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Attached is an overview of what cannabis is, what it does, its legal and scientific history, and the current science on its use. The content is drawn from multiple sources but any errors are my responsibility alone.

Cannabis Basics
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Cannabis, Marijuana, and Hemp

Cannabis is a genus of plants which historically had three species — sativa, indica, and ruderalis — although modern science has rejected those morphological (i.e. appearance-based) categorizations in favor of **chemovars**, or categorizations based on the chemical output of the plant. *See* page 12. "Marijuana" once a slang term is now a legal term for cultivars (less formally known as strains)[1] of the Cannabis genus with THC content greater than 0.3% by dry weight, while "hemp" describes cannabis with less than 0.3% THC. Cannabis contains a cornucopia of medicinal molecules and has been described as "the plant of 1001 molecules." Cannabis is dioecious, meaning there are sexually distinct male and female plants.

"**Marihuana**" is an anglicized spelling from the Mexican slang "**marijuana.**" This term is often used to indicate cultivars grown for higher cannabinoid content, including the main euphoric and psychoactive cannabinoid, delta-9 tetrahydrocannabinol, commonly known as THC (although the plant produces many tetrahydrocannabinols). These cultivars are grown for medical or adult use. Federal and Texas penal statutes use the anglicized spelling "marihuana." The term may also be used for the parts of the plant that contain high concentrations of cannabinoids, namely the flowers and to a lesser extent the leaves.

Hemp is a legal term indicating a very low THC-content cultivars (non-euphoric and psychoactive) grown for nutrition, fiber, oil, paper, and a variety of other purposes including medicinal with CBD- or CBG-rich cultivars, legally (but arbitrarily) defined as less than 0.3% THC content per dry weight as explained in more detail below. "Hemp" is currently used to describe a wide variety of products derived from cannabis many of which are intoxicating.

Marijuana, hemp, and cannabis are all the same plant, but the medicinal and psychoactive effects vary by variety or cultivar, growing conditions, timing of harvest, and how the resulting material is both prepared and consumed. While "marijuana" is a non-scientific, legal term, this paper will use it to indicate high-THC cultivars of cannabis when necessary to avoid confusion.

The Cannabis plant produces a resin containing **cannabinoids** (a group of compounds that are bioactive through the body particularly the central nervous and immune systems), **terpenes** (a group of strong-smelling compounds found in many plants also known as essential oils), and **flavonoids** (a group of substances also found in many plants with antioxidant effects). Because cannabinoid receptors, unlike opioid receptors, are not located in the brainstem area controlling respiration, **lethal overdoses from cannabis do not occur**.

The highest concentration of cannabinoids and resin occur in the flowers of the plant. Consequently, cultivators of cannabis for medicinal purposes (or adult use) only cultivate female plants and avoid any contact with male plants or pollen (such as from hemp strains). This concern for cross-pollination is so great that Pueblo County, Colorado, established hemp growing zones in 2015 creating five-mile buffers to protect marijuana grows.[2] For similar reasons, marijuana is

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[1] **Strains** (more properly cultivars) are genetic variations of cannabis exhibiting differing properties including the amounts and ratios of cannabinoids and terpenes.

[2] Michelle Miguel, *Pueblo County Establishes Zoning Regulations for Hemp Grow*s, Mar. 18, 2015, https://www.krdo.com/news/local-news/pueblo-county-establishes-zoning-regulations-for-hemp-grows/35138867.

often grown indoors whether in greenhouses or completely contained and climate-controlled structures where hemp is most often grown outdoors.

The **legal line between hemp and marijuana** as stated in the Farm Bill and Texas statute is:

> . . . the plant Cannabis sativa L. and any part of that plant, including the seeds of the plant 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.

TEX. AGRIC. CODE § 121.001 (emphasis added); *see also* 7 U.S.C. § 1639o(1). Three things about this definition that are not helpful:

1. While there is **a natural break in the concentration of THC** between low- and high-THC cultivars of cannabis, that concentration **is closer to 1%**. Toth, Jacob A. et al., *Development and validation of genetic markers for sex and cannabinoid chemotype in* Cannabis sativa *L.*, GCB BIOENERGY 2020:00:1-10. (See graph from Toth Fig. 5 below.)

2. **Cannabis contains many forms of tetrahydrocannabinols, not just delta-9**. In fact, THCA is what naturally occurs in marijuana in large quantities but converts to delta-9 when heated through a process called decarboxylation. By including all cannabinoids but delta-9 the definition allows a wide variety of cannabinoids — including many that are intoxicating — to be sold as "hemp."

3. **This description was never meant to apply to anything but plant material given the "dry weight" clarification**. However, the definition is routinely applied to cannabis products such as gummies or beverages which have no readily achievable dry weight.

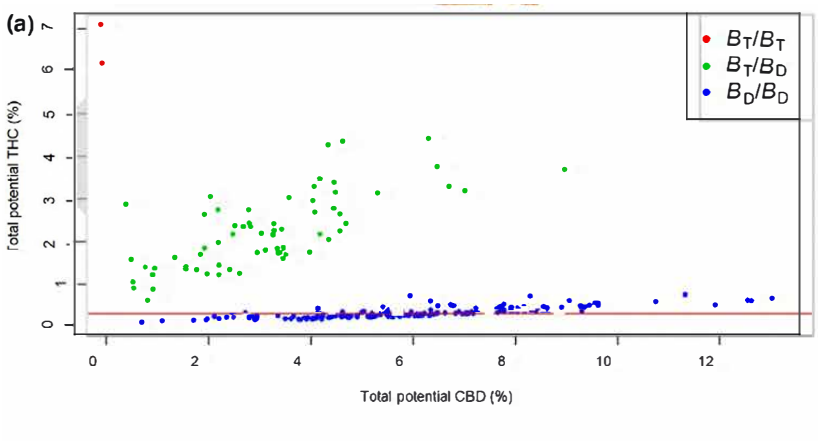


FIGURE 5 Genotype to phenotype relationships. (a) Total potential tetrahydrocannabinol (THC) and cannabidiol (CBD) concentration (% dry mass) in individual plants for which B locus genotype was also determined. The red line indicates 0.3% total potential THC (b) Δ^9-THC concentration by genotype. The red line indicates 0.3% dry weight Δ^9-THC. (c) Total potential THC concentration by genotype. The red line indicates 0.3% dry weight total potential THC. (d) Total potential CBD:THC concentration ratio. All means differ (ANOVA $p <$ 1e-4). Tabular data can be found in Table S2

How Cannabis Works

The **Entourage Effect** is a term coined in 1998 by a group of Israeli-based scientists to describe how the components of cannabis working together have a better therapeutic effect than any one component alone. For example, Marinol, a synthetic THC approved by the FDA in the 1980s for cancer patients, never took off because patients preferred whole plant use for its effects.

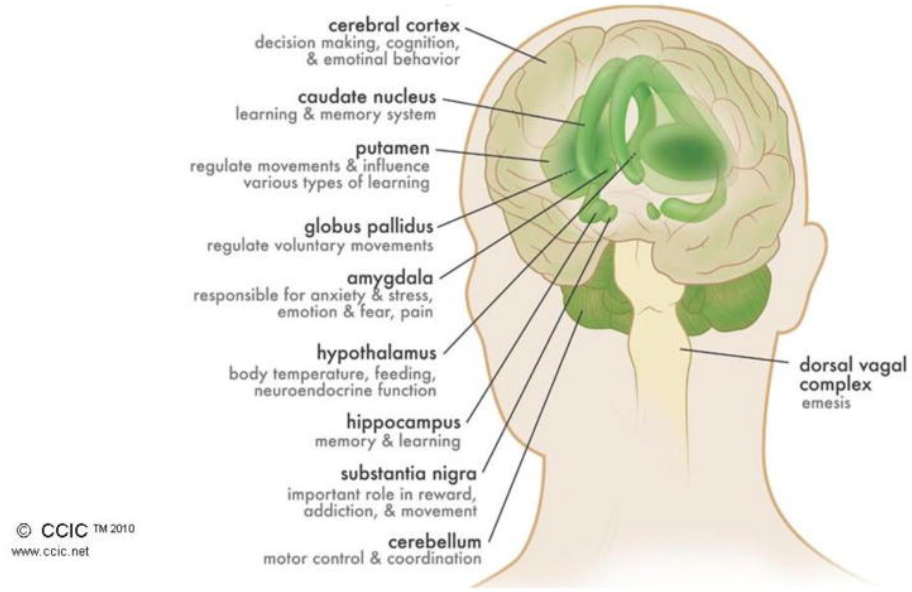
Cannabis has two major classes of bioactive compounds: **cannabinoids** and **terpenes**. Depending on where they arise, cannabinoids are described as:

- endocannabinoids – produced naturally in the body of animals
- phytocannabinoids – found in cannabis and other plants
- synthetic cannabinoids – manufactured artificially

Cannabis also includes flavonoids, polyphenols, and other classes of compounds in addition to cannabinoids and terpenes.

We have an **Endocannabinoid System** (ECS) made up of receptors in both the brain and the body and naturally occurring cannabinoids. **Receptors** are signaling devices that work like the ignition in a car. Once the right key (here a cannabinoid) comes along it connects and turns a switch chemically. Major **endocannabinoid receptors** include:

- CB1 – or Cannabinoid Receptor Type 1. Found in the brain, reproductive system, and nervous system.
- CB2 – or Cannabinoid Receptor Type 2. Found in the spleen, immune system, lymphoid, thymus, tonsils, pancreas, and near the skin.



Distribution of CB1 Receptors in the Brain. This figure illustrates the structures of the human brain with the highest density of CB1 receptor concentrations. Each identified brain structure is also notated with its attributed function. The figure is reproduced with permission from the Canadian Consortium for the Investigation of Cannabinoids and was published in Int. J. Drug Policy, 2017 Apr; 42: 39-49 as Figure 1.

Some naturally occurring **endocannabinoids** include:

- Anandamide (arachidonoyl ethanolamine) (AEA) – an endogenous ligand[3] of CB1 and CB2. Binds to CB1 and to a lesser extent CB2. Also found in black truffles and chocolate.
- 2-AG – 2-arachidonoloylglycerol, acts as a full agonist[4] to both CB1 and CB2; present at higher levels in the brain than anandamide.

Endocannabinoids interact with other compounds in the body, such as fatty acids and compounds derived from cannabis to modulate the body's use of energy, protect cells, and stimulate growth of certain cells. For example, anandamide is structurally similar to another naturally occurring endogenous compound, oleoyl serine (OS or HU-639) an anabolic regulator which stimulates osteoblasts assisting in bone growth (thus, is a potential treatment for osteoporosis). *See* https://www.youtube.com/watch?v=Olaczu7rhqI . (Dr. Raphael Mechoulam lecture explaining bone research). Research also indicates that CBD stimulates bone growth. Kogan et al., *Cannabidiol, a Major Non-Psychotropic Cannabis Constituent Enhances Fracture Healing and Stimulates Lysyl Hydroxylase Activity in Osteoblasts*, J. BONE & MINERAL RESEARCH (2015).

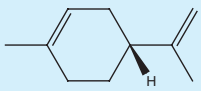
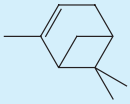
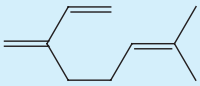
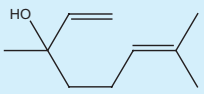
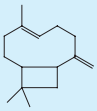
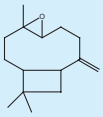
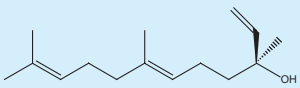
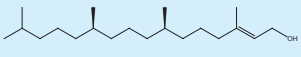
Cannabinoids are **hydrophobic** molecules, meaning they cannot travel long distances in the aqueous medium surrounding the cells from which they are released. Thus, they act locally on nearby target cells and have a restricted sphere of influence.

Terpenes are also bioactive and give cannabis (or basil or pine trees) its smell. Terpenes act synergistically with cannabinoids. **Myrcene** is a common terpene (and also found in hops) and is thought to contribute to sedation, blocking inflammation, and pain relief. **Limonene** (also found in lemons) is an immunostimulant and anxiolytic. **Linalool** (also found in lavender) is an anticonvulsant, anti-anxiety, analgesic, and sedative. *See* Table 2, Cannabis Terpenoid Activity Table, Russo, Ethan B., *Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects*, BRITISH J. PHARMACOLOGY (2011) 163:1344-64. The table on the following page lists major terpenes found in cannabis, their chemical structure, their pharmacological activity, and which cannabinoids each interacts with synergistically.

[3] A **ligand** is a molecule that binds to a receptor.
[4] An **agonist** is a chemical that binds to a receptor and activates a physiological response.

Table 2

Cannabis Terpenoid Activity Table

Terpenoid	Structure	Commonly encountered in	Pharmacological activity (Reference)	Synergistic cannabinoid
Limonene		 Lemon	Potent AD/immunostimulant via inhalation (Komori *et al.*, 1995)	CBD
			Anxiolytic (Carvalho-Freitas and Costa, 2002; Pultrini Ade *et al.*, 2006) via 5-HT_{1A} (Komiya *et al.*, 2006)	CBD
			Apoptosis of breast cancer cells (Vigushin *et al.*, 1998)	CBD, CBG
			Active against acne bacteria (Kim *et al.*, 2008)	CBD
			Dermatophytes (Sanguinetti *et al.*, 2007; Singh *et al.*, 2010)	CBG
			Gastro-oesophageal reflux (Harris, 2010)	THC
α-Pinene		 Pine	Anti-inflammatory via PGE-1 (Gil *et al.*, 1989)	CBD
			Bronchodilatory in humans (Falk *et al.*, 1990)	THC
			Acetylcholinesterase inhibitor, aiding memory (Perry *et al.*, 2000)	THC?, CBD
β-Myrcene		 Hops	Blocks inflammation via PGE-2 (Lorenzetti *et al.*, 1991)	CBD
			Analgesic, antagonized by naloxone (Rao *et al.*, 1990)	CBD, THC
			Sedating, muscle relaxant, hypnotic (do Vale *et al.*, 2002)	THC
			Blocks hepatic carcinogenesis by aflatoxin (de Oliveira *et al.*, 1997)	CBD, CBG
Linalool		 Lavender	Anti-anxiety (Russo, 2001)	CBD, CBG?
			Sedative on inhalation in mice (Buchbauer *et al.*, 1993)	THC
			Local anesthetic (Re *et al.*, 2000)	THC
			Analgesic via adenosine A_{2A} (Peana *et al.*, 2006)	CBD
			Anticonvulsant/anti-glutamate (Elisabetsky *et al.*, 1995)	CBD, THCV, CBDV
			Potent anti-leishmanial (do Socorro *et al.*, 2003)	?
β-Caryophyllene		 Pepper	AI via PGE-1 comparable phenylbutazone (Basile *et al.*, 1988)	CBD
			Gastric cytoprotective (Tambe *et al.*, 1996)	THC
			Anti-malarial (Campbell *et al.*, 1997)	?
			Selective CB_2 agonist (100 nM) (Gertsch *et al.*, 2008)	THC
			Treatment of pruritus? (Karsak *et al.*, 2007)	THC
			Treatment of addiction? (Xi *et al.*, 2010)	CBD
Caryophyllene Oxide		 Lemon balm	Decreases platelet aggregation (Lin *et al.*, 2003)	THC
			Antifungal in onychomycosis comparable to ciclopiroxolamine and sulconazole (Yang *et al.*, 1999)	CBC,CBG
			Insecticidal/anti-feedant (Bettarini *et al.*, 1993)	THCA, CBGA
Nerolidol		 Orange	Sedative (Binet *et al.*, 1972)	THC, CBN
			Skin penetrant (Cornwell and Barry, 1994)	–
			Potent antimalarial (Lopes *et al.*, 1999, Rodrigues Goulart *et al.*, 2004)	?
			Anti-leishmanial activity (Arruda *et al.*, 2005)	?
Phytol		 Green tea	Breakdown product of chlorophyll	–
			Prevents Vitamin A teratogenesis (Arnhold *et al.*, 2002)	–
			↑GABA via SSADH inhibition (Bang *et al.*, 2002)	CBG

Representative plants containing each terpenoid are displayed as examples to promote recognition, but many species contain them in varying concentrations. 5-HT, 5-hydroxytryptamine (serotonin); AD, antidepressant; AI, anti-inflammatory; CB_1/CB_2, cannabinoid receptor 1 or 2; GABA, gamma aminobutyric acid; PGE-1/PGE-2, prostaglandin E-1/prostaglandin E-2; SSADH, succinic semialdehyde dehydrogenase.

Types of Cannabinoids

Cannabis contains dozens if not hundreds of cannabinoids and hundreds of bioactive compounds of which only THC is euphoric and psychoactive (causes a "high" in higher doses). Major cannabinoids include:

- Tetrahydrocannabiniol (**THC**) – a bioactive or medicinal component of cannabis that comes in many forms such as:
    - **delta-9 tetrahydrocannabiniol (Δ9-THC)** – the main medicinal component of cannabis which is psychoactive and euphoric;
    - **delta-8 tetrahydrocannabiniol (Δ8-THC)** – a phytocannabinoid which is not as euphoric as delta-9, but occurs in very small quantities in the plant;
    - **tetrahydrocannabinolic acid (THC-A)** – an anti-inflammatory and neuro-protectant. Occurs in large amounts in cannabis flower and is not (in theory) psychoactive. Heating THC-A readily converts it to Δ9-THC in a process called **decarboxylation** in which the sample loses 12% of its mass**.** Some cannabis physicians consider THC-A to have more potential medical use than CBD;
    - **tetrahydrocannabivarin (THCV)** – A less euphoric THC and the subject of research for diabetes treatment, believed to be an appetite suppressant, anti-anxiety/PTSD, help with Alzheimer's and tremors, and with bone growth; more common in African cannabis varieties; and
    - **11-hydroxy-THC** – produced by liver when cannabis is ingested. Has a longer half-life than Δ9-THC. A more potent psychoactive and sedative than Δ9-THC and is also much longer lasting than inhaling Δ9-THC.

- Cannabidiol (**CBD**) – the component the original 2015 Compassionate Use Act legalized for use treating intractable epilepsy. Useful in higher doses for Dravet's Syndrome or Lennox-Gastaut Syndrome. Also an anti-inflammatory and anxiolytic but requires enormous doses which may be unaffordable in a poorly regulated market. In certain ratios may attenuate THC's effects (particularly the unwanted side effect of psychoactivity) while exaggerating helpful effects.
- Cannabigerol (**CBG**) – non-psychoactive shown to promote apoptosis in cancer cells and inhibit tumor growth in mice; binds to CB2.
- Cannabichromene (**CBC**) – antitumor effects.
- Cannabinol (**CBN**) – Results from THC degradation as the plant matures; higher affinity for CB2 than CB1; causes sleepiness.

Cannabis clinicians and researchers are developing an increasing interest in the acid forms of cannabinoids such as THCA and CBDA as medicine.

Which Cannabinoids are Intoxicating? Synthetic?

"Intoxicating" and "synthetic" are terms that are the continual subject of heated legislative debate in hemp regulation. The following chart breaks down what cannabinoids are common in the current hemp market.

	Natural	"Semi-Synthetic" "Artificial" or Converted*	Synthetic
Intoxicating	Δ9-THC	Δ8-THC* Δ10-THC Δ7-THC Δ6-THC THC-O	THCP† HHC EXO-THC HHCP THCH CB9A
Not Intoxicating	Full Spectrum hemp Broad Spectrum hemp Cannabidiol (CBD/CBDA) Cannabidivarin (CBDV) Cannabigierol (CBG/CBGA) Cannabichromene (CBC) Cannabicitran (CBT) Cannabicyclol (CBL) Cannabielsoin (CBE) Cannabinol (CBN) Tetrahydrocannabivarin (THCV)	 CBN* THCV*	None in the marketplace

See CO Stat. § 44-10-209 (distinguishing intoxicating and non-intoxicating cannabinoids).

*Note: Some cannabinoids naturally occur in the plant but only in very small amounts. In the marketplace, these low-yield cannabinoids are commonly manufactured from CBD. Some states use "artificial" or "semi-synthetic" to describe this category.

† THCP has been reported as naturally occurring in cannabis but only in very small quantities. It is extremely potent and manufactured chemically for the products on the market.

Glossary

Full Spectrum – Hemp extract rich in cannabidiol (CBD) which contain all natural cannabis plant compounds — cannabinoids, terpenes, and flavonoids. Contains small amounts (under 0.3%) of Δ9-tetrahydrocannabinol (THC).

Broad Spectrum – Contains naturally occurring compounds like full spectrum hemp extract but manufacturers remove all or most of the THC. This process also may remove minor (non-intoxicating) cannabinoids which hinders efficacy. May contain trace amounts of THC.

Isolate – A pure form of a cannabinoid such as CBD which contains 0% THC. Does not contain any terpenes or flavonoids.

THC as Medicine

While THC can be psychoactive it is the main medicine in cannabis. As do many medicines, THC has a side effect, in its case euphoria, which an able medical professional can manage in the normal course of patient care. Medical uses of THC are supported by medical research a few examples of which are listed below:

- THC is a neuroprotectant meaning it can protect brain cells from damage. Hampson et al., *Cannabidiol and (-) Δ9 tetrahydrocannabiniol are neuroprotective antioxidants*, PROC. NAT'L ACAD. SCI. USA, Vol. 95, pp. 8268-73 (July 1998).

- An analysis of outcomes with traumatic brain injury patients who tested positive for THC versus those that did not showed a significantly higher survival rate in those who used cannabis concluding that a positive THC screen is associated with decreased mortality in adult patients sustaining TBI. Nguyen et al., *Effect of Marijuana Use on Outcomes in Traumatic Brain Injury*, THE AM. SURGEON, Vol. 80, pp. 979-83 (Oct. 2014).

- THC also alleviates pain. For example, one study demonstrated that a relatively low-dose of THC in cannabis flower (1.29% and 3.53%) consumed by vaporization relieved pain with very tolerable side effects. Wilsey et al., *Low-Dose Vaporized Cannabis Significantly Improves Neuropathic Pain*, THE J. OF PAIN, Vol. 14, No. 2, pp. 136-48 (Feb. 2013).

Cannabis users may develop a tolerance to cannabinoids. But unlike opioids, cannabinoids cannot cause respiratory arrest. There is no risk for overdose in the manner that opioids kill people by shutting down the respiratory system. Extremely high doses of THC can cause severe adverse effects. CBD however is much more likely to counter-indicate with certain pharmaceuticals (just as St. John's Wort or grapefruit may do) than THC, so it is critical that consumers are warned of the risk and physicians know their patients are taking CBD.

Our bodies contain a natural antidote to THC in pregnenolone, a naturally occurring steroid and the precursor to all steroids. Pregnenolone functions as a natural protectant to THC intoxication and its volume in the brain increases as THC is added.

Cannabis's Medical Uses

Cannabis has broad categories of known medicinal uses due to its varying properties of its numerous components whether used alone, in medical preparations using small numbers of the components, or in whole-plant preparations to take advantage of the entourage effect.

Categories of uses and relevant conditions and diseases include:

- analgesic (chronic pain, migranes)
- antiemetic (for nausea and vomiting) and cachexia (cancer, AIDS, anorexia)
- anti-inflammatory (Crohn's, IBS, rheumatoid arthritis)
- endo-cannabinoid deficiency (autism, a complex condition in a category of its own)
- spasticity (Multiple Sclerosis)
- neuroprotectant and slowing cell damage (Alzheimer's, Parkinson's, Multiple Sclerosis, ALS, diabetes type 1)
- seizures (epilepsy)
- anxiolytic (anxiety) and depression (PTSD)
- sleep disorders/insomnia
- bone growth

As a general matter, cannabis promotes homeostasis, or a balance of body chemistry. Below are some sources for details and support for the use of cannabis for particular conditions via peer-reviewed medical research:

National Academies of Sciences, Engineering, and Medicine, *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research* (2017), *available at* https://www.ncbi.nlm.nih.gov/books/NBK423845/pdf/-Bookshelf_NBK423845.pdf.

National Cancer Institute, Cannabis and Cannabinoids (PDQ), Health Professional Version, *available at* https://www.cancer.gov/about-cancer/treatment/cam/hp/cannabis-pdq/ (updated Aug. 16, 2018) (surveying medical literature).

Russo, Ethan B., *Clinical Endocannabinoid Deficiency (CECD): Can this Concept Explain Therapeutic Benefits of Cannabis in Migraine, Fibromyalgia, Irritable Bowel Syndrome and other Treatment-Resistant Conditions?*, NEUROENDOCRINOLOGY LETTERS, 2004; 25(1/2):31-39. *See also* https://ethanrusso.org/category/library/.

Society of Cannabis Clinicians, Research Library, *available at* https://www.cannabisclinicians.org/resources/research-library-3/.

Bioavailability and Methods of Delivery

Medical cannabis can come in a wide variety of forms from raw flower or oil extract to processed items like lozenges, sublingual strips, skin patches, even topicals such as lotions and creams. The method of delivery affects the speed of onset and absorption. **Edibles** refers to anything that can be ingested containing cannabis or cannabis derivatives including gummies, sublingual strips, lozenges, chocolates, etc. Raw plant material can be consumed by methods other than smoking such as by using a **vaporizer** or a machine that heats cannabis to release the active medicinal agents creating a vapor that can be inhaled. Vaporizing does not burn the material which minimizes chemical changes that could be counterproductive to a patient.

Bioavailability is the degree and rate at which a substance is absorbed into the living system or made available at the site of physiological activity. Bioavailability varies by methods of administration. For example, intravenous administration results in 100% bioavailability where sublingual, oral, inhalation, or topical application results in less than 100%. The percentages below are drawn from medical research, but the actual percentage will vary by the individual product and the individual user. For example, the bioactivity of smoking can range down to 1%. Moreover, the bioavailability varies by individual cannabinoid.

- **Oral/Ingested** – 10-20%. Bioactivity depends on stomach contents and is low because of the first pass metabolism of the digestive system but can be enhanced if prepared with fatty acids such is an oil extract as doing so helps bypass the first pass metabolism of digestion. Onset may exceed an hour; duration, 6-8 hours.
- **Nasal/Oral Mucosa (sublingual)** – <5% to 20-30%. Bioactivity is higher because the first pass metabolism is bypassed by absorption into the high abundance of capillaries below the tongue. Onset 15-45 minutes; duration, 45 minutes to two hours.
- **Suppository** – 13% up to double Oral. Onset in 10-15 minutes; duration, 2-8 hours.
- **Inhalation by smoking/combustion** – 40%. Because inhalation bypasses the digestive system entirely and administers the compounds via lung tissue and into the blood stream, the effects are felt much faster than when ingested. Quick (3-10 minutes) onset; duration, 2-4 hours. Lower bioavailability for CBD than THC.
- **Inhalation by vaporizing/no combustion** – 40%. Same quick effect as smoking. If done correctly, occurs as lower temperature than smoking which reduces the risk of certain harmful by-products that occur when cannabis is subjected to high temperatures.
- **Topical/Transdermal** – Effective for localized relief from pain, tension, muscle ache, and inflammation and binds to CB2 receptors. CBN and CBD absorb 10x better than THC. Non-psychoactive and not edible. Onset ½ to 2 hours; duration, 1-8 hours.

Inhalation versus ingestion. The main advantage of the inhalation techniques is rapid onset of effect and ease of dose titration.[5] THC levels fall to 30-40% of peak within an hour. With orally ingested methods, THC peaks are only reached one to six hours after a dose. When ingested THC degrades in the liver to 11-hydroxy-THC which has potent psychoactive effects and enhances sedation. Inhalation generates less 11-hydroxy-THC. **Consequently, a physician may prefer**

[5] **Titration** of a dose means determining how much of a substance is needed to reach a desired effect.

recommending to a patient inhalation during the day, but ingestion for nighttime and sleeping. The former acts fast for a short duration while the latter is slow acting for a longer duration. Many patients need both.

The complexity and variability of the plant and the individualized reactions of a patient make it imperative that dosing is highly individualized. Any recommendation for use should consider:

- Bioavailability
- Chemical profile of the product
- Concentration (mg/ml)
- Amount consumed over time

THC metabolizes very differently than alcohol and takes several days for most of the THC consumed to leave the body. Other compounds can affect THC's affect. Grapefruit increases the THC concentration and duration while St. John's Wort can decrease it. A litany of drugs can hasten metabolism of THC: caffeine, clozapine, olanzapine, estradiol, lidocaine, melatonin, naproxen, olanzapine, and others. CBD can inhibit the metabolism of antihistamines, antiretrovirals, antipsychotics, beta blockers, haloperidol, opioids, most statins, SSRIs, and other. Cannabis use with anticholinergics can enhance tachycardia and hypertensive effects.

Strains, Cultivars, and Chemotypes

Strain is a slang word commonly used to describe different types of cannabis. **Variety** or **Cultivar** are more appropriate words for types of cannabis produced by cultivation. **Landrace** is used to describe indigenous strains that are naturally occurring (or have so long been cultivated by humans that they appear naturally occurring in the wild).

In medical and adult use legal states, cannabis is marketed and labeled in dispensaries by strain name, such as Blue Dream, Swazi Gold, or Pineapple Express. This practice arose from the black market's tendency to name strains based on their perceived qualities and origins. Sativas, which were the subspecies traditionally grown in the western hemisphere, were cross-bred with the shorter, bushier indicas to limit the size of the plant, but this also raised the THC levels in the plants. Strains are often coded in dispensaries by Sativa, Indica, or Hybrids, although the distinction among the three has become more and more blurred with the innovations of cultivators in cross-breeding. In reality, these terms are marketing terms with no true indication of the contents of the products being sold. A Nevada study conducted before adult use went into effect in July 2017 found that despite 396 strain names testing revealed only three chemovars and twelve genotypes were present creating a false impression that there was a variety of medical cannabis available to patients. Riemann-Philipp, U., et al., *Cannabis Chemovar Nomenclature Misrepresents Chemical and Genetic Diversity; Survey of Variations in Chemical Profiles and Genetic Markers in Nevada Medical Cannabis Samples*, CANNABIS AND CANNABINOID RESEARCH, Vol. X, No. X (2019).

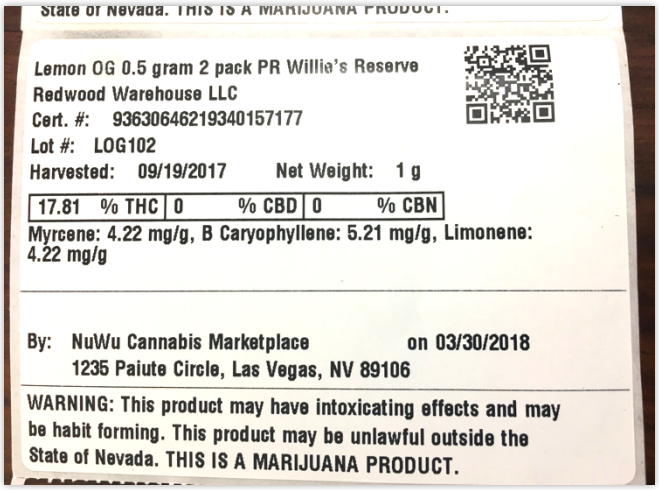
Because it is the chemical make-up of cannabis that counts for its effects on humans, the terms **chemotype** or **chemovar** are being used more often to describe variations within the species.

Modern researchers characterize cannabis chemotypes by the following numerated types (with whether they are legally marijuana or hemp noted):

- Type 1 – higher ratio of THC to CBD (marijuana)
- Type 2 – 1:1 CBD:THC (marijuana)
- Type 3 – higher ratio of CBD to THC (maybe hemp)
- Type 4 – CBG dominant (hemp)
- Type 5 – high fiber yield; very small detectable cannabinoids (hemp)
- Type 6 – THCV dominant (hemp?)

Testing Cannabis

Effective medicine requires effective testing to determine the **cannabinoid profile** or the quantity and type of cannabinoids and other components in a given batch of flower or processed medicine. Profiles are determined by gas chromatography (GC) or more reliably by GC combined with mass spectrometry (GC/MS). Liquid chromatography (LC) can differentiate between acid and neutral forms. Most states require testing for THC and CBD levels but so far only Nevada requires a full profile of both cannabinoids and terpenes. The image to the right is a sample, batch-specific disclosure Nevada requires with every sale of a cannabis product.



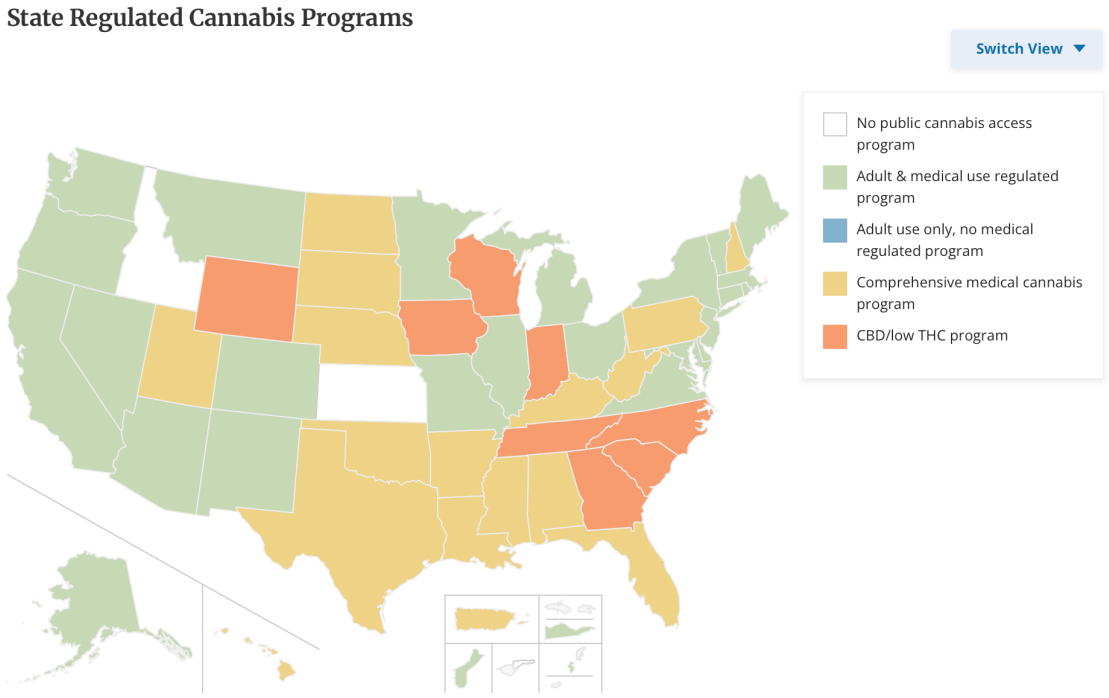
Currently, Texas requires testing of hemp before it is harvested for THC potency and cannabis products used for human consumption for THC and any contaminants. A healthy testing regime screens for pesticides, heavy metals (particularly common with outdoor cultivation), and pathogens. Powdery mildew, for example, is very common in cannabis when not carefully cultivated and hazardous when the flower is consumed, but is stripped out by the process of making oils. Conversely pesticides are concentrated when oils are made from contaminated product. **A healthy regulatory regime would require a "full spectrum" analysis of the cannabinoids and terpenes** present **in that particular batch** of raw flower or processed product so that patients and their physicians as well as consumers know exactly what compounds are in the product and at what doses so they can in turn learn what formulation and dosage works best for that patient or a consumer's goal.

Some states, like Nevada, license testing companies and require that they be third-party with no shared financial interests or owners with cannabis cultivation, production, or dispensing licensees. Ensuring no cross-interest may be simple with smaller companies but more difficult with publicly traded or larger companies which may have thousands of "owners." The federal securities laws require the disclosure of anyone owning more than 5% of a company's stock, so some states set 5% as the disclosure threshold.

Finally, a cautious state should be prepared to test the testing companies. **Unless the state itself has full-spectrum testing capability** whether in-house or through a contractor it will be unable to ensure that the system to protect patients and consumers is secure and reliable.

Current Legal Status of Cannabis

Despite 42 states and the District of Columbia having legalized cannabis for medical purposes, cannabis is still federally illegal. The National Conference of State Legislatures' map below illustrates the status as of mid-2025. Eight states currently allow only CBD/low-THC products in their medical products. (Texas began as a "low-THC" state but in practice no longer is one.) In addition, 24 states have legalized adult cannabis use.



See https://www.ncsl.org/health/state-medical-cannabis-laws. The District of Columbia allows limited adult possession and cultivation, but no regulated production and sales for adult use.

Since 2020, New Mexico, Connecticut, New York Virginia, Rhode Island, Maryland, Missouri, Delaware, Minnesota, and Ohio have legalized marijuana for adult use while Alabama, Mississippi, Kentucky, and Nebraska have legalized medical use.

Both the federal and state Controlled Substances Acts ("CSA") use the scientific term *Cannabis sativa L.* in criminalizing the plant. The definition from Texas law below is similar to that in federal law:

> "Marihuana" means the plant Cannabis sativa L., whether growing or not, the seeds of that plant, and every compound, manufacture, salt, derivative, mixture, or preparation of that plant or its seeds. The term does not include:

(A) the resin extracted from a part of the plant or a compound, manufacture, salt, derivative, mixture, or preparation of the resin;

(B) the mature stalks of the plant or fiber produced from the stalks;

(C) oil or cake made from the seeds of the plant;

(D) a compound, manufacture, salt, derivative, mixture, or preparation of the mature stalks, fiber, oil, or cake; or

(E) the sterilized seeds of the plant that are incapable of beginning germination.

TEX. HEALTH & SAFETY CODE § 481.002(26).

Thus, while one can possess part of a "marihuana" cannabis plant in Texas, one cannot legally cultivate those plant varieties outside the Compassionate Use Act's three (soon to be 15) licensees.

The federal CSA delegates scheduling to the Drug Enforcement Administration (DEA) which has steadfastly refused to reschedule cannabis for the last fifty years. The federal government's attitude toward cannabis varies by agency and even within agencies. Cannabis-related intellectual property can be patented but not trademarked even though the U.S. Patent and Trademark Office regulates both functions. Both the Biden and the Trump administrations stated rescheduling should happen. An administrative trial was set in January 2025 to do so, but was postponed after the DEA was caught having improper *ex parte* contacts with Smart Approaches to Marijuana (SAM), a pro-prohibition group. Rescheduling could happen before the 2027 Session, or not.

Despite the Schedule I CSA designation of having no medical use, the federal government has distributed cannabis to patients on a case-by-case basis starting in 1978 through its Compassionate Use Investigational New Drug Program. Moreover, the United States holds a patent for its medical use.

In 2013, the Department of Justice ("DOJ") issued the **Cole Memorandum** which directed U.S. Attorneys to not enforce federal marijuana laws in states with states with "strong and effective regulatory and enforcement systems" except when other priorities were implicated such as fighting cartels or illicit trafficking. In January 2018, former Attorney General Jeff Sessions rescinded the Cole Memorandum, but legal states pushed back, resulting in a political stalemate and strategic enforcement. For example, when California rolled out adult-use licensing, federal enforcement focused on unlicensed grows and outlaw operations on federal land.

The **Rohrabacher–Farr amendment** (a.k.a. the **Rohrabacher–Blumenauer amendment**) to the omnibus spending bill prohibits the DOJ from spending any funds to interfere with state-legal medical cannabis programs and was most recently re-upped in May 2018. The federal courts have broadly enforced the amendment. *See U.S. v. McIntosh*, 833 F.3d 1163 (9th Cir. 2016) (rejecting DOJ's argument that Rohrabacher-Farr did not prohibit the prosecution of individuals). With the current lack of a federal budget, the amendment's status going forward is unclear.

Two large problems for the cannabis industry with federal law are **banking** and **taxation**. The federal prohibition makes most banking institutions refuse to accept cannabis derived funds forcing the industry to function on a cash basis which creates severe security issues. While many cannabis businesses are eventually able to find banks that will open accounts, typically in credit

unions or state banks, the accounts may be closed without warning. **Section 280E** of the Internal Revenue Code prohibits the deduction of expenses for "marihuana distribution" rendering it virtually impossible to turn a profit. Section 280E has been interpreted by the IRS in a way that exempts cultivation and processing companies while applying fully to dispensaries. Most federal legislative efforts are focused on fixing these two areas, in addition to decriminalizing cannabis or re-scheduling it.

The 2018 Farm Bill

In late December 2018, President Trump signed the 2018 Farm Bill which contained provisions to permanently legalize hemp — and all cannabinoids except for delta-9 THC derived from marijuana. Moreover, under the Farm Bill, these products can now cross state lines. The law amends the federal CSA to exempt hemp and its products from the definition of "marihuana." States have to enact their own hemp laws to de-schedule hemp from state CSAs. The law also requires states to propose a hemp program to the U.S. Department of Agriculture ("USDA") for approval which must include requirements such as licensing of hemp grows and tracking their geographic location so that law enforcement can know which crops are legal. If a state does not do so, hemp growers can simply register with the USDA. An important effect for health care policy is that CBD derived from hemp is now legal federally but currently has no clear requirements for testing or labeling at the federal level leaving that policy work to the states.

The Texas Compassionate Use Act – 2025 Version

(Health & Safety Code ch. 487
Occupations Code ch. 169)

What can patients access in TCUP:

- "Marijuana" derived cannabinoids.
- Pulmonary inhalation products (don't call them vapes!) — ***if and when*** DPS approves them
- "Low-THC cannabis" meaning a product with not more than 10 mg of THCs "in each dosage unit"
- Each prescription limited to a 90-day supply with up to 4 refills

Basic requirements:

- TCUP patients must be a Texas resident
- A registered TCUP physician (who must be a specialist) determines the risk of the medical use of "low-THC" cannabis by the patient is reasonable in light of the potential benefit for the patient

What conditions qualify a patient:

- epilepsy;
- a seizure disorder;
- multiple sclerosis;
- spasticity;
- amyotrophic lateral sclerosis (ALS);
- autism;
- cancer;
- an incurable neurodegenerative disease (see lengthy list in HHSC regulations);
- post-traumatic stress disorder;
- a condition that causes chronic pain;
- traumatic brain injury;
- Crohn's disease or other inflammatory bowel disease;
- a terminal illness or a condition for which a patient is receiving hospice or palliative care; or
- a medical condition that is approved for a research program under Subchapter F, Chapter 487, Health and Safety Code, and for which the patient is receiving treatment under that program

Other new provisions:

A physician may submit to the Department of State Health Services ***a request*** that the department report to the legislature that low-THC cannabis may be beneficial to treat a specific medical condition not listed. The request must be accompanied by medical evidence such as peer-reviewed published research demonstrating that low-THC cannabis may be beneficial to treat that medical condition. The executive commissioner by rule shall prescribe the manner in which a physician may submit a request under this subsection.

Executive Order GA-56: What's happening and what's coming

- The Texas Alcoholic Beverage Commission (TABC) and the Department of State Health Services (DSHS) issuing emergency regulations to prohibit sales to those under 21 on pain of cancelation of a permit, license or registration issued by the agency.
- DSHS revamping hemp rules to:
    - Revise requirements for measuring THC to account for conversion of THCA into delta-9 for consumable hemp products
    - Revise application and renewal fees
    - Update labeling requirements regarding the amount and concentration of cannabinoids, recommended serving size, and warnings to consumers
    - Strengthen recordkeeping requirements for sales, inventory, and product testing results
- DSHS to coordinate with (likely delegate to) TABC for enforcement
    - Sharing data on licensees, enforcement actions, etc.
    - Identifying and transferring funding to TABC for delegated powers and duties
- TABC, DSHS, Texas A&M AgriLife Extension Services, and any other relevant agency to jointly study implementation of rules similar to the provisions of HB309, 2d C.S. (Cain bill, a variation of the King committee substitute + King floor amendment (SB3, R.S.))
- DPS to coordinate with other law enforcement and regulatory agencies to deter and address violations consistently across the state.

TCUP Timeline

???: Satellite locations of original three licensees approved

???: Pulmonary inhalation products approved

Dec. 1, 2025: Nine new licenses chosen

Apr. 1, 2026: Three additional licenses chosen

???: Satellite locations of new licensees approved

By next Regular Session: Maybe a new licensee is operational?

THC Caps in Hemp Products

Grouped by the type of state — ***legal*** marijuana, ***full medical*** marijuana, ***low-THC*** medical cannabis, or ***no legal*** status. Cap applies to edibles and beverages unless otherwise noted. Ratios are CBD:THC or all other cannabinoids:THC.

State	Status	Cap (mg THC/dose)/Ratio
Alaska	Legal	0 mg
Arizona	Legal	0 mg
California	Legal	0 mg
Colorado	Legal	1.75 mg & 15:1
Connecticut	Legal	*Edibles*: 0.5 mg *Beverages*: 3 mg
Maryland	Legal	0.5 mg
Minnesota	Legal	*Edibles*: 5 mg *Beverages*: 10 mg
Montana	Legal	0 mg
New Jersey	Legal	0.5 mg (Enforcement enjoined)
New York	Legal	1 mg & 15:1 ratio
Oregon	Legal	2 mg
Rhode Island	Legal	1 mg
Vermont	Legal	1.5 mg (more allowed if 20:1 ratio)
Virginia	Legal	2 mg *or* 25:1
Washington	Legal	0 mg
Alabama	Full Medical	10 mg
Hawaii	Full Medical	*Edibles*: 1 mg *Beverages*: 0.5 mg
Kentucky	Full Medical	*Edibles*: no cap for adult use/2.5 mg & 15:1 unregulated *Beverages*: 5 mg
Louisiana	Full Medical	5 mg
North Dakota	Full Medical	5 mg & 15:1
Utah	Full Medical	5 mg & THC < 10% of total cannabinoids
Georgia	Low-THC Medical	10 mg
Iowa	Low-THC Medical	4 mg
Tennessee	Low-THC Medical	15 mg
Idaho	None	0 mg

Note that “low-THC” states have the highest caps for hemp products. Why? Unlike legal marijuana states, there is no place for consumers to go but the black market.

Intoxication and Other Public Health Risks

Driving Under the Influence. Because the body processes cannabinoids very differently from alcohol, namely by storing them in fat, the body will have levels of THC and other cannabinoids long after any intoxication effects are gone. Compare to alcohol breath tests that measure instantaneous blood-levels that reliably predict intoxication and impairment levels. While some in the industry claim a simple field test could be developed to test for THC intoxication, doing so reliably is highly unlikely for the added reasons that different personal body chemistry and different usage histories will result in different levels of impairment on the same dosage.

Current Texas law exempts registered medical cannabis patients from criminal charges for possession. TEX. HEALTH & SAFETY CODE § 481.111(e)(1). However, being a registered medical cannabis patient in Texas rightly does not provide a defense against driving while intoxicated.

Other states that have legalized medical cannabis have enacted laws to prohibit the use of cannabis in a vehicle similar to open container laws for alcohol. *See* http://www.ncsl.org–/research/transportation/driving-with-cannabis-in-a-vehicle.aspx. While a scientifically reliable method of gauging intoxication is difficult, law enforcement can rely on simple field tests for motor skills. In short, just as it is illegal in Texas to drive while impaired by prescription drugs, it has been and will be illegal to drive while impaired by cannabis.

"Dabbing" and Extreme Concentrates or High Doses. "Dabbing" is a slang term for vaporizing butane hash oil ("BHO") at very high temperatures using a "rig." BHO is made by passing butane over cannabis plant material, then attempting to purge the butane by using a vacuum at room temperature or in an oven resulting in a sticky resinous substance with THC levels ranging from 50-90% when heated. Different processes can produce a different looking end product described based on its appearance as shatter, budder, crumble, wax, etc. Because the product has not been heated the THC-A has not yet become THC, so BHO is not orally active and must be vaporized for users to get a "high." Users do this by using a rig with a "nail" that is heated to 700°F+ then touching a small amount of the BHO which is instantly vaporized. The rig traps the vapors which the user then inhales the high-THC vapors with one inhalation resulting in an instant and intense high.

This can be dangerous for a variety of reasons:

- Butane extraction, especially when performed underground or by amateurs, can cause explosions and fires.
- Terpenes which are present in BHO degrade at the very high temperatures used in dabbing to irritants such as methacrolein and carcinogens such as benzene. Meehan-Atrash et al., *Toxicant Formation in Dabbing: The Terpene Story*, ACS OMEGA, Vol. 2, pp 6112-17 (2017).
- Habitual dabbing can result in lung injury including severe symptoms that mimic pneumonia. *See* Anderson, R.P., et al., *Lung injury from inhaling butane hash oil mimic pneumonia*, RESPIRATORY MEDICINE CASE REPORTS, 171-73 (Jan. 2019)

In addition, consuming high doses of THC can trigger a variety of health issues whether cardiovascular or psychiatric.

Opioids and Cannabis

Reports and data from around the country indicate that cannabis can be useful for addressing opioid addiction in individuals and reducing overall deaths from addiction. The following is a brief survey of peer-reviewed articles addressing the effects of cannabis on opioid use and abuse.

Bachhubler, MD, Marcus A., Saloner, PhD, Brendan, Cunningham, MD, MS, Chinaso O., Barry, PhD, MPP, Colleen L, *Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States* (1999-2010), JAMA INTERNAL MED., 2014:174(10) — After analyzing both states with longtime medical cannabis laws (like California) and states that legalized during the period reviewed, **finds a 25% drop/lesser rate of opioid overdoses** in states with medical cannabis.

Ibrahim, MM, Porreca, F., Lai, J., Albrecht, P.J., Rice, F.L., Khodorova, A., Makriyannis, A., Vanderah, T.W., Mata, H.P., Malan, T.P., Jr., *CB2 cannabinoid receptor activation produces antinociception by stimulating peripheral release of endogenous opioids*, PROC. NAT'L ACAD. SCI. USA, 2005 Feb. 22; 102(8):3093-8 – Explains a mechanism of how cannabis eases pain and can address opioid use as the lab rat studies demonstrated that triggering CB2 receptors triggers the production of endogenous opioid beta-endorphins.

Johnson JR, Burnell-Nugent M, Lossignol D, et al., *Multicenter, double-blind, randomized, placebo-controlled, parallel-group study of the efficacy, safety, and tolerability of THC:CBD extract and THC extract in patients with intractable cancer-related pain*, J. PAIN SYMPTOM MANAGE 39 (2): 167-79, 2010 – Concludes that THC:CBD extract is efficacious for pain relief in patients with advanced cancer pain not fully relieved by strong opioids.

Liang D, Bao Y, Wallace M, Grant I, Shi Y., *Medical cannabis legalization and opioid prescriptions: evidence on US Medicaid enrollees during 1993-2014*, ADDICTION, 2018 Jul 10 – State-wide medical cannabis legalization appears to have been associated with reductions in both prescriptions and dosages of Schedule III (e.g., codeine) but not Schedule II, (e.g., hydrocodone and oxycodone) opioids received by Medicaid enrollees in the United States.

Lozano-Rojas, Felipe, Victoria Bethel, Sumedha Gupta, Shelby R. Steuart, W. David Bradford, Amanda J. Abraham, *Cannabis Laws and Opioid Use Among Commercially Insured Patients With Cancer Diagnoses*, JAMA HEALTH FORUM, 2025:6(1), Oct. 17, 2015 – Finds that opioid use by cancer patients drops significantly when medical or recreational cannabis becomes \ available.

Vigil, Jacob M., Stith, Sarah S., Adams, Ian M., Reeve, Anthony P., *Associations between medical cannabis and prescription opioid use in chronic pain patients: A preliminary cohort study*, PLOS ONE 12(11) (2017) – Finds that enrollment in New Mexico's medical cannabis program lowered the use of prescription opioids and recommends further investigation into cannabis as an alternative to opioids for pain.

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Status of Cannabis Research
And How to Read it Critically

Despite its status as a Schedule I drug at the federal and state levels cannabis research has exploded in recent years. The greatest strides have been made by a team based in Israel, which did not prohibit research, led by Dr. Raphael Mechoulam, the scientist who first identified THC as the psychoactive component of cannabis. He and his colleagues also identified the existence of the endocannabinoid system and coined the phrase "the entourage effect" to describe how cannabinoid and other components of cannabis work better together than in isolation.

The National Institute of Health's database of medical and public health research, PubMed, has close to 20,000 articles regarding cannabis and the number is growing exponentially. The database contains a wide range of types of research and not just medical research on humans. Cannabis research should be read critically given the wide range of cannabis products used. Use of extracted CBD or THC in a pharmaceutical or edible may affect people very differently from whole plant use. Dosages matter in pharmaceuticals in general but in cannabis that factor is even more important because cannabinoids are **biphasic**, meaning they have different and even opposite effects at different dosages.

Thus, when weighing a study on the safety and efficacy of cannabis one should consider:

(1) what form of cannabis is used,

(2) its content,

(3) what dosage, and

(4) how it is administered.

For example, a widely cited article about the efficacy of cannabis medicine using a meta-analysis of other studies, Whiting et al., *Cannabinoids for Medical Use: A Systematic Review and Meta-Analysis*, JAMA, Vl. 313, 2456-73 (2015), contains an analysis on efficacy for pain that relies on only one study using smoked whole plant and the rest using oral nabiximols (a 1:1 ratio THC:CBD spray). While the study concluded that there was a 30% or greater improvement in pain, the smoked whole plant study showed a greater improvement than the nabiximols studies. *See id*., Figure 2.

Research is fast evolving and clinicians are finding new uses for cannabis medicine including for rare conditions. For example, cannabis has been successfully used to treat Ehlers-Danlos Syndrome. *See* https://invisibleproject.org/enedina-stanger-ramos/.

Why U.S. Cannabis Research is So Difficult

Texas passed a cannabis medical research law in 1979 on the local and consent calendars, yet it appears to have never been used despite all the major medical research institutions in Texas. *See* TEX. HEALTH & SAFETY CODE ch. 481, subch. G.

The federal government created a monopoly on cannabis research through the National Institute of Drug Abuse ("NIDA"). Researchers must use cannabis grown through the NIDA program, which historically was grown outdoors in Mississippi and is of very low quality. (You can see a side-by-side picture here: https://www.washingtonpost.com/news/wonk/wp/2017/03/13/government-marijuana-looks-nothing-like-the-real-stuff-see-for-yourself/?utm_term=.38dafecd006f). Thus, many researchers do not want to use the government cannabis because it is so unlike what is available from a regulated medical cannabis program.

In practice, the federal government imposes a series of hurdles on medical cannabis research:

First – the U.S. Food and Drug Administration ("FDA") must approve any drug study. This alone can take years.

Second – An Institutional Review Board ("IRB") must approve the design of the study and that it is ethical and safe for patients.

Third – Researchers must meet any state-required standards and procedures.

Fourth – Researchers using a Schedule I substance must get DEA approval and a license. The problem is the DEA has been incredibly reluctant to grant those licenses. Despite making some statements in recent years they would open it up (in response to pressure from former Sen. Orrin Hatch and others), the DEA has not done so in practice.

Fifth – Until 2015, researchers had to clear another federal governmental hurdle by passing a Public Health Service ("PHS") (which is within Health and Human Services) interdisciplinary review process. Cannabis was the only Schedule I drug that had that requirement.

Sixth – Once a research team went through all that, then you have to convince NIDA to actually provide the cannabis, which is much more easily said than done. NIDA has had a monopoly on the cannabis for research and would often refuse to issue it.

In 2001, a Professor Lyle Cracker applied to cultivate cannabis for research purposes so he could use a better quality than the federal government's cannabis. The DEA first claimed they lost his application, then after a federal court ordered them to respond they rejected the application. Professor Cracker appealed to an Administrative Law Judge who issued an 87-page ruling supporting his application. But the DEA denied it again. Then the DEA sat on the Professor's motion to reconsider for two years. All in all, Prof. Cracker litigated ***for 12 years*** and lost.

Back in 2005, the Texas Medical Association sent a letter to the DEA in support of Prof. Cracker's efforts to study cannabis and stated that "**TMA believes that the medical use of marijuana is an issue that should be resolved through scientific research**."

The DEA said in 2018 that it would speed up its application process for research on Schedule I drugs. But little has changed. In practice the DEA only moves in response to litigation.

State Regulation of Cannabis
Basic Safeguards and How Texas Can Do It Better

Now that the vast majority of states have state-legal medical cannabis regimes and many states have legalized marijuana, patterns have emerged for what basic regulatory requirements a cannabis program should have and where other states have come short in providing safe and effective cannabis medicine to patients and products to consumers. The list below summarizes some key points and makes recommendations create a better, safer regime in Texas that is focused on science-based harm reduction and effective therapies for patients.

Typical requirements:

- **Criminal background checks** for every director, manager, and employee. (Texas already has this.)
- **"Seed-to-sale" software tracking** all product to prevent diversion and **labeling** the source, recommendation information, batch identification, content, and potency. (Texas already has this for TCUP by regulation to a large degree, but lack supply chain tracking for hemp products.)
- **Full-spectrum, third-party, independent testing** by ISO-certified labs. (Texas allows self-testing of TCUP products and does not require full spectrum of all cannabinoids and terpenes present.)
- **Licensing** of all sources of cannabis and cannabis product whether by vertical integration (as Texas now has in TCUP) or tiered licensing (which Texas has for hemp products). A typical licensing structure is three-tiered by cultivation, processing and retail/dispensary. Other license categories to support the system may include testing, transportation, delivery, and research.
- **Defining what conditions may participate.** Early medical cannabis laws listed conditions and expanded over time. However, this approach has become frowned upon because it is both legislators practicing medicine and looks at the medicine the wrong way. Medicines do not pick a diagnosis like Crohn's disease; rather they have a function, such as anti-inflammatory which may help a variety of conditions including Crohn's. Moreover, the research on cannabis is growing rapidly and legislatures cannot keep up effectively. Finally, picking and choosing which categories of patients may legally use cannabis medicine and alleviate their and their families' suffering is cruel. Simply letting physicians practice medicine is a better policy.
- **THC levels tested and labeled so physicians, patients, and consumers can dose appropriately.** Raw flower is labeled by percentage of THC and other cannabinoids while processed medicine is labeled by milligrams per dose. Physicians can then determine appropriate dosing and consumers can ensure they are taking what they intend.
- **Allow whole-plant medicine.** THC and CBD are but two of dozens of medically useful components in cannabis. Only allowing isolate extracts shortchanges patients and hamstrings physicians.

What could be done better:

- **Regulate TCUP and hemp products cohesively.** It's all from the same plant, so unless the entire market is considered with developing policy, nothing will work as intended.

- **Encourage and track research** whether in clinical practices or a research institution setting, including physicians reporting dosages and formulations along with their effectiveness for particular functions and any minor adverse events or side effects. Track public health concerns such as youth access or mental health outcomes.

- **License and regulate testing labs.** Until the state can "test the testers" a cannabis program is rife for abuse.

- Require **severe adverse event reporting** to the state for data collection such as for events that require hospitalization.

- Ensure anyone who qualifies for medical cannabis or assists those who do, such as home health care workers, **will not be subject to arrest or otherwise punished** using a simple registration to prevent diversion and protect those possessing cannabis under the state-legal program from arrest. Products should be available in assisted living facilities, for school children under a nurses supervision, etc. Parents should not be punished in custody matters nor should probationers avoiding hard drugs be sent to prison for using TCUP or hemp products.

- **Encourage cannabis use rather than opioids** where medically appropriate which can save lives.

- **Invest in educating the public and the medical community** about cannabis medicine such as any counterindications with pharmaceuticals.

- **Limit access to high-THC dose product** and perhaps ban super-concentrates which have no medical use and can easily be misused as there are some known adverse effects for high-dose THC in the medical literature.

- **Prohibited additives or synthetic, novel cannabinoids.** Or at the very least require strict disclosure to consumers when products contain additives or man-made ingredients.

A Cannabis Legal & Regulatory Timeline

- 1893 - British government establishes **the *Indian Hemp Drugs Commission*** to study cannabis which produces an eight-volume report concluding "the moderate use of hemp drugs is practically attended by no evil results at all."

- 1906 - The **Pure Food and Drug Act** requires the labeling of cannabis content in over-the-counter remedies and sets the main standards for pharmaceuticals to this day: safety and efficacy.

- 1914 - El Paso outlaws "marihuana" after a policeman in Juarez is murdered by a man allegedly in a marihuana-induced frenzy becoming the first U.S. jurisdiction to do so.

- 1914 - **The Harrison Act** establishes federal control over narcotics (opium and cocaine).

- 1919 - Texas outlaws "marihuana" after the Mexican Revolution prompts a wave of immigrants who more widely disseminate marijuana use in Texas.

- 1925 - the **U.S. Army** investigates cannabis use in the **Panama Canal Zone** among soldiers convening a committee of lawyers, military officers, public health officials, and mental health experts which finds no evidence of any "appreciable deleterious influence" on users and that reports of soldiers flipping out after smoking "appear to have little basis in fact."

- 1930 - Harry Anslinger, who worked against smuggling during Prohibition, becomes the head of the **Federal Bureau of Narcotics** ("FBN") and begins a decades-long effort to criminalize cannabis use and prohibit any research into its medical efficacy often by vilifying Mexicans and jazz musicians.

- 1931 – 29 states have outlawed cannabis under the name marijuana.

- 1932 – Apparently unable to pass a federal ban, the FBN begins promoting the **Uniform State Narcotic Act** to states.

- 1936 – The film **Reefer Madness** released with Anslinger's encouragement.

- 1937 - American Medical Association legal counsel Dr. William Woodward testifies to Congress that marijuana is not the danger Anslinger and the FBN describes but is largely ignored.

- 1937 - The federal **Marihuana Tax Act** imposing enormous taxes on marijuana leads to a de facto federal prohibition ($1/ounce for registered handlers; $100/ounce for unregistered).

- 1943 – The needs of the U.S. effort during World War II change the federal attitude toward cannabis, and American farmers registered in the "Hemp for Victory" program which distributed seeds and draft deferments harvest 375,000 acres of hemp

- 1944 - New York mayor Fiorello **LaGuardia** asks the **New York Academy of Medicine** to study marijuana. The Academy conducts the most comprehensive study since the *Indian Hemp Drugs Commission* and concludes that marijuana does not lead to addiction, crime, or use of narcotics nor does it induce violence, sex crimes, or insanity.

- 1951 - **The Boggs Act**, initially directed at heroin addiction, lumps marijuana in with harmful drugs and imposes mandatory minimum sentences. Marijuana is included at the urging of Anslinger, despite the testimony of Dr. Harris Isbell, the research director at the Public Health Service Hospital's "narcotics farm."

- 1956 – Similar to the Boggs Act, the **Narcotics Control Act** sets mandatory sentences for drug-related offenses including marijuana with a first offense for possession carrying 2-10 years and a fine up to $20,000.

- 1968 – The Bureau of Narcotics and Dangerous Drugs is created by a merger of the FBN and the FDA's Bureau of Dangerous Drugs

- 1970 - President Richard Nixon pushes for the **Controlled Substances Act** to classify drugs in schedules based on the potential for abuse, harmfulness, and known level of medical utility giving the power to schedule a drug to the Attorney General rather than to the Department of Health, Education, and Welfare. Meanwhile Congress repeals most of the mandatory penalties for drug offenses.

- 1971 - Specifically to study and determine marijuana's proper classification in the schedules, Nixon creates the nearly all-Republican *Presidential Commission on Marihuana and Drug Abuse* appointing Ray Shafer, former Pennsylvania Governor.

- 1972 - ***The Shafer Commission***, in a 1,184-page report, concludes marijuana "carries minimal risk to public health," is not a gateway drug, while tobacco and alcohol are, and concludes marijuana should not only be rescheduled but decriminalized. Nixon disowns his own

Commission's findings and announced that “America's public enemy number one is drug abuse” keeping marijuana a Schedule I drug.

- 1973 – The **Drug Enforcement Agency** is created by a merger of the Bureau of Narcotics and Dangerous Drugs and the office of Drug Abuse Law Enforcement.

- 1976 – Robert Randall sued the federal government for the right to use cannabis to treat his glaucoma, and — backed by science — wins. But the government will not let him grow his own supply, instead launching the **Compassionate Investigational New Drug Program**.

- 1979 – Texas enacts a tetrahydrocannabinols “Therapeutic Research Program” — which passes out of the House on the consent calendar — to allow participation for cancer and glaucoma patients in the federal Compassionate Investigational New Drug Program. The program appears to have never been implemented by the health department but is codified at Health & Safety Code ch. 481.

- 1986 – the **Anti-Drug Abuse Act** reinstates mandatory minimum sentences. Possession of 100 marijuana plants receives the same penalty as 100 grams of heroin. Later amended to provide the ‘three strikes and you’re out” policy providing life sentences.

- 1988 – In response to a petition to reschedule marijuana, DEA administrative law judge Francis Young concludes: “In strict medical terms marijuana is far safer than many foods we commonly consume. For example, eating 10 raw potatoes can result in a toxic response. By comparison, it is physically impossible to eat enough marijuana to induce death. Marijuana in its natural form is one of the safest therapeutically active substances known to man." Young finds that its Schedule I classification is "unreasonable, arbitrary and capricious." On appeal, her ruling does not survive agency deference to the DEA.

- 1994 – John Ehrlichman gives an interview to Dan Baum who was researching a book on drug policy, and admits: “You want to know what this was really all about. The Nixon campaign in 1968, and the Nixon White House after that, had two enemies: the antiwar left and black people. You understand what I'm saying. We knew we couldn't make it illegal to be either against the war or black, but by getting the public to associate the hippies with marijuana and blacks with heroin, and then criminalizing both heavily, we could disrupt those communities. We could arrest their leaders, raid their homes, break up their meetings, and vilify them night after night on the evening news. Did we know we were lying about the drugs? Of course we did.” Baum doesn’t publish the quote until a 2016 Harper’s Magazine article.

- 2007 - Brian Vicente sues on behalf of Damien LaGoy, an AIDS and Hepatitis C patient to secure safe access to medical marijuana by challenging a Colorado rule limiting caregivers to five patients each. The *LaGoy* case prompts a dramatic revision of medical marijuana regulations in Colorado to make the medicine more accessible to patients.

- 2013 - **Cole Memorandum** declares that Department of Justice (DOJ) will defer to state and local law enforcement to address marijuana issues in states with "strong and effective regulatory and enforcement systems to control the cultivation, distribution, sale and possession of marijuana" allowing medical marijuana programs to continue.

- 2015 – Texas passes the Compassionate Use Act to allow "low-THC" cannabis for "intractable epilepsy" only and cannabis of < 0.5% THC only

- 2018 – U.S. Attorney General Jeff Sessions rescinds the Cole Memorandum, but the **Rohrabacher-Blumenauer Amendment** continues to prevent the DOJ from spending any funds to interfering with state-legal medical cannabis programs or participants. Thirty-one states (plus the District of Columbia, Puerto Rico and Guam) have legalized cannabis for medical purposes, fifteen have CBD/low-THC programs like the Texas, and nine have adult use, leaving only four states with no legal program at all.

- 2018 – President Trump signs the 2018 Farm Bill which de-schedules and legalizes hemp and cannabinoids derived from hemp except for D9-THC <0.3% at a federal level.

- 2019 – Texas passes a hemp law and expands TCUP to allow all seizure disorders, MS, spasticity, ALS, autism, terminal cancer and "incurable neurodegenerative disease" but does not raise the THC cap

- 2021 – Texas raises the TCUP THC cap to 1%, adds PTSD and medical research. Cancer patients no longer have to be dying

- 2025 – Texas adds chronic pain, TBI, Crohn's/IBS, hospice & palliative care. Changes 1% THC cap to 10 mg "per dosing unit"

A Cannabis Western Scientific Timeline

- 1839 – Irish physician Dr. W.B. O'Shaughnessy introduces cannabis as medicine to Europe after working for the British East India Company promoting it for its analgesic, sedative, anti-inflammatory, antispasmodic, and anticonvulsant effects.

- 1890 – Dr. J. Russell Reynolds publishes an article in *Lancet* calling cannabis "when pure and administered carefully" "one of the most valuable medicines we possess." He recounts his success in treating patients for dementia, depression, neuralgia, migraines, and epilepsy. He cautions that dosages should be adjusted for individual patients as different people react differently to the same dosage.

- 1893 – The British government establishes the Indian Hemp Drugs Commission to study cannabis use in India which produces a lengthy report a year later on the medical and sociological practices and effects. The report concludes that "the moderate use of hemp drugs is practically attended by no evil results at all."

- 1940s – First cannabinoids identified, CBD and CBN.

- 1942 – Cannabis removed from the U.S. Pharmacopoeia.

- 1964 – Working in Israel, the only western country allowing cannabis research, Dr. Raphael Mechoulam determines THC's structure.

- 1980 – Mechoulam publishes positive results on the use of CBD on epileptics.

- 1986 – Synthetic delta-9-THC approved by the FDA under the trade name Marinol (dronabinol generically); the DEA sets Marinol as Schedule II.

- 1988 – First endocannabinoid receptor, CB1, identified.

- 1992 – The first endocannabinoid, Anandamide (the bliss molecule), an endogenous ligand for cannabinoid receptors identified.

- 1993 – A second endocannabinoid receptor, CB2, identified.

- 1995 – 2-arachidonoylglycerol (2AG), a second endocannabinoid identified.

- 2017 – National Academy of Sciences calls for removing research barriers for cannabis.

- Oct. 2025 – a search of « cannabis » in PubMed.com returns in excess of 39,000 articles (up from 19,000 in 2019).

Medical Cannabis Cultivation Stages

Mother

- Each stage takes place in a different room so the climate can be precisely controlled
- Genetics safeguarded
- Female "Mother" plant for each strain cultivated kept in controlled state to provide cuttings or tissues from which cloned plants are grown

Propagation

- Growth cultivated from cuttings or tissue cultures (not seeds)
- Monitored carefully to guard against disease and promote health
- Trimmed to promote growth and thinned to select the best specimens

Vegetation

- Once roots form, each plant is moved to vegetation for growth phase, kept under specialized lights
- Climate control maintains desired growing conditions
- Plants are monitored daily and trimming continues

Bloom

- A change in light patterns triggers flowering and plant maturity
- Continue to monitor each plant closely for disease, mildew, or other quality issues
- Cannabinoid-rich resin forms on flowers
- Timing of harvest affects cannabinoid profile

Harvest, Dry, Cure, Trim

- Entire plant is harvested and wet weighed
- Plants are slowly and carefully dried and cured with climate carefully monitored to avoid mildew and other possible failures; dry weighed when cured (~10% of wet weight)
- Skilled-labor intensive trimming of plant material to separate leaves from flower

Store & Secure

- Stored in food-quality containers which must be periodically burped until curing is complete
- Final plant product secured in locked safe room with limited access
- Stored until production demand requires its use

Processing & Packaging

- Multiple methods of extraction and processing each of which will have a different yield of product
- Tested to determine cannabinoid and terpene profile and to screen for pesticides and other contaminants
- As demand requires, packaged for distribution

Glossary

Δ^9-tetrahydrocannabinol (THC)—the main naturally occurring psychoactive constituent of cannabis.

adjusted odds ratio (aOR)—an odds ratio that controls for confounding variables.

Ashworth scale—a clinical measure of muscle spasticity based on an assessment of a patient's muscle tone in different muscle groups.

association—the statistical relation between two or more events, characteristics, or other variables.

broad spectrum – Contains naturally occurring compounds like full spectrum hemp extract but manufacturers remove all or most of the THC. This process also may remove minor (non-intoxicating) cannabinoids which hinders efficacy. May contain trace amounts of THC.

bud—the flower of the cannabis plant.

cannabidiol (CBD)—a constituent of cannabis that has been traditionally considered non-psychoactive.

cannabinoid—one of a class of chemical compounds that act on cannabinoid receptors, cannabinoids can be naturally derived from the cannabis plant or manufactured.

cannabis—a broad term that can be used to describe the various products and chemical compounds derived from the *Cannabis sativa* or *Cannabis indica* species.

cannabis use disorder (CUD)—according to the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, a problem-causing pattern of cannabis use leading to clinically significant impairment or distress, as manifested by at least two distinguishing symptoms (e.g., cannabis is taken in larger amounts or for longer periods than intended; experience of craving; continued cannabis use despite the experience of physical, social, or interpersonal problems caused by cannabis use) occurring within a 12-month period.

case series—an analysis of a series of people with the disease (there is no comparison group in case series). Case series studies provide weaker evidence than case-control studies.

case-control study—an observational analytic study that enrolls one group of persons with a certain disease, chronic condition, or type of injury (case-patients) and a group of persons without the health problem (control subjects) and compares differences in exposures, behaviors, and other characteristics to identify and quantify associations, test hypotheses, and identify causes.

clones—cuttings taken from a mother plant then grown into adult plants. Using clones rather than seeds to propagate plants keeps the genetics more consistent.

cohort study—an observational analytic study in which enrollment is based on one's status of exposure to a certain factor or membership in a certain group. Populations are followed, and disease, death, or other health-related outcomes are documented and compared. Cohort studies can be either prospective or retrospective.

comparator—the agent to which the experimental arm of a study is compared (e.g., placebo, usual care, active control).

control—comparator against which the study treatment is evaluated (e.g., concurrent [placebo, no treatment, dose–response, active], and external [historical, published literature]).

converted cannabinoids — cannabinoids converted from another substance, often CBD, that occur in nature. Manufacturers convert rather than extract because it is more cost effective.

cross-sectional study—a study in which a sample of persons from a population are enrolled and their exposures and health outcomes are measured simultaneously; a survey.

cultivar—a plant variety that has been produced in cultivation by human-selective breeding that requires asexual propagation such as by cuttings or graftings to remain genetically consistent. E.g., a granny smith apple

dose—the quantity of a drug that is used at one time or in fractional amounts during a given period of time.

dronabinol—a synthetic cannabinoid for oral administration, similar to tetrahydrocannabinol (THC). It is the active ingredient in Marinol®.

endocannabinoids — cannabinoids produced naturally in the body of animals

The Entourage Effect — a term to describe how the components of cannabis work together to have a better therapeutic effect than any one component alone

evidence—information on which a conclusion about a cause-effect relationship is based. The most direct evidence for health effects in humans is usually based on studies of health endpoints that are conducted in humans, including randomized trials and nonrandomized epidemiologic studies. Additional evidence can be provided by studies of intermediate endpoints or markers in humans as well as by nonhuman studies.

exclusion criteria—a list of characteristics in a protocol, any one of which may exclude a potential subject from participation in a study.

full spectrum—Hemp extract rich in cannabidiol (CBD) which contain all natural cannabis plant compounds — cannabinoids, terpenes, and flavonoids. Contains small amounts (under 0.3%) of Δ9-tetrahydrocannabinol (THC).

hazard ratio (HR)—the weighted relative risk of an outcome (e.g., death) during the entire study period; often reported in the context of survival analysis.

health effects—the positive and negative health outcomes resulting from exposure to cannabis or cannabis-derived products.

immature plant— a plant that has not yet flowered and does not have buds

incidence—the number of new cases of a condition, symptom, death, or injury that develop during a specified period of time.

inclusion criteria—the criteria in a protocol that prospective subjects must meet to be eligible for participation in a study.

isolate – A pure form of a cannabinoid such as CBD which contains 0% THC. Does not contain any terpenes or flavonoids.

marijuana—a *Cannabis sativa* plant-derived product typically composed from the plant's dried leaves, stems, seeds, and buds with a THC content above 0.3% by dry weight.

meta-analysis—a statistical technique for combining (pooling) the results of a number of studies that address the same question and report on the same outcomes to produce a more precise summary estimate of the effect on a particular outcome. Meta-analyses are frequently used in systematic reviews.

morbidity—any departure, subjective or objective, from a state of physiological or psychological health and well-being (e.g., disease, injury, disability).

mortality—death or loss of life.

nabilone—a synthetic cannabinoid for oral administration, similar to tetrahydrocannabinol (THC). It is the active ingredient in Cesemet®.

narrative review—narrative reviews tend to be mainly descriptive, do not involve a systematic search of the literature, and thereby often focus on a subset of studies in an area chosen based on availability or author selection. Generally, narrative reviews offer lower-quality evidence than systematic reviews.

novel cannabinoids—cannabinoids that are manufactured and do not occur in nature

observational study—a study in which the investigator observes rather than influences exposure and disease among participants. Case-control and cohort studies are examples of observational studies.

odds ratio (OR)—one measure of treatment effectiveness. It is the odds of an event happening in the experimental group expressed as a proportion of the odds of an event happening in the control group. The closer the OR is to 1, the smaller the difference in effect is between the experimental intervention and the control intervention. If the OR is greater (or less) than 1, then the effects of the treatment are more (or less) than those of the control treatment. Note that the effects being measured may be adverse (e.g., death or disability) or desirable (e.g., survival). When events are rare, the OR is analogous to the relative risk (RR), but as event rates increase, the OR and RR diverge.

outcome—events or experiences that clinicians or investigators examining the impact of an intervention or exposure measure because they believe such events or experiences may be influenced by the intervention or exposure.

phytocannabinoids — cannabinoids produced naturally by plants

pooled estimate—an average derived from multiple studies with varying data but with a common measurement. Typically found in systematic reviews and meta-analyses.

potency—the amount of drug required to produce a specific level of effect.

preclinical—research studies that use cell culture or animal models to test scientific hypotheses. These studies are performed prior to clinical studies that use human subjects.

prevalence—the number or proportion of individuals within a given population who share a specific characteristic.

primary literature—peer-reviewed accounts of original research that contribute new evidence to science. By comparison, systematic reviews and literature reviews analyze existing evidence. Examples of the types of primary literature used in the report are randomized controlled trials, cohort studies, cross-sectional studies, case-control studies, and case series.

problem cannabis use—a symptom of cannabis use disorder. Problem cannabis use includes the experience of persistent or recurrent social, interpersonal, occupational, academic, recreational, psychological, or physical problems caused or exacerbated by cannabis use.

randomized controlled trial (RCT)—a trial in which participants are randomly assigned to one of two or more groups, at least one of which (the experimental group) receives an intervention that is being tested and another (the comparison or control group) receives an alternative treatment or placebo. This design allows assessment of the relative effects of interventions.

relative risk (RR)—a ratio of the risk of an event among an exposed population to the risk among the unexposed.

Rohrabacher-Farr or Rohrabacher-Blumenauer Amendment—a rider on the federal omnibus spending bill that prohibits DOJ from spending funds to interfere with state-legal medical cannabis programs, rendering them as a practical matter quasi-legal.

route of administration—the path by which a drug is taken into the body.

Section 280E—a provision of the Internal Revenue Code that prohibits deduction of expenses for "marihuana distribution" making it very difficult to turn a profit with marijuana dispensaries and other state-legal operations.

synthetic cannabinoids—cannabinoids that are manufactured artificially. This term is also used to describe "novel cannabinoids" meaning those that do not occur in nature.

systematic review—research that summarizes the evidence on a clearly formulated question according to a predefined protocol. Systematic and explicit methods to identify, select, and appraise relevant studies and to extract, collate, and report their findings are used. Statistical meta-analysis may or may not be used. Systematic reviews were the optimal data source for identifying associations between cannabis exposure and all of the health endpoints discussed in this report.

titration—determining how much of a substance is needed to reach a desired effect. Self-titration is when a patient can control their consumption precisely and consume only as much as needed to reach a desired effect

trim—the trimmings of a cannabis plant, largely from leaves.

variety —a naturally occurring, genetically distinct plant population within a species that produces offspring true to its type.