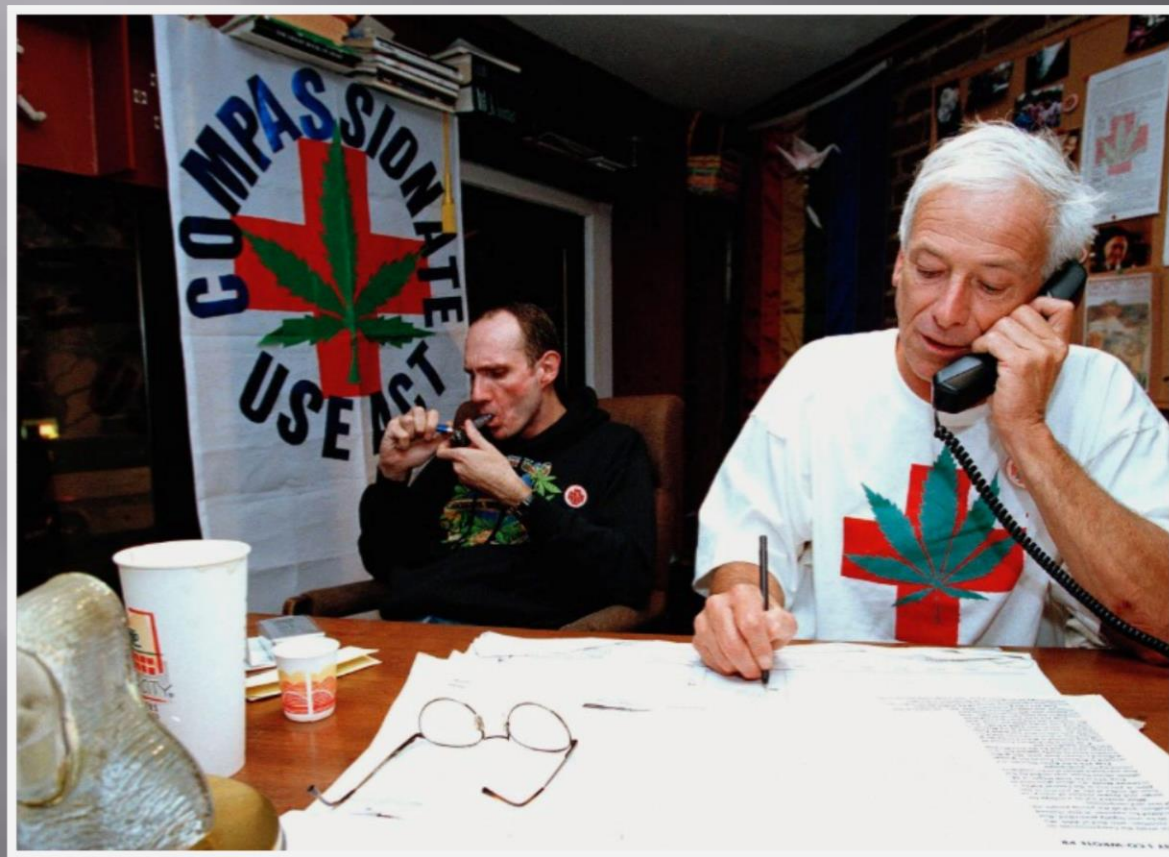


## 1989: George H. Bush

Escalates “War on Drugs”, we need more jails, more prisons and more courts and more prosecutors”.



1996: November 1996, Proposition 215  
approved by voters allowing medical  
marijuana in California





## 1998-2001: Multiple states follow, legalizing medical marijuana

Alaska, Oregon, Washington and Arizona



2013: “Charlotte’s Web”. Charlotte Figi 6 y/o with 300 grand mal seizures/week (Darvet Syndrome), treated with Hemp Extract (high in Cannabidiol)





## 2014-2016: Marijuana reform sweeps the country

As of December 2016, 28 states and D. of C. have legalized medical cannabis. 8 states and D.C. have legalized recreational marijuana. Still illegal at the federal level.





# Cannabis

- ▣ Cannabis Sativa- Known as Marijuana.
  - Subspecies that has psychoactive properties
- ▣ Cannabis Sativa L.- A subspecies known as hemp.
  - Nonpsychoactive form, used in manufacturing products such as oil, cloth and fuel.
  - The L is in honor of botanist Carl Linnaeus

# Cannabis Sativa

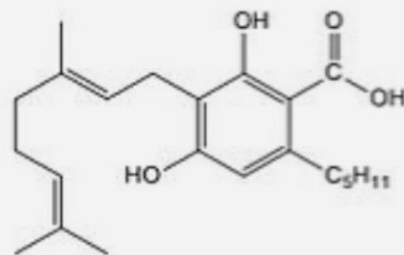
- ▣ Most popular illicit drug in the United States
- ▣ 22.2 million American is age is 12 an older reported using cannabis in the past 30 days
- ▣ 90% of adult cannabis users in the United States said the primary use was recreational
- ▣ 10% report using solely for medical purposes
- ▣ 36% reported mixed medical in recreational use

# Cannabis Sativa

- ▣ There are at least 113 active cannabinoids identified in cannabis sativa.
- ▣ Cannabidiol (CBD) is a major phytocannabinoid, accounting for up to 40% of the plant's extract.
  - Low psychoactivity (Hippies' Disappointment)
- ▣ Delta (9) tetrahydrocannabinol (THC)
- ▣ Endocannabinoid receptors
  - CB1- THC
  - CB2- CBD

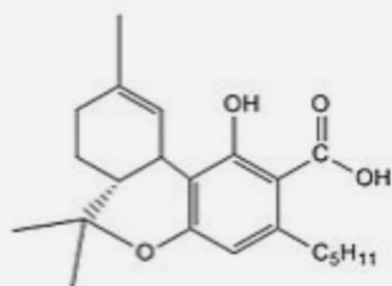


cannabigerolic-acid (CBGA)

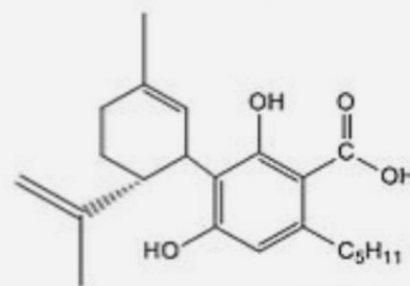


THCA Synthase

CBDA Synthase



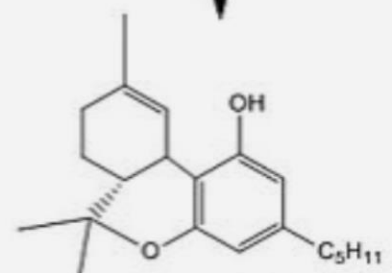
tetrahydrocannabinolic acid (THCA)



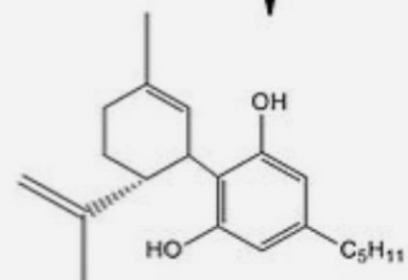
cannabidiolic acid (CBDA)

O<sub>2</sub> (decarboxylation)

-CO<sub>2</sub> (decarboxylation)



tetrahydrocannabinol (THC)



cannabidiol (CBD)

[illegible]

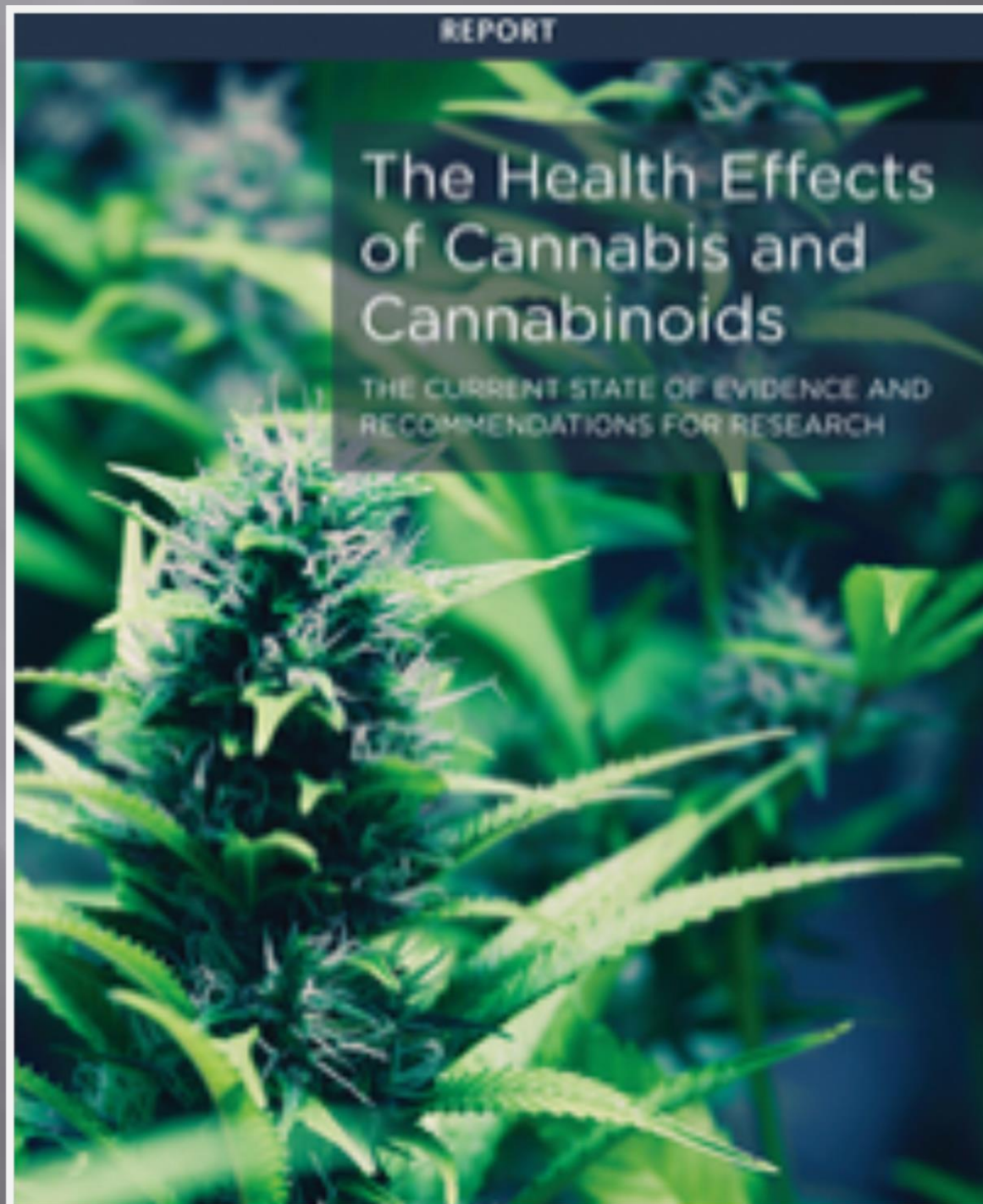




REPORT

# The Health Effects of Cannabis and Cannabinoids

THE CURRENT STATE OF EVIDENCE AND  
RECOMMENDATIONS FOR RESEARCH



# The National Academies of Sciences, Engineering, Medicine

- ▣ An expert committee carried out a study and wrote a report after reviewing 10,000 scientific abstracts regarding health effects of recreational and therapeutic use of cannabis.
- ▣ Reached 100 conclusions.
- ▣ Proposed ways to expand and improve the quality of cannabis research and enhance data collection efforts.

The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research. January 2017

# Standardized Weight of Evidence

- ▣ 5 levels of evidence
  - -CONCLUSIVE
  - -SUBSTANTIAL
  - -MODERATE
  - -LIMITED
  - -NO or INSUFFICIENT



# Conclusive/Substantial Evidence of Effectiveness

- ▣ For the treatment of chronic pain in adults.
- ▣ Antiemetic's in the treatment of chemotherapy-induced nausea and vomiting.
- ▣ For improving patient-reported multiple sclerosis symptoms.

# Moderate Evidence for Effectiveness

- ▣ Improving short-term sleep outcomes in individuals with sleep disturbance associated with obstructive sleep apnea syndrome, Fibromyalgia, chronic pain, and multiple sclerosis.

# Limited Evidence of Effectiveness for

- ▣ increasing appetite and decreasing weight loss associated with HIV/AIDS
- ▣ improving clinician measured multiple sclerosis spasticity symptoms
- ▣ improving symptoms of Tourette syndrome
- ▣ improving anxiety symptoms, as assessed by a public speaking test, in individuals with social anxiety disorders



# limited evidence of a statistical association between cannabinoids and:

- ▣ Better outcomes (mortality, disability) after a traumatic brain injury or intracranial hemorrhage.

# Limited evidence that cannabis or cannabinoids are ineffective for:

- ▣ improving symptoms associated with dementia.
- ▣ improving intra-ocular pressure associated with glaucoma
- ▣ reducing depressive symptoms in individuals with chronic pain or multiple sclerosis

There is no evidence or insufficient evidence to support or refute a conclusion the cannabis or cannabinoids on effective treatment for the following:



# No or insufficient evidence:

- ▣ Cancers including glioma
- ▣ Cancer associated anorexia cachexia syndrome and anorexia nervosa
- ▣ Symptoms of irritable bowel syndrome
- ▣ Epilepsy
- ▣ Spasticity in patients with paralysis due to spinal cord injury
- ▣ Symptoms associated with amyotrophic lateral sclerosis

# Conclusions for: Injury and Death

- ▣ There is substantial evidence of statistical association between cannabis use and increased risk of motor vehicle crashes.
- ▣ There is moderate evidence of statistical association between cannabis use and increased risk of overdose injuries, including respiratory distress, among pediatric population in the United States where cannabis is legal.

# Conclusions for: Prenatal, Perinatal, and Neonatal Exposure

- ▣ There is substantial evidence of an association between maternal cannabis smoking and lower birth weight of the off spring
- ▣ There is limited evidence of association between maternal cannabis smoking and pregnancy complications for the mother and admission of the infant to the neonatal intensive care unit
- ▣ There is insufficient evidence regarding later outcomes in the off spring ( SIDS, cognitive achievement or later substance use)



# No or insufficient evidence:

- ▣ Chorea and certain neuropsychiatric symptoms associated with Huntington's disease
- ▣ Dystonia
- ▣ Achieving abstinence in the use of addictive substances
- ▣ Mental health outcomes in individuals with schizophrenia or schizophreniform psychosis

# Conclusions for: Mental Health

- ▣ There is substantial evidence of a statistical association between cannabis use and the development of schizophrenia or other psychoses, with the highest risk come on the most frequent users.

# Conclusions for: Mental health

- ▣ There is moderate evidence of a statistical association between cannabis use and:
  - better cognitive performance among individuals with psychotic disorder
  - increased incidence of suicidal ideation and suicide attempts with a higher incidence among frequent users
  - increased incidence of suicide completion
  - increased incidence of social anxiety disorder with regular cannabis use

# Conclusions for: Mental health

- ▣ There is limited evidence of a statistical association between cannabis use and:
  - The likelihood of developing bipolar disorder, particularly among regular or daily users
  - Increased symptoms of anxiety ( near daily cannabis use)
  - Increased severity of posttraumatic stress disorder symptoms among individuals with posttraumatic stress disorder



# Conclusions for: Psychosocial

- ▣ There is moderate evidence of statistical association will between cannabis use and impairment in the cognitive domains of learning, memory, and attention (acute).
- ▣ There is limited evidence of statistical association between cannabis use and:
  - Impaired academic achievement and education outcomes
  - Increased rates of unemployment and/or low income
  - Impaired social functioning or engagement in developmentally appropriate social rolls

# Conclusion for: Abuse of Other Substances

- ▣ There is moderate evidence of a statistical association between cannabis use and:
  - The development of substance dependence and or substance abuse disorder for substances including tobacco, alcohol, and other illicit drugs
- ▣ There is limited evidence of a statistical association between cannabis use and:
  - The initiation of tobacco use
  - Changes in the rates in use pattern of other licit and illicit substances

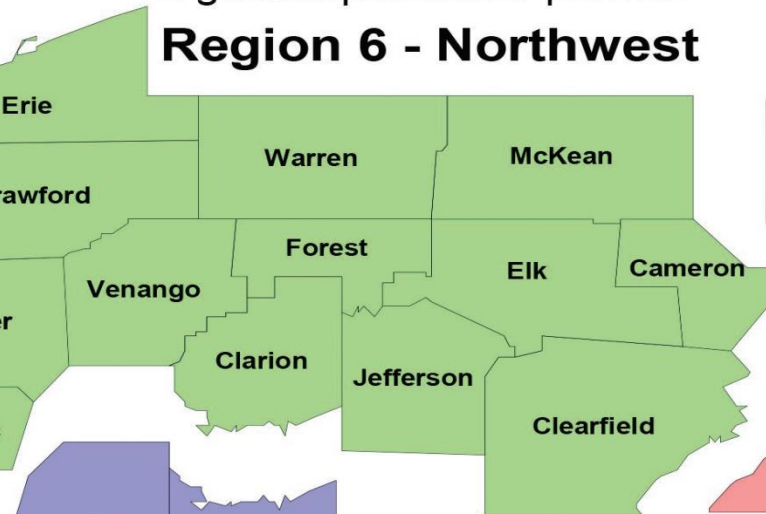
# Act 16 of 2016- The Medical Marijuana Program Pennsylvania

- ▣ Under act 16 the term medical marijuana refers to marijuana obtained for a certified medical use by Pennsylvania resident with a series medical condition and is limited in Pennsylvania to the following forms;
  - Pill
  - Oral
  - Topical forms, including Gel, creams or ointments
  - A for medically appropriate for administration by vaporization or nebulization, excluding dry leave or plant form
  - Tincture
  - Liquid

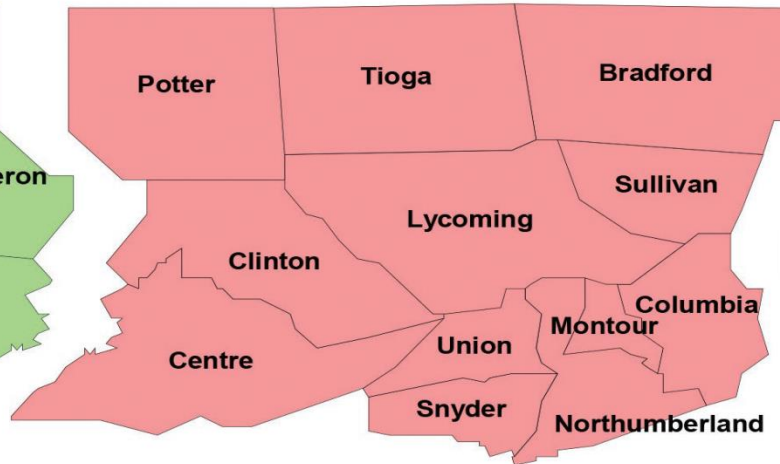
# Pennsylvania Department of Health

## Medical Marijuana Regions

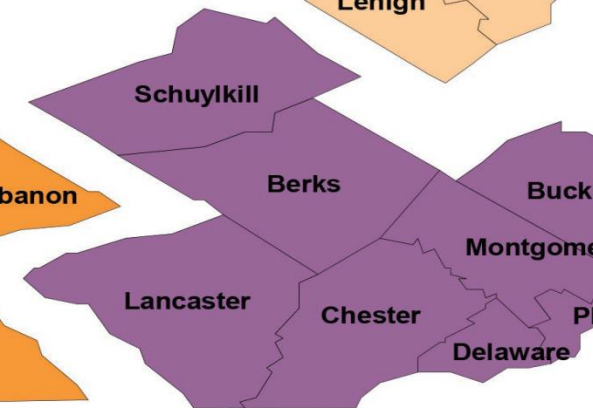
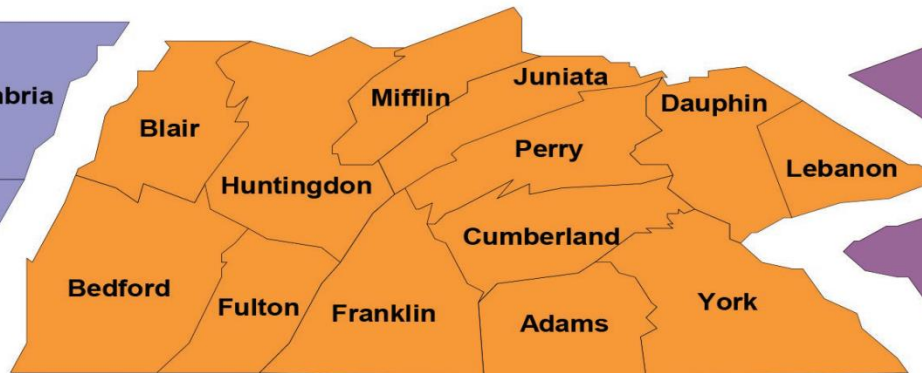
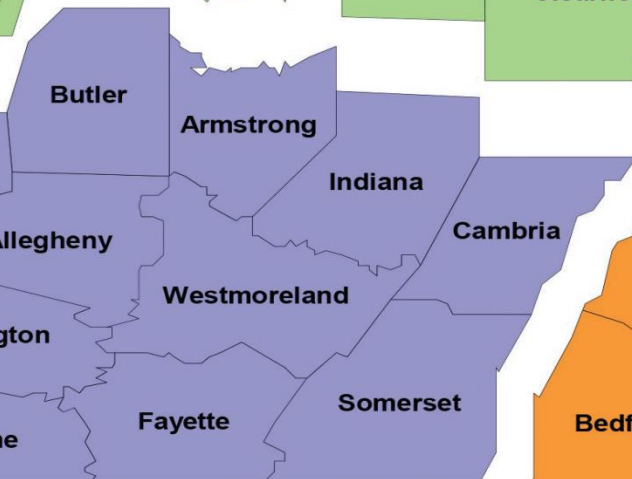
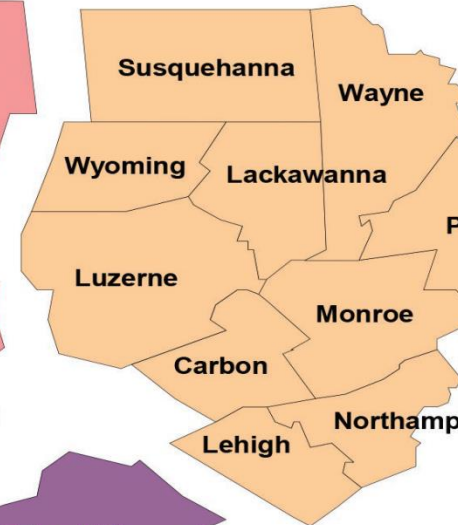
2 dispensary permits  
2 grower/processor permits  
**Region 6 - Northwest**



2 dispensary permits  
2 grower/processor permits  
**Region 4 - Northcentral**



4 dispensary permits  
2 grower/processor permits  
**Region 2 - Northeast**



**Region 5 - Southwest**  
2 dispensary permits  
2 grower/processor permits

**Region 3 - Southcentral**  
4 dispensary permits  
2 grower/processor permits

**Region 1 - Southeast**  
10 dispensary permits  
2 grower/processor permits



# “Serious Medical Conditions”

- ▣ Severe chronic or intractable pain of neuropathic origin or severe chronic or intractable pain in which conventional therapeutic intervention in opiate therapy is contraindicated or ineffective.

# What is a “Serious Medical Condition” Under the Act?

- ▣ Amyotrophic lateral sclerosis
- ▣ Autism
- ▣ Cancer
- ▣ Crohn’s disease
- ▣ Damage to the nervous tissue of the spinal cord with objective neurological indication of intractable spasticity
- ▣ Epilepsy
- ▣ Glaucoma

# “Serious Medical Conditions”

- ▣ HIV/AIDS
- ▣ Huntington's disease
- ▣ Inflammatory bowel syndrome
- ▣ Intractable seizure
- ▣ Multiple sclerosis
- ▣ Neuropathies
- ▣ Parkinson's disease
- ▣ Posttraumatic stress disorder
- ▣ Sickle cell anemia

# Drugs Currently Available

- ▣ Two products approved and on the market:
  - Nabilone (Cesamet)- a THC synthetic analogue
    - ▣ Approved to treat chemotherapy induced nausea
    - ▣ Usually taken 1-2 hours before chemotherapy
  - Dronabinol (Marinol)- a synthetic THC
    - ▣ Approved for chemotherapy-induced nausea
    - ▣ appetite stimulant for AIDS patient's
- ▣ “Charlotte’s Web” Hemp Extract-marketed as a dietary supplement with claim efficacy to treat Dravet syndrome.



# Non FDA Approved Medications

## ▣ Sativex

- An oromucosal spray formulated from extract of cannabis sativa plant.
- Principal cannabinoids are THC and CBD
- Used to treat MS spasticity in 16 country's outside the United States
- Regulatory filing ongoing in 12 other countries principally in the Middle East and Latin America

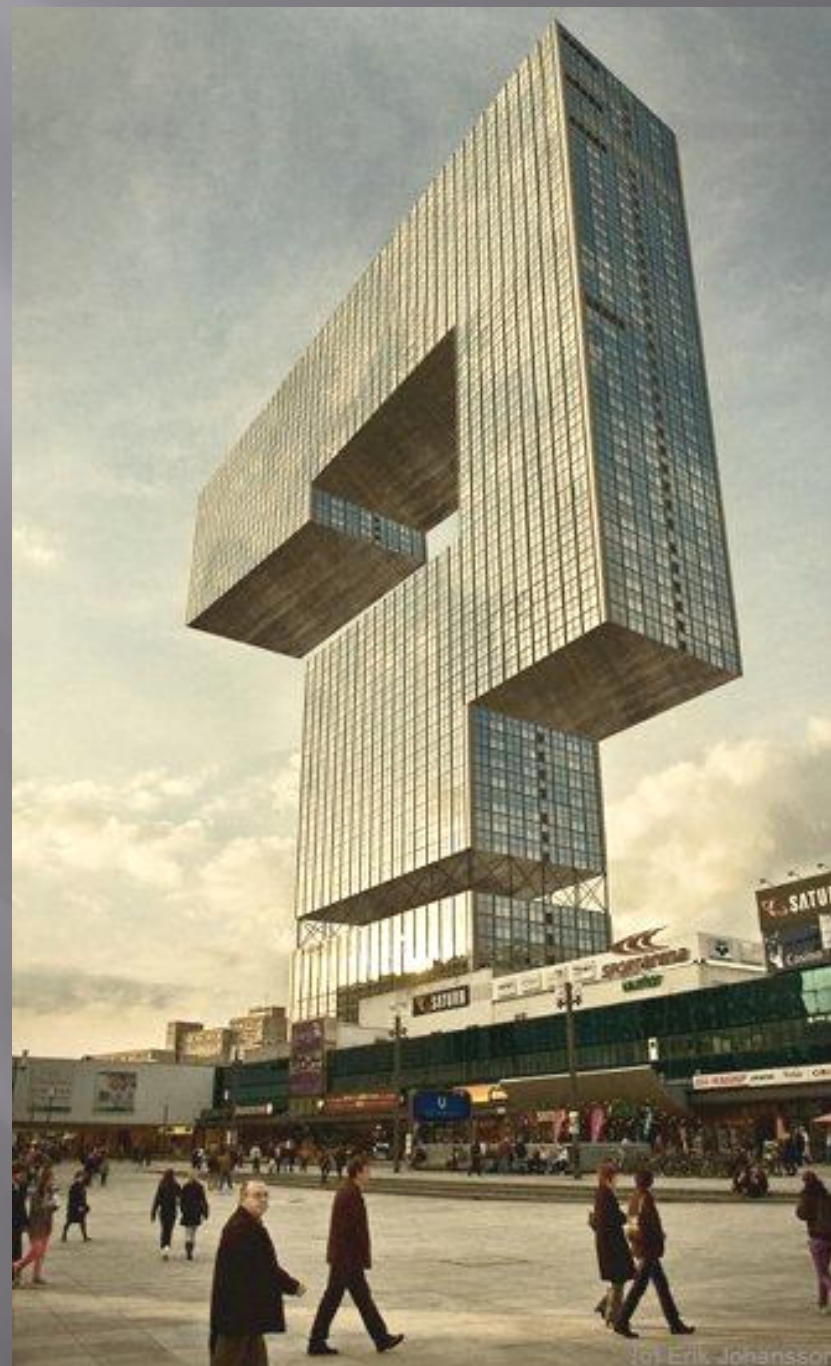
# Non FDA Approved Medications

## ▣ Epidiolex

- Currently in phase 3 clinical trials in the United States
- A proprietary oral solution of pure plant derived cannabidiol (CBD)
- Developed to treat severe, warfarin, early onset, treatment resistant epilepsy syndromes including Dravet syndrome, Lennox-Gastaut syndrome, Tuberous Sclerosis Complex and Infantile Spasms

# Summary of Statement of Task

- ▣ Develop a comprehensive, in-depth review of existing evidence regarding the health effects, both harms and benefits, of cannabis and cannabinoid use.
- ▣ Makes short and long-term recommendations regarding a research agenda to identify the most critical research questions and advance the cannabis and cannabinoid research agenda



[6] Erik Johansson