

As High As The Rockies – The Canadian Marijuana Opportunity

The Marijuana Opportunity Is As High As The Rockies – Looking At The Large Market Potential

The Canadian marijuana market is expected to grow fast and based on our model, it is still well under-penetrated, leaving room for significant growth and potential new entrants (assuming their facilities can be financed). **We have forecast the peak Canadian marijuana market size to be over C\$2.5B in 2020, assuming full legalization down the road (over C\$1.1B in 2020 without full legalization) - some of these sales are being cannibalized to the black market via dispensaries.** Details of each segment within this industry are provided in this report, as **we have constructed a detailed marijuana model to look at the Canadian opportunity.** Our marijuana model assumes that the Canadian market would follow a similar growth trajectory and market penetration trend as has occurred in Colorado and Oregon. We have done a price sensitivity analysis of four different marijuana prices, looking at the total Canadian market size. Even if investors assume that our estimates are too high and assume our numbers are 50% lower than modelled estimates, the market potential is significant.

Medical Marijuana Is Regulated By MMPR – The Good & The Bad

The Marihuana for Medical Purposes Regulations (MMPR), overseen by Health Canada, authorizes three key activities: (i) the possession of dried marijuana (or oil) for medical purposes by eligible patients, who have the support of an authorized healthcare practitioner; (ii) the production of dried marijuana or oil by licensed producers; and, (iii) the sale and distribution of dried marijuana or oil by licensed producers to eligible patients. By strictly regulating the medical marijuana industry, MMPR helps ensure a safe and consistent product. However, due to the added incurred expenses imposed by the MMPR, we believe investors should focus on low cost producers.

The Path of Legalization is Not Clear; However, It was a Liberal Government Campaign Promise

One of the reasons the Liberal government was elected in Canada was due to their campaign promise to legalize marijuana. Nanos Research was commissioned by the Globe & Mail to survey 1,000 Canadians. According to this survey, just over two thirds of Canadians support marijuana legalization. Canada is a member country of three international treaties criminalizing possession and production of non-medical marijuana: The Single Convention on Narcotic Drugs of 1961, as amended by the 1972 Protocol; The Convention on Psychotropic Substances of 1971; and The United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988. The Canadian government needs to navigate and comply with these three international treaties. **While the majority of Canadians support legalization, the path is not clear and the Federal government with a Liberal majority may have a difficult time steering around three international treaties.** From April 19-21, 2016, the United Nations is scheduled to hold a "General Assembly Session on the World Drug Problem" (UNGASS) – the legalization of marijuana is on that agenda. Due to the massive deficit being taken on, the Canadian government needs to find new sources of revenue including possible taxation of legalized marijuana. If the Federal government wants to maximize its tax revenue, it would likely have to shut down illegal dispensaries.

Marijuana – The Active Chemicals And Medical Science

In this report, **we have reviewed some of the scientific and medical literature, the botany, the chemistry and the science of why cannabis is a viable treatment option for certain medical conditions, such as pain management.**

A Big Opportunity Always Has Risks

One of the key risk factors for the industry focuses on the willingness of physicians to prescribe medical marijuana to patients. Risks also include execution of management teams in their build-out capacity, patient acquisition costs, financial capacity to implement plans, as well as if legalization is prevented by world treaties. If a significant number of limited producers are approved by MMPR, the industry could see pricing pressure.

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Note: All financial figures in this report are in Canadian dollars, unless stated otherwise.

CANADA - MMPR – MEDICAL MARIHUANA PURPOSES REGULATIONS

The Marihuana for Medical Purposes Regulations (MMPR) came into effect April 2014 and is overseen by Health Canada.

Specifically, Health Canada via the MMPR authorizes **three key activities**:

- the possession of dried marijuana (or oil) for medical purposes by eligible patients, who have the support of an authorized healthcare practitioner;
- the production of dried marijuana or oil by licensed producers; and,
- the sale and distribution of dried marijuana or oil by licensed producers to eligible patients.

The MMPR treats marihuana as a narcotic, which is used specifically for medical purposes by creating conditions for a new, commercial industry that is responsible for its production and distribution. The regulations create conditions for a commercial industry that is responsible for the production and distribution of marijuana for medical purposes. These regulations ensure Canadians with a medical need can access quality controlled marijuana grown under secure and sanitary conditions.

As of the date of this report, there are 30 MMPR licenses held by approximately 21 licensed producers (LPs). Of key importance is that there are over 1300 applicants in line for a license, and it typically can take one to two years to obtain a license. Security clearance is the biggest hurdle, but financing is also important as there are considerable costs in ensuring the facilities are compliant with government regulations.

Under the new process for medical marijuana under the MMPR, patients are no longer required to obtain a license to possess marijuana from Health Canada. Patients are required to obtain a “medical document” (similar to a drug prescription) from their physician or nurse practitioner (if allowed by provincial legislation). Once the patient has their medical document they can then provide this to the Licensed Producer (LP) from which they wish to purchase medical marijuana. To change Licensed Producers, the client must obtain a new medical document and re-submit all materials to the new Licensed Producer.

Licensed Producers are not allowed to market their products to the public, this is referred to as direct to consumer marketing (DTC). On June 30, 2014, Health Canada provided an advertising bulletin to all Licensed Producers outlining their concerns regarding the use of promotional materials and advertisements. LPs are allowed to promote their medical marijuana products to physicians in the same manner as pharmaceutical companies do for their drugs.

The MMPR also provides that Licensed Producers are allowed to sell to each other in order to overcome potential short y and demand imbalances.

Dispensaries are not currently being regulated by MMPR. Should patients be concerned?

Some patients are sourcing product from marijuana dispensaries which are operating illegally in Canada (black market). These dispensaries are not currently being regulated by the MMPR. It is quite possible that the marijuana being purchased by patients from these dispensaries could have issues with illegal pesticide/fungicide/bactericide chemicals (potentially resulting in health issues) as the growth and production facilities are not being carefully monitored by MMPR. Why should patients be worried by lack of dispensary regulation by the MMPR? In Colorado, marijuana was pulled from the market due to unapproved pesticide use. For example, if myclobutanil, a fungicide was being used during marijuana production in high doses – that chemical can turn into cyanide when it is heated (smoked).

THERE HAS BEEN A LONG HISTORY OF MEDICAL MARIJUANA USE

Marijuana made its first appearance, in our known history, about 10,000 years ago in China and Taiwan. In 140 – 208 AD, the ancient Chinese doctor Hua Tuo was the first recorded person to use cannabis as an anesthetic. He mixed a cannabis powder with wine for the patient to imbibe prior to surgery. Because of its widespread usefulness, cannabis became one of the 50 “fundamental” herbs in traditional Chinese medicine. There was extensive medical cannabis in ancient Egyptian culture and India for a wide spectrum of medical ailments.

Medical cannabis use was first integrated into Western medicine in the mid 19th century. Cannabis was the main ingredient in many “wonder” potions, which were said to help with everything from muscle spasms, stomach cramps to general pain relief.

Selected Key Events of Medical Marijuana in North America (U.S. and Canada)

In the United States:

- 1906: Marijuana was criminalized
- 1978: New Mexico passes the first state law recognizing the medical value of marijuana.
- 1996: California becomes the first state to legalize medical marijuana. Legalization of medical marijuana in other states is summarized below:
- 1998: Alaska, Oregon, Washington
- 1999: Maine
- 2000: Colorado, Hawaii, Nevada
- 2004: Montana
- 2006: Rhode Island
- 2007: New Mexico, Vermont
- 2008: Michigan
- 2010: Arizona, New Jersey
- 2011: Delaware, Washington, D.C.
- 2012: Connecticut, Massachusetts
- 2013: New Hampshire, Illinois
- 2014: Maryland, Minnesota

To date, a total of 23 states and Washington D.C. have legalized marijuana for medical use. Seven states have pending legislation.

In Canada:

According to an October, 2014 report by the Centre for Addiction and Mental Health, Canada has one of the highest rates of cannabis use in the world. More than 40% of Canadians have used cannabis in their lifetime and about 10% have used it in the past year. No other illegal drug is used by more than 1% of Canadians every year.

- 1923: Cannabis was criminalized and added to the Schedule of the Opium and Narcotic Control Act.
- 1969: Canadian government established a Commission of Inquiry Into the Non-Medical Use of Drugs, known as the Le Dain commission after its chairman, Gerald Le Dain.
- 1972: The Le Dain commission recommended decriminalizing simple cannabis possession and cultivation for personal purposes.
- 1999: Two Canadian patients got the federal OK to smoke pot.
- 2000: Court ruled that Canadians had a constitutional right to use cannabis as a medicine.
- 2001: Canadian Medical Marijuana Access Regulations (MMAR) granted legal access to cannabis for individuals with HIV/AIDS and other illnesses. Since then, authorized patients can grow their own marijuana or obtain it from authorized producers.
- 2013: New regulations (Marijuana for Medical Purposes Regulations, “MMPR”) changed the Canadian medical marijuana access rules, shifting to licensed commercial growers for supply and away from homegrown operations.

- 2014: The federal government said the unforeseen growth of its medical marijuana program has “seriously compromised” the goal of providing the drug to patients while ensuring public safety. According to the Federal documents, the number of people authorized to possess marijuana under the federal program has risen to 37,000 in 2015 from fewer than 100 in 2001. Patients and producers authorized under the old regulations (MMAR) were required to destroy stocks of pot and cannabis seeds, although a Federal Court had granted a temporary injunction allowing continued use of home-grown medical marijuana until legal arguments could be heard.

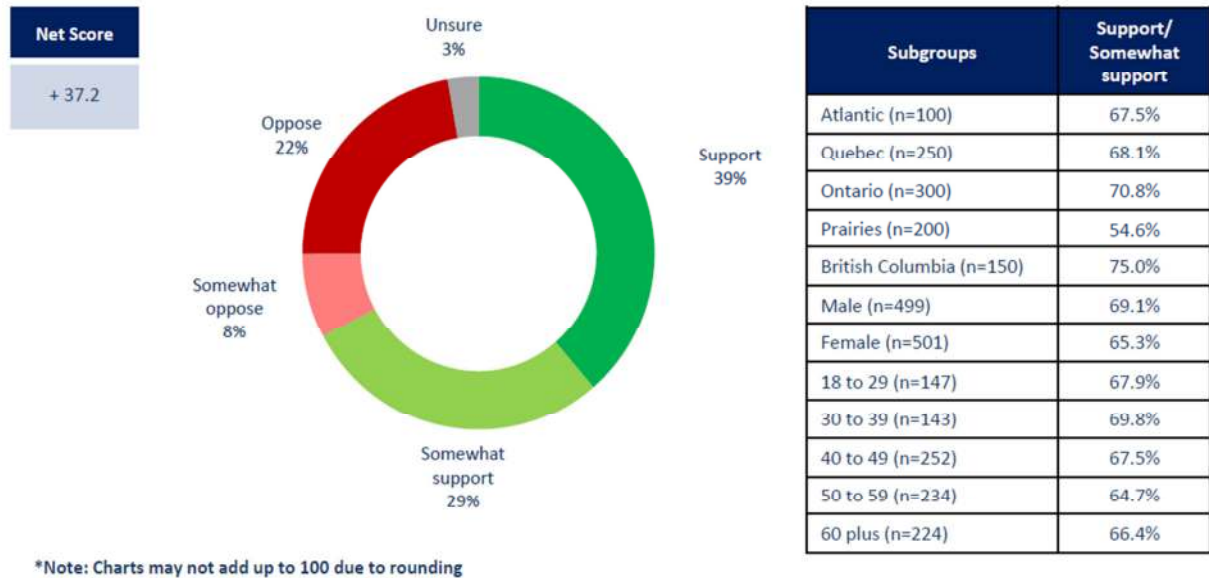
Globe & Mail/Nanos Research Survey Indicates Majority of Canadians Favour Legalization

Nanos Research was commissioned by the Globe & Mail to conduct a telephone and online random survey of 1,000 Canadians, 18 years of age or older, between February 22nd and 24th, 2016 as part of an omnibus survey. Participants were randomly recruited by telephone using live agents and administered a survey online. The sample included both land- and cell-lines across Canada. The results were statistically checked and weighted by age and gender using the latest Census information and the sample was geographically stratified to be representative of Canada.

Here were the key results of the Nanos survey:

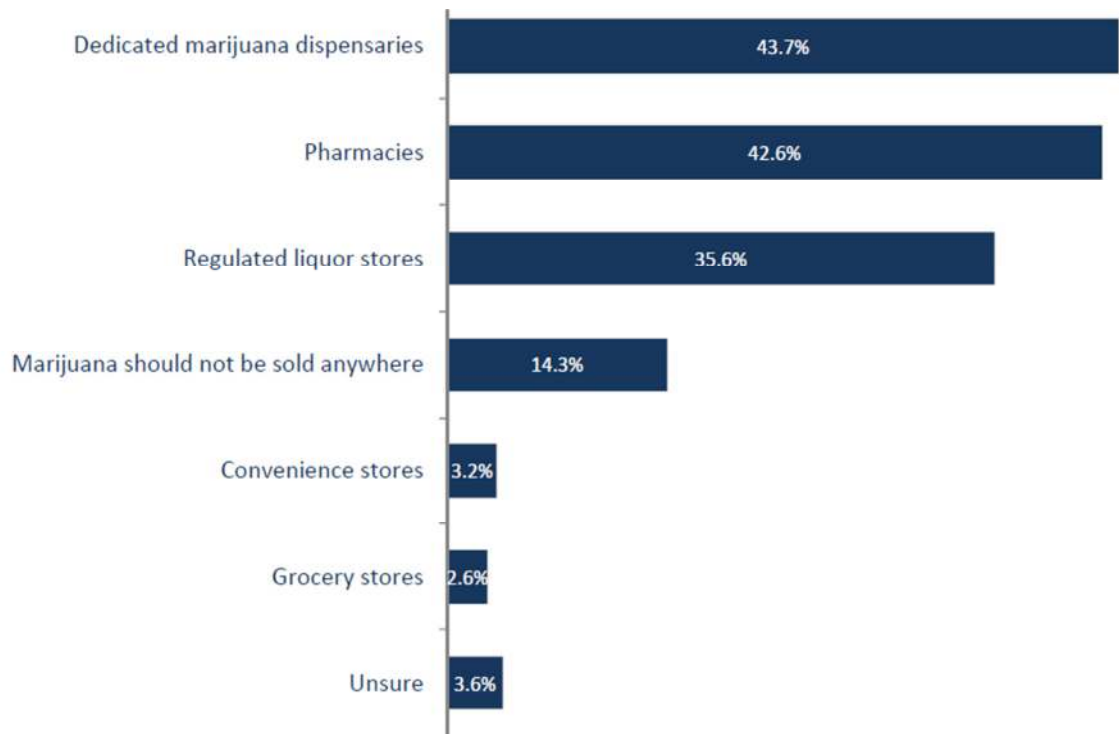
- Support for legalization of marijuana – Just over two thirds of Canadians support (39%) or somewhat support (29%) the legalization of marijuana, while 30% somewhat oppose (eight percent) or oppose (22%) legalization.
- Growing marijuana at home – Canadians are split in terms of whether or not people should be able to grow marijuana in their homes, with 49% who somewhat agree (24%) or agree (25%) that this should be allowed, while 12% somewhat disagree and 36% disagree.
- Marijuana as a “gateway drug” – Thirty-nine percent of Canadians either agree (19%) or somewhat agree (21%) that marijuana is a gateway drug that could lead to more harmful drugs, while 20% somewhat disagree and 37% disagree that marijuana is a gateway drug.
- Marijuana use among youth – Just over half of Canadians (51%) either somewhat agree (20%) or agree (30%) that legalizing recreational marijuana will lead to more young people (21 and younger) using the drug. Eighteen percent of Canadians somewhat disagree and 27% disagree with this statement.
- Points of sale for marijuana – Canadians would prefer that marijuana be sold through either dedicated dispensaries (44%) or pharmacies (43%), followed by regulated liquor stores (36%). Three percent of Canadians think marijuana should be sold through grocery stores, while 14% believe marijuana should not be sold anywhere.

Figure 1: Support for Legalizing Marijuana



Source: The Globe and Mail/Nanos Research, RDD dual frame hybrid telephone and online random survey, February 22nd to 24th, 2016, n=1000, accurate 3.1 percentage points plus or minus

Figure 2: Where Should Marijuana Be Sold?



Source: The Globe and Mail/Nanos Research, RDD dual frame hybrid telephone and online random survey, February 22nd to 24th, 2016, n=1000, accurate 3.1 percentage points plus or minus

These survey results are similar to The Harris Poll that was conducted in the U.S. and press released on May 7, 2015. A total of 2,221 American adults were surveyed online between February 11 and 17, 2015 by The Harris Poll. Currently, four in five adults (81%) favor legalizing marijuana for medical use, up from 2011 when three quarters of Americans (74%) indicated the same. Meanwhile, half of Americans are supportive of legalizing marijuana for recreational use (49%), up from the two fifths (42%) who felt that way in 2011.

Centre for Addiction and Mental Health (CAMH) - Minimum Requirements to Guide Regulation of Legal Cannabis Use

As Canada's leading hospital for mental illness, in an October, 2014 report, the Centre for Addiction and Mental Health (CAMH) offered evidence-based conclusions about cannabis and measures aimed at reducing harm. CAMH reviewed the evidence on cannabis control and have drawn the following conclusions:

- Cannabis use carries significant health risks, especially for people who use it frequently and/or begin to use it at an early age.
- Criminalization heightens these health harms and causes social harms.

A public health approach focused on high-risk users and practices – similar to the approach favoured with alcohol and tobacco – allows for more control over the risk factors associated with cannabis-related harm.

From these conclusions follows another:

- Legalization, combined with strict health-focused regulation, provides an opportunity to reduce the harms associated with cannabis use.

Regulating legal cannabis markets with improved public health as the main objective would be a complex undertaking spanning production, distribution (supply), and consumption (possession and use). In an October, 2014 report generated by the Centre for Addiction and Mental Health CAMH offered ten basic principles that the foundation believed should be used as minimum requirements to guide regulation of legal cannabis use:

- 1) **Establish a government monopoly on sales.** Control board entities with a social responsibility mandate provide an effective means of controlling consumption and reducing harm.
- 2) **Set a minimum age for cannabis purchase and consumption.** Sales or supply of cannabis products to underage individuals should be penalized.
- 3) **Limit availability.** Place caps on retail density and limits on hours of sale. Curb demand through pricing. Pricing policy should curb demand for cannabis, while minimizing the opportunity for continuation of lucrative black markets. It should also encourage use of lower-harm products over higher-harm products.
- 4) **Curtail higher-risk products and formulations.** This would include higher-potency formulations and products designed to appeal to youth.
- 5) **Prohibit marketing, advertising and sponsorship.** Products should be sold in plain packaging with warnings about risks of use.
- 6) **Clearly display product information.** In particular, products should be tested and labelled for THC and CBD (cannabidiol) content.
- 7) **Develop a comprehensive framework to address and prevent cannabis-impaired driving.** Such framework should include prevention, education, and enforcement.
- 8) **Enhance access to treatment and expand treatment options.** Include a spectrum of options from brief interventions for at-risk users to more intensive interventions.
- 10) **Invest in education and prevention.** Both general (e.g. to promote lower-risk cannabis use guidelines) and targeted (e.g. to raise awareness of the risks to specific groups, such as adolescents or people with a personal or family history of mental illness) initiatives are needed.

Risk of International Treaties Preventing Legalization

Canada is a member country of three international treaties criminalizing possession and production of non-medical marijuana, respectively. These three treaties are The Single Convention on Narcotic Drugs of 1961, as amended by the 1972 Protocol; The Convention on Psychotropic Substances of 1971; and The United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988. Article 3, paragraph 2 of the 1988 UN Convention requires that: “Each Party shall adopt such measures as may be necessary under its domestic law, when committed intentionally, the possession, purchase or cultivation of narcotic drugs or psychotropic substances for personal consumption contrary to the provisions of the 1961 Convention, the 1961 Convention as amended or the 1971 Convention.” (Marijuana is one such substance.) Besides domestic legalization, the Canadian government needs to figure out how to comply with the three international treaties. Although there is no international treaty where reservations cannot be made, the government has to explain why it’s doing it, why it feels it has to do it, and how it can benefit Canada in term of improving enforcement and decreasing crime rate. Global Affairs Canada, the lead government department on international treaties, has taken action to examine a range of international issues on fully legalizing marijuana. We expect the entire progress of reconciling the international compliance issues to take some time to work through.

What path(s) can the Liberal Government take to legalize marijuana in Canada and not face international repercussion?

1. Canada is a sovereign country - free to make its own laws through a democratically elected government in the House of Commons.
2. Other UN member countries have already improved their marijuana laws without sanction.
3. Canada can lead an international movement to amend international conventions to reflect changes in medical evidence and international marijuana consumption rates.
4. Canada has the right to withdraw from these UN conventions, as granted in the articles of each convention - exercisable by written notification to the UN Secretary-General. Withdrawal would take effect one year after the date of notification was received.

United Nations is going to be Looking at the Legalization of Marijuana

From April 19-21, 2016, the United Nations is scheduled to hold a “General Assembly Session on the World Drug Problem” (UNGASS) – legalization of marijuana is going to be on that agenda. At the meeting, several South American countries, as well as Mexico, plan on discussing what they perceive as more effective policy approaches to respond to the current realities of the drug problem, which could include decriminalization/legalization of illicit drugs (including marijuana), harm reduction and/or a call to renegotiate the international drug control treaties.

What Canadian Laws Need to Be Changed?

A new legal framework must repeal Schedule II of the Canadian Controlled Drugs and Substances Act, establish new penalties for operating outside of the legal system and create a new taxation and regulatory structure.

Government Taxation of Marijuana

Due to the massive deficit being taken on, the Canadian government needs to find new sources of revenue including possible taxation of legalized marijuana. If the Federal government wants to maximize its tax revenue, it would likely have to shut down illegal dispensaries. Looking at Colorado as an example, in 2014 and 2015, the state generated US\$76M and US\$134M of tax revenue from the marijuana industry, respectively. If illegal dispensaries continue, the government (and tax payers) could be losing on potential tax revenue.

Figure 3: Why The Federal Government has Incentives to Eventually Shut Down Dispensaries



Source: *Legalization of Marijuana – Policy Paper 2013 - Liberal Party of Canada in BC*

What is Cannabis?

Cannabis is a complex drug that is comprised of approximately 80 unique cannabinoids along with many other compounds. The main component in cannabis that is responsible for the psychoactive, or mood altering effects is called delta-9-tetrahydrocannabinol (THC). The level of THC in cannabis, and thus its potency, is not always consistent across the same plant nor necessarily between plants grown if they are different cultivars.

The way in which cannabis is grown can affect the amount of THC in the plant, and therefore the potency. Cannabis sativa is the species of plant that most commonly produces the preparations known as marijuana, hash or hashish. Female plants are usually grown in isolation, so the flowering tops of the plant remain unfertilised. These unfertilised flowering tops, known as sinsemilla, have particularly high THC levels. Crossbreeding and genetic modification can also produce cannabis plant strains which also lead to higher levels of THC.

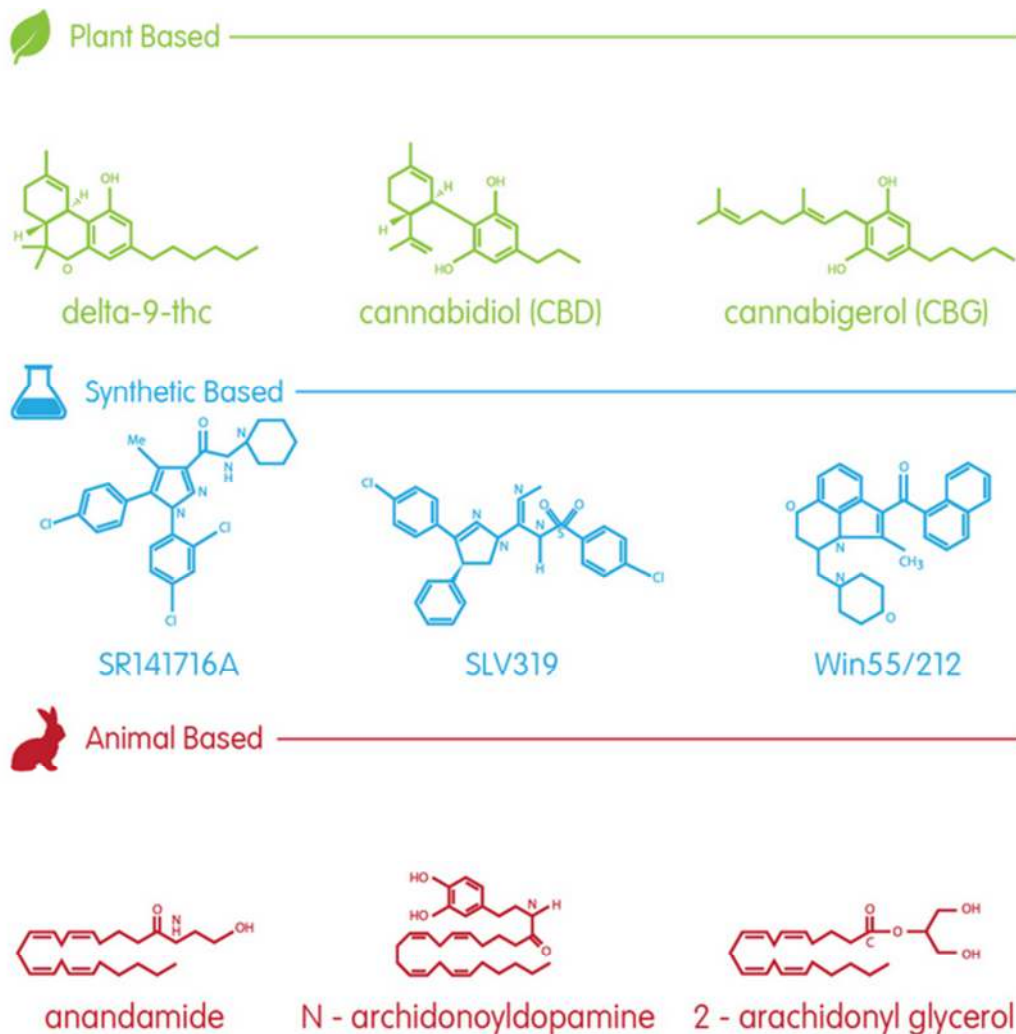
The flowering tops, or 'buds' of the female cannabis plant typically have the highest concentrations of THC, followed by the leaves. Much lower THC levels are found in the stalks and seeds of the cannabis plant and these are of minimal commercial value. The cannabis plant can be prepared in different ways for use, and these different forms have different potency.

The Science Behind Marijuana (Mechanism of Action and Pharmacokinetics)

Mechanism of Action: The extraction of active pharmaceutical ingredients (APIs) from marijuana plant has been done for centuries since the use of it. It was not until the 1930s and 1940s that Todd (*Todd AR. Nature. 1940*) in the UK and Adams (*Adams R, et al. J Am Chem Soc. 1941*) in the USA isolated pure APIs (cannabinoids) - mainly cannabidiol, various tetrahydrocannabinols (THC), and cannabichromene. They also showed that the only three isoforms of THC were responsible for the psychoactive effects and cannabidiol had other non-psychoactive pharmacological activity. Finally, Mechoulam (*Mechoulam R, et al. J Am Chem Soc. 1972*) in Israel, and Claussen and Korte (*Claussen U, et al. Z Naturforsch. 1966*) in Germany, achieved the complete synthesis of the pure APIs, established their molecular structures, and began the study of their structure-activity relationships. This work led to the synthesis of new cannabinoid derivatives and analogues that do not exist in nature. Armed with these pure and potent chemicals, Devane (*Devane WA, et al. Mol Pharmacol. 1988*) identified specific binding sites (cannabinoid receptors) of cannabinoids in the brain, and showed that the receptor-binding affinities of the different cannabinoid compounds paralleled their respective potencies of biological activity. Since cannabinoids themselves do not exist in the brain, the existence of the receptors implied that some other endogenous chemicals in the brain normally binds to them. Devane (*Devane WA, et al. Science. 1992*) later reported the isolation of anandamide (arachidonyl-ethanolamine), a lipid material related to prostaglandins, that is formed locally in the brain, binds to the these receptors, exerting actions similar to those of the cannabinoids but less potent. Arachidonyl-glycerol and several other such chemicals have been identified subsequently. As noted in Figure 3, cannabinoid molecules can be

produced by three pathways: 1) phytocannabinoids are produced by the Cannabis plant, 2) endocannabinoids are created by humans and animals, and 3) synthetic cannabinoids have been produced artificially by pharmaceutical companies.

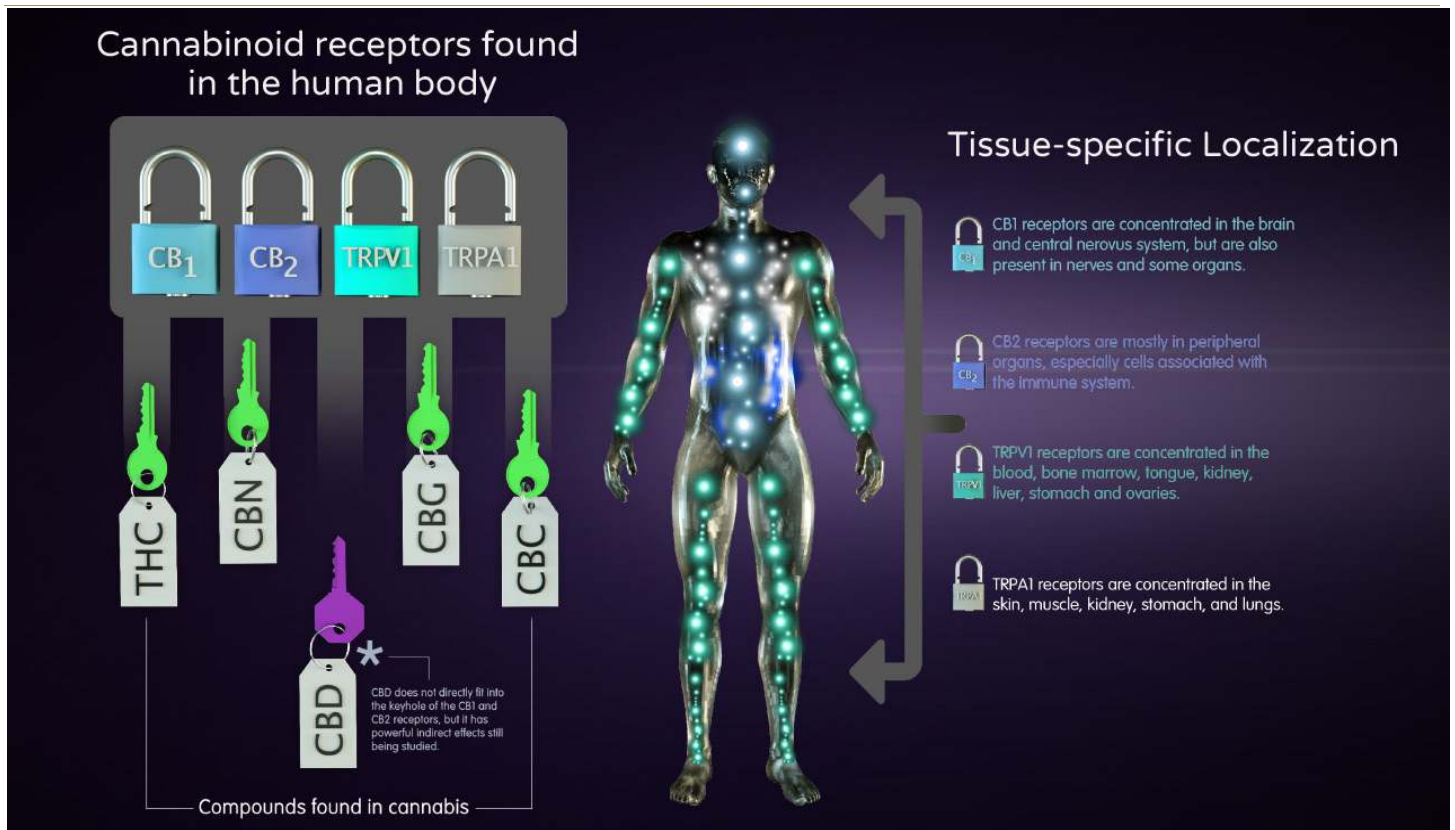
Figure 4: Sources of Cannabinoid Molecules



Source: GB Sciences

The cannabinoid (CB) receptors were found to be of at least two different types (Adams IB, et al. *Addiction*. 1996. & Howlett AC. *Ann Rev Pharmacol Toxicol*. 1995): the CB1 receptors present mainly in various parts of the brain (cerebral cortex, cerebellum, basal ganglia, limbic system, hypothalamus, hippocampus), and the CB2 receptors present exclusively in peripheral tissues such as the immune system, bone marrow, lung, pancreas and smooth muscle. Both receptor types are linked to the inhibitory G protein, through which they act to inhibit cAMP by decreasing adenylyl cyclase activity. Decreased cAMP prevents the activation of various Ca^{2+} channels in the cell membrane, while increasing K^+ influx. The functional results of CB receptors signaling vary in different types of neuron. Inhibitory neurons are activated by CB receptors, with increased GABA release (Pertwee RG. *Pharmacol Ther*. 1987); while in motor neurons cell excitability and neurotransmitter release are decreased. The isolation of the different types of receptor has made it possible to develop wholly synthetic compounds with high selective affinity for one or other type, some acting as agonists and others as antagonists. The availability of these receptor-specific ligands (cannabinoids and cannabinoids-related derivatives) has permitted rapid advances in analyzing the cellular mechanisms underlying various pharmacological effects of the cannabinoids.

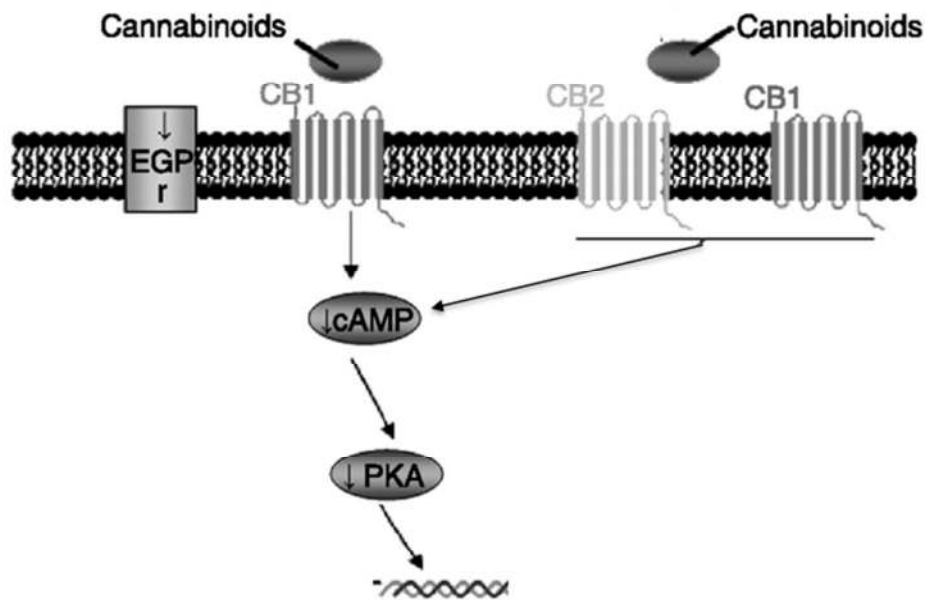
Figure 5: Location of Cannabinoids (CB) Receptors in the Body



Source: GB

Sciences

Figure 6: Cannabinoids (CB) Receptors Signaling Pathway

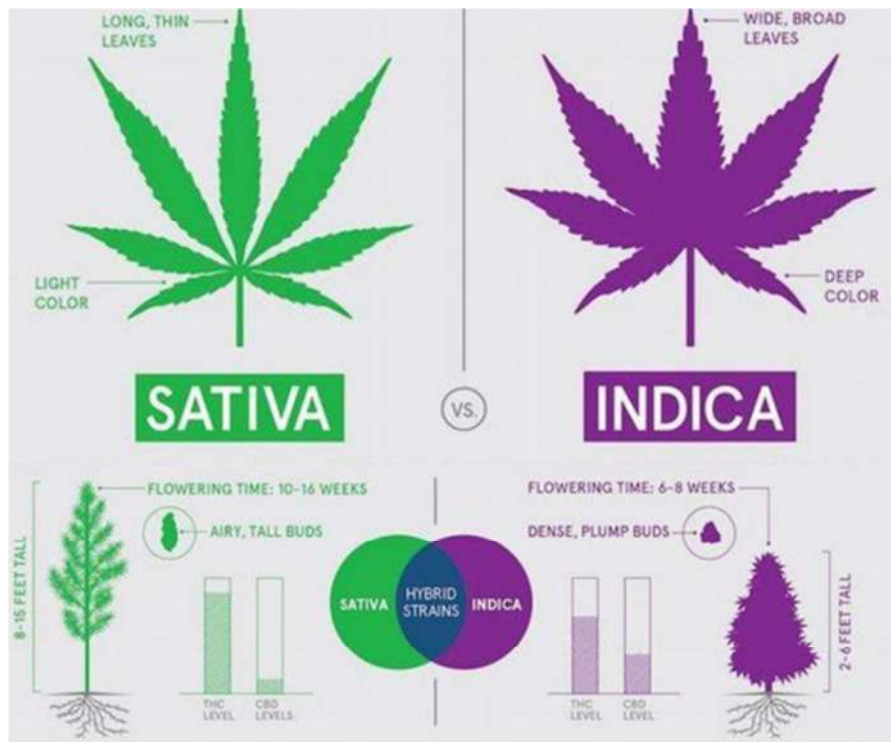


Source: Bifulco M, et al. *Endocr Relat Cancer*. 2008 (Adapted by Mackie Research Capital)

Marijuana has Two Different Species

There are two species of marijuana: *Cannabis indica* and *Cannabis sativa*. Cross-breeding of the two types has led to a wide variety of hybrid strains with unique characteristics. In Canada, there are approximately 60 phenotypes (observable characteristics, such as height, biomass, leaf shape etc) of marijuana plants that are being grown by the different LPs. The way to distinguish the two strains of marijuana, indica versus sativa, is by the plant morphology (appearance). Indica plants are short, densely branched and have wider leaves. Indica plants are better suited for growing indoors. Whereas sativa plants are tall, loosely branched and have long, narrow leaves. Sativa plants are usually grown outdoors and can reach heights of up to 20 feet.

Figure 7: Looking at the Morphology of Sativa vs. Indica Species



Source: Industry Sources adapted by MRCC

THC is a measure of Cannabis potency

The amount of tetrahydrocannabinol (THC) present in a cannabis sample is generally used as a measure of cannabis potency. Based on information from the UNODC World Drug Report 2009 series, the secretion of THC is most abundant in the flowering heads and surrounding leaves of the cannabis plant. Specifically, the THC content varies in the different parts of the plant: from 10-12 per cent in flowers, 1-2 per cent in leaves, 0.1-0.3 per cent in stalks, to less than 0.03 per cent in the roots. The amount of resin secreted is influenced by environmental conditions during growth (light, temperature and humidity), sex of the plant and time of harvest.

What Are Terpenes?

Terpenes are fragrant organic compounds (oils) that give cannabis its aromatic diversity. Between 10% and 30% of cannabis extracts are composed of terpenes, which are aromatic molecules produced in the resin of the plant. Many terpenes affect the aroma and flavor profile of cannabis.

As noted in Figure 7, the average content of different terpenes by mg/g in flowers entrants in either indica or sativa categories is shown. Sativas typically have higher myrcene and terpinolene, while linalool, limonene and caryophyllene predominate in the indicas. A U.S. company, Steep Hill labs has indicated that any strain with more than 0.5% myrcene is an indica and anything less is a sativa.

Figure 8: Typical Concentrations of Terpenes in Indica and Sativa Cannabis Strains (mg/g)

Terpene	Strain	
	Indica	Sativa
Myrcene	4.4	7.6
Terpinolene	0.1	3.4
Linalool	1.2	0.4
Limonene	3.6	1.3
Caryophyllene	4.6	2.6

Source: *Industry Sources*

Limonene (a Terpene) – Strong Smell of Oranges

Limonene is a colorless liquid hydrocarbon classified as a cyclic terpene. The more common d-isomer possesses a strong smell of oranges. In natural and alternative medicine, d-limonene is marketed to relieve gastroesophageal reflux disease and heartburn. Some natural homeopathic medicines utilize limonene to help promote weight loss, prevent and treat cancer, and treat bronchitis.

Figure 9: Structure of Limonene

Source: *PubChem*

Myrcene (a Terpene) – Pleasant Smell

Myrcene has an analgesic effect and is believed to be key product responsible for the medicinal properties of lemon grass tea. Myrcene's anti-inflammatory properties are derived by stimulating prostaglandin E2 which suppresses T cell receptors.

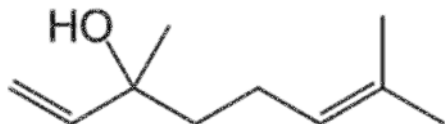
Figure 10: Chemical Structure of Myrcene

Source: *PubChem*

Linalool (a Terpene) - Floral Scent

Linalool is a naturally occurring terpene alcohol chemical.

Figure 11: Structure of Linalool

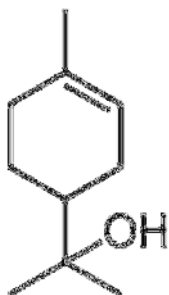


Source: PubChem

Terpineol - Lilac and Pine Needle Scent

Terpineol is a naturally occurring monoterpene alcohol that has antibacterial properties.

Figure 12: Structure of Terpineol

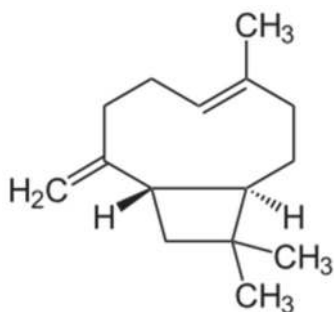


Source: PubChem

Caryophyllene

Caryophyllene is a natural bicyclic sesquiterpene that is an FDA approved food additive. Caryophyllene is the primary terpene that contributes to the spiciness of black pepper and also a major terpene in cloves, hops, rosemary, and cannabis. Caryophyllene has shown to have various medicinal properties such as anticancer activity, anti-inflammatory and analgesic (pain relief).

Figure 13: Chemical Structure of Caryophyllene



Source: PubChem

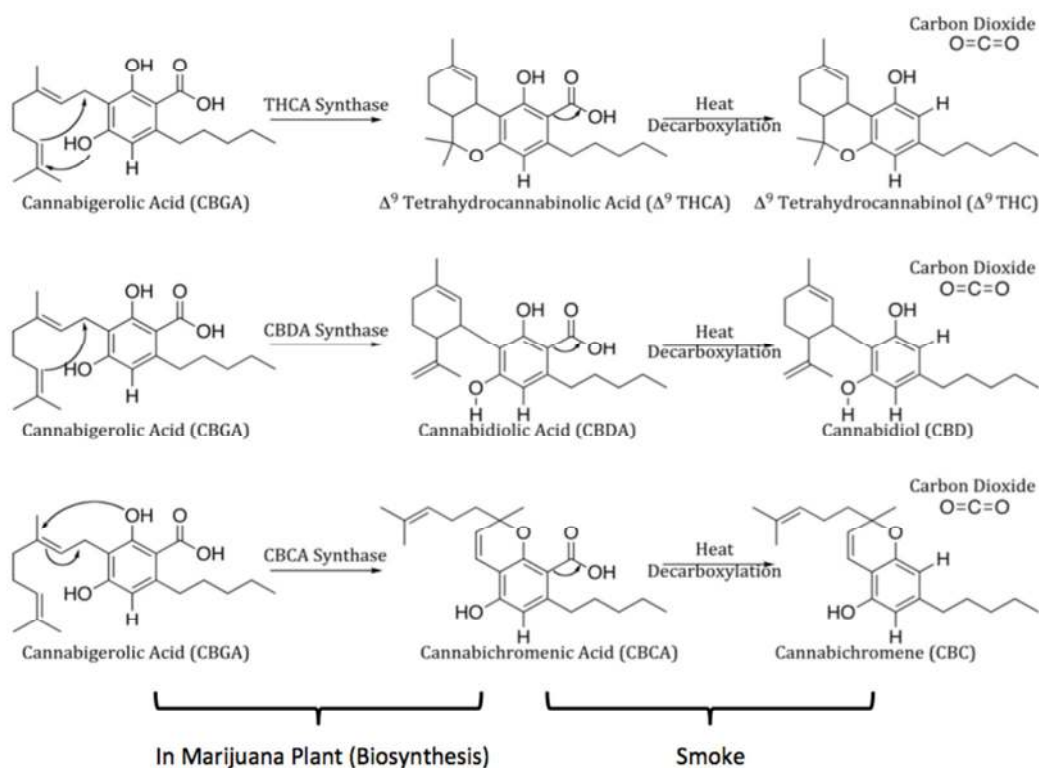
Production of medical marijuana often relies on the use of gamma irradiation as a decontamination technique to destroy most bacteria (it does not destroy viruses or mycotoxins). Gamma irradiation can be used to cover up biological contamination resulting from poor production, processing or handling practices. Gamma irradiation has been shown to destroy terpenes like myrcene and linalool (Fan *et al.* J. Agric. Food Chem. 2002, 50:7622-7626). It is many of the terpenes found in cannabis that provide aroma and flavor, as well as have medicinal properties.

Marijuana strains (typically indica) that produce high levels of THC express genes which code for the enzyme THCA synthase. This enzyme converts CBG into THCA (See Figure 14), which becomes THC when heated. Strains (typically sativa) express genes that code for the enzyme CBDA synthase. This enzyme converts CBG into CBDA, the precursor of CBD, instead. Thus, indica plants have high THC:CBD ratios and sativa plants have high CBD:THC ratios. It should be noted that many strains produce varying amounts of both enzymes.

Cannabinoids Synthesis by Smoke (Heat) - This is why the Raw Ingredients have to be Heated to Produce Oil

Smoking is the most common way to absorb the active ingredients of dried marijuana. As we discuss above, the API (active pharmaceutical ingredients) in marijuana are cannabinoids - cannabidiol, THC, and cannabichromene. Refer to Figure 14 to see how cannabinoids are synthesized by smoke (heat). In order for oils to be used by patients or recreational users, cannabis has to be heated to convert the components of cannabis into their active ingredients.

Figure 14: Synthesis of Cannabinoids by Smoke



Source: www.weedmaps.com and adapted by MRCC

Pharmacokinetics: Cannabinoids can be administered by a variety of routes:

Smoking: Smoking is undoubtedly the best-known method of administration, and is the typical manner of using administration of medical marijuana. Much of the total THC in crude cannabis is not free THC but tetrahydrocannabinolic acid. The heat just ahead of the advancing zone of combustion in a cigarette or pipe of cannabis converts the THC acid to free THC (see Figure 14), and volatilizes the THC so that it can be inhaled with the smoke, deep into the lung. The high lipid-solubility of the THC allows it to cross the alveolar membrane rapidly, entering the blood in the pulmonary capillaries. The bioavailability of THC by this route ranges from 18 to 50% in

different studies. Much of the variation is due to individual differences in smoking technique, relating to volume of the "draw", depth of inhalation into the lungs, and duration of retention of the smoke in the alveoli (*Azorlosa JL, et al. J Pharmacol Exp. 1995*). Effects from smoking cannabis products are felt within minutes and reach their peak in 10-30 minutes. Typical marijuana smokers experience a high that lasts approximately 2 hours. Most behavioral and physiological effects return to baseline levels within 3-5 hours after drug use, although some investigators have demonstrated residual effects in specific behaviors up to 24 hours, such as complex divided attention tasks.

Edibles: Oral administration of cannabinoids results in a slow and variable absorption, with a bioavailability of 10-20%, and usually less than 15%. Edibles are a discreet and convenient way to consume cannabis, particularly for those who cannot tolerate smoke. Edibles are made by infusing cannabis with food, many find that edibles offer a high that is more calm and relaxing than smoking pot. Edibles actually come in many shapes and sizes: These include brownies, cookies, gummies, cakes, hard candies, chocolate bars and more. On the other hand, the effects of edibles can be hard to predict and tend to differ between individuals.

In the U.S. some edible products are manufactured to contain as much as 100 milligrams of THC, and therefore should be used for multiple servings. Other edibles have lower dosages of THC such as 5 or 10 milligrams. Marijuana edibles take longer to start working – usually 30 to 60 minutes. However, the effects can last between 4 to 12 hours depending on the dose. Since patients/recreational users may find it hard to determine how much your body needs to medicate or get high, ideally people should wait at least one hour to assess the effect. In the U.S., there have been multiple hospitalizations as a result of overdosing on edibles. Signs of an edibles overdose include paranoia, lack of coordination and hallucinations.

Health Canada has introduced medical cannabis oil to the MMPR and has implemented certain safety precautions that producers must follow before the oil can be made available for sale. One of the primary safety precautions put in place is a limit of THC or concentration of Cannabis that can be found in the oil based medicine. The current MMPR limit of THC concentration in oil is 30mg/ml. This means that for each one milliliter of oil, the producer must ensure that no more than 30 milligrams of THC is present. In order to meet this requirement, the Licenced Producer (LP) must dilute the cannabis resin so that the concentration of THC meets this specification.

Eye Drops: Because of their high lipid solubility, topical administration is possible in such locations as the eye or the nasal mucosa. However, this has been of very limited applicability, as THC tends to be an irritant to the eye. However, newer vehicles that permit lipid-soluble materials to be applied to the eye in aqueous solution may make this route of greater interest again.

Skin Patch: In theory, percutaneous absorption, as from a drug-impregnated skin patch, should be possible, but the absorption would be very slow and not clinically useful.

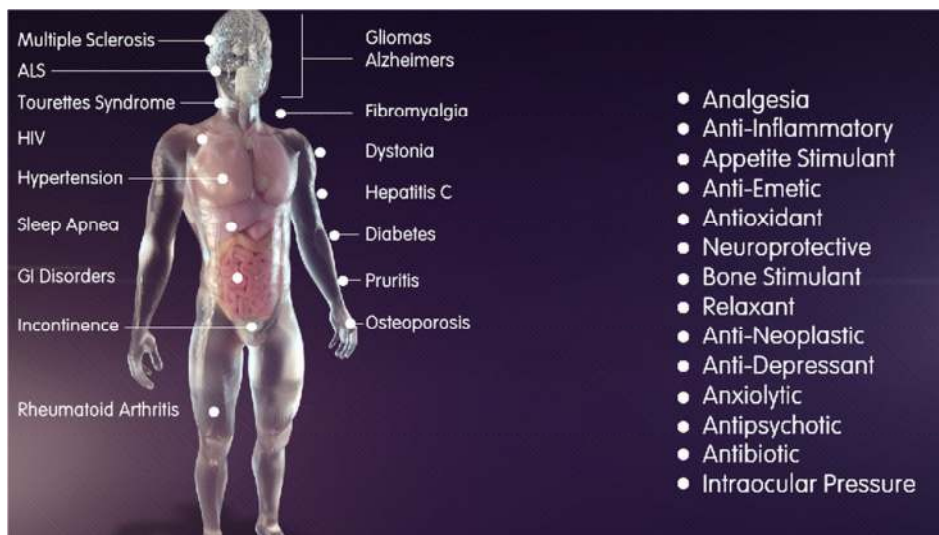
Intravenous (unlikely): Intravenous injection or infusion is possible, but because of the very low water-solubility of cannabinoids a special formulation must be used, such as a complex of the cannabinoid with plasma protein, or a solution in a water-miscible organic solvent. Without such formulations, almost no active material could be delivered. Intravenous toxicity would be likely due essentially to injection of insoluble particulate material.

Like other highly lipid-soluble drugs, THC in the plasma is largely transported as a loosely bound complex with plasma protein. This complex dissociates readily, so that the free THC rapidly crosses cell membranes and enters the tissues in proportion to their respective blood flow rates. THC is metabolized with half-life of about 2 - 3 days. Chronic use appears to produce little or no increase in the rate of metabolism (*Ohlsson A, et al. Biomed Mass Spectrometry. 1982*), so that there is a potential risk of cumulative increase in the tissue concentrations over time, in daily users.

Pharmacological Effects of Marijuana:

As noted in Figure 15, medical marijuana has been used to treat a variety of diseases.

Figure 15: Diseases that Medical Marijuana is Used For Treating



Source: GB Sciences

The pharmacological effects of crude marijuana and pure cannabinoids (collectively called “Marijuana”) can be divided into acute and chronic effects. We briefly summarize each effect below:

Acute Therapeutic Effects:

- **Central Nervous System (CNS)** – Marijuana acts essentially as a CNS depressant, so that its main acute effects in many ways resemble those of alcohol. It produces pain relief, drowsiness and decreased alertness, being synergistic with alcohol, barbiturates and other CNS depressants in this respect. Cognitive effects include impairment of short-term memory, slowed reactions, decreased accuracy of psychomotor task performance, and decreased selectivity of attention. Antinauseant and antiemetic effects of marijuana have also been well demonstrated. All of the foregoing effects are produced mainly through CB1 receptors.
- **Cardiovascular (CV) Effects** – One of the most consistent and reliable signs of acute action of cannabis is tachycardia, with increased cardiac output and correspondingly increased myocardial oxygen requirement. These effects are generally mild, and of no pathological significance, but the increased myocardial workload could in theory become dangerous in an individual with some degree of coronary insufficiency.
- **Respiratory System** – One of the manifestations of smooth muscle relaxation by marijuana is bronchodilatation, with resulting decrease in airway resistance. Since marijuana smoke is similar to tobacco smoke, the consequences of chronic exposure to marijuana smoke are similar to those of tobacco smoke.
- **Ophthalmology** – Marijuana has been shown repeatedly to lower the intraocular pressure (useful for treating glaucoma), by a mechanism that is not yet understood (*Green K. Arch Ophthalmol. 1998*). This effect can be produced by systemic administration at doses that also produce the characteristic CNS effects, and inconsistently by local application to the eye.

- **Immune System** – *In vitro* exposure to very high concentrations of marijuana results in decreased function of macrophages, lymphocytes and NK cells. *In vivo*, however, the observations are highly variable in different studies, and it is not yet clear whether there is or is not a significant effect of marijuana smoking on immune functions. The effects on immune cells are probably produced via CB2 receptors.

Cannabis Use Carries Health Risks

Cannabis' health harms increase with intensity of use. Particularly when used frequently (daily or near-daily), cannabis is associated with increased risk of problems with cognitive and psychomotor functioning, respiratory problems, dependence, and mental health problems. Most significant from a public health perspective is the potential impact of cannabis use on the skills necessary for safe driving and the substantial increase of risk of motor-vehicle accidents.

Chronic Adverse Effects:

- **Central Nervous System (CNS)** – Prolonged daily use of marijuana is linked to a variety of cognitive changes, including poor memory, vagueness of thought, decreased verbal fluency and learning deficits that are not always fully reversible when the use of marijuana is stopped. High-dose daily use can give rise to a chronic intoxication syndrome.
- **Respiratory System** – Two relatively large-scale studies of pulmonary function in chronic marijuana and tobacco smokers give contradictory findings with respect to chronic obstructive pulmonary disease (COPD): One study found a clear linkage of COPD to tobacco smoking, but not to marijuana smoking; in contrast, a larger study found a significant link between COPD and marijuana smoking, as well as an additive effect of tobacco and marijuana. The reason for the difference between the findings of the two studies is not yet entirely clear (might be due to selection of trial subjects). In some studies, chronic inflammatory chest disease has been reported to be present in over 60% of long-term daily smokers of marijuana. A significant increase of the risk of lung cancer in long-term marijuana smokers was demonstrated in a case-control study (Zhang ZF, et al. *Cancer Epidemiol Biomark Prev.* 1999).
- **Endocrine System** – Heavy smokers of marijuana have shown various endocrine changes, including decreased testosterone levels and reduced sperm counts in males, and decreased LH and prolactin levels in the luteal phase of the menstrual cycle in females, resulting in shorter periods and more anovulatory cycles.

Addiction (Dependence) – About 9% of cannabis users develop dependence (Lopez-Quintero C et al. 2011, *Drug and Alcohol Dependence* 115: 120). People who develop cannabis dependence may have difficulty quitting or cutting down and may persist in using it despite negative consequences; those who stop suddenly may experience mild withdrawal symptoms including irritability, anxiety, upset stomach, loss of appetite, disturbed sleep and depression (Anthony J *Cannabis Dependence: Its Nature, Consequences and Treatment.* Cambridge: Cambridge University Press. 2006 and Kalant H (2004) *Progress in Neuro-Psychopharmacology and Biological Psychiatry* 28: 849). Long-term frequent users have a higher risk of dependence than occasional users. By way of comparison, the estimated probability of developing dependence is 68% for nicotine, 23% for alcohol, and 21% for cocaine (Lopez-Quintero C et al. 2011, *Drug and Alcohol Dependence* 115: 120).

Medical Use of Marijuana – No Single Indication Officially Approved by Any Authority (FDA, EMA, etc.)

To date, the FDA has not approved a marketing application for marijuana for any indication. The FDA or other regulatory agencies usually requires human data from multiple rigorous, well-designed (randomization, well-controlled) clinical trials to demonstrate the efficacy and safety of a product before approval. One product, Marinol by Abbvie, containing synthetic cannabinoid, THC, has been approved by FDA as a treatment for anorexia associated with weight loss in AIDS patients. Another FDA-approved drug, Cesamet by Meda Pharmaceuticals, contains the active ingredient nabilone, which has a chemical structure similar to THC and is synthetically derived. We summarize some main medical uses of marijuana (crude marijuana and pure cannabinoids) and selected clinical trials below:

- **Antinauseant and Antiemetic** – The anti-emetic properties of marijuana have been studied in humans more widely than any other indication. Nausea and vomiting following chemotherapy was felt to be one of the best-supported therapeutic uses of marijuana by the British Medical Association in their review of 23 studies, and was also supported by the American Institute of Medicine. Pooling available data from 768 U.S. cancer patients receiving chemotherapy in state-sponsored clinical studies showed that oral THC provided 76-88% relief of nausea and vomiting, while smoked marijuana supported 70-100% relief in various surveys (*Musty RE, et al. Journal of Cannabis Therapeutics. 2001*).
- **Analgesia (pain)** – All neuropharmacological studies leave no doubt that there is an analgesic action of marijuana at appropriate doses. Several short-term studies showed that marijuana decreased post-operative (*Jain AK, et al. J Clin Pharmacol. 1981*), dental (*Raft D, et al. Clin Pharmacol Ther. 1977*), cancer (*Royes R, et al. Clin Pharmacol Ther. 1975*), and visceral (*Holdcroft A, et al. Anaesthesia. 1997*) pain. However, large and well-controlled studies are still needed to demonstrate the efficacy of marijuana as analgesic. Cannabinoids and opioids are two different analgesic and act on different receptors, respectively (cannabinoids on CB1/2 receptors while opioids on mu, delta, kappa receptors). However, both signaling pathways have the same G-protein-coupled mechanism that blocks the release of pain-propagating neurotransmitters in the brain and spinal cord. The shared mechanism creates the possibility that a combination of the two drugs, at lower doses than would be used for either alone, might result in improved analgesia with lower risk of the typical side effects of each drug.

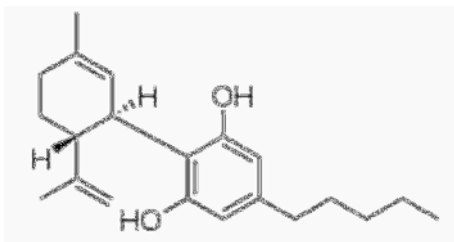
Can Medical Marijuana Reduce Opioid Use?

A cross-sectional retrospective survey of 244 medical cannabis patients with chronic pain who patronized a medical cannabis dispensary in Ann Arbor, Michigan between November 2013 and February 2015 (*Boehnke et al J Pain. 2016 Mar 18. pii: S1526-5900(16)00567-8*) was conducted. Among study participants, medical cannabis use was associated with a 64% decrease in opioid use (n=118), along with decreased number and side effects of medications, and an improved quality of life (45%). This study suggests that many chronic patients are essentially substituting medical cannabis for opioids and other medications for chronic pain treatment, and finding the benefit and side effect profile of cannabis to be greater than these other classes of medications. One limitation of the study is that it was conducted with people at a dispensary who are presumed to be believers in the medical benefits of marijuana. These participants were also surveyed after they had been using marijuana, which may decrease the accuracy of their recollections. While this study was not controlled, it suggests that cannabis should be an effective pain medication and agent to prevent opioid overuse.

- **Relief of Muscle Spasticity** – Numerous claims have been made for the ability of marijuana to relieve muscle spasms, especially in multiple sclerosis, but most of these claims are unverified case reports, rather than well-controlled clinical studies. A self-report study, based on interviews with 112 multiple sclerosis patients in UK and U.S. who smoked marijuana, found that the main benefits claimed by the users were decreased spasticity and pain, but other claimed benefits included decreased bladder spasm and improved balance and walking (*Gonsroe P, et al. Eur Neurol. 1997*). In contrast, an experimental study of 10 multiple sclerosis patients and 10 healthy controls, each smoking one marijuana cigarette, found that marijuana caused worse posture and balance in both groups, but more so in the patients than in the controls (*Greenberg HS, et al. Clin Pharmacol Ther. 1994*). To date, there have been no well-controlled studies comparing marijuana with other drugs currently used for the relief of spasm.
- **Glaucoma** – Both oral THC and smoked marijuana have been shown to reduce the intraocular pressure (IOP) (*Devane WA, et al. Mol Pharmacol. 1988*). The therapeutic objective of preventing retinal and optic nerve damage in glaucoma requires a continuously sustained fall in IOP. To produce such a sustained effect with marijuana, a better formulation of THC with increased half-life would be required. But it is still not possible to avoid the psychoactive effects at THC doses that would provide a useful reduction of IOP. Potential future developments would rest on synthetic analogs with a superior separation of effects.
- **Anticonvulsant (Epilepsy)** – The anticonvulsant effect of marijuana has been well shown in animal models. In a small-scale, double-blind, and controlled study, epilepsy patients who did not have adequate therapeutic benefit with conventional agents despite good compliance had significantly reduced frequency of seizure when taking oral cannabinoid as add-on (*Cunha JM, et al. Pharmacology. 1980*). However, two other double-blind placebo-controlled clinical trials showed no therapeutic effect (*Ames FR. S Afr Med J. 1986 and Joy JE, et al. Natl Academy Press. 1999*).

GW Pharmaceuticals' (GWPH-NASDAQ) Epidiolex (cannabidiol) generated positive Phase 3 results for the treatment of Dravet syndrome. Cannabidiol (see Figure 16) is one of at least 85 active cannabinoids identified in cannabis - it is a major phytocannabinoid, accounting for up to 40% of the plant's extract. Epidiolex achieved the primary endpoint of a significant reduction in convulsive seizures assessed over the entire treatment period compared with placebo ($p=0.01$). Epidiolex has both orphan drug designation and fast track designation from the U.S. Food and Drug Administration (FDA) in the treatment of Dravet syndrome, a rare and debilitating type of epilepsy for which there are currently no treatments approved in the U.S. The Phase 3 study randomized 120 patients into two arms, Epidiolex 20mg/kg/day ($n=61$) and placebo ($n=59$). Epidiolex or placebo was added to current anti-epileptic drug (AED) treatment regimens. On average, patients were taking approximately 3 AEDs, having previously tried and failed an average of more than 4 other AEDs. The average age of trial participants was 10 years and 30 percent of patients were less than 6 years of age. The median baseline convulsive seizure frequency per month was 13. Epidiolex was generally well tolerated in this study. The most common adverse events (occurring in greater than ten percent of Epidiolex-treated patients) were: somnolence, diarrhea, decreased appetite, fatigue, pyrexia, vomiting, lethargy, upper respiratory tract infection and convulsion. Of those patients on Epidiolex that reported an adverse event, 84 percent reported it to be mild or moderate. Ten patients on Epidiolex experienced a serious adverse event compared with three patients on placebo. Eight patients on Epidiolex discontinued treatment due to adverse events compared with one patient on placebo. The primary efficacy endpoint was a comparison between Epidiolex and placebo measuring the percentage change in the monthly frequency of convulsive seizures during the 14-week treatment period compared with the 4-week baseline observation period. In this study, patients taking Epidiolex achieved a median reduction in monthly convulsive seizures of 39 percent compared with a reduction on placebo of 13 percent, which was highly statistically significant ($p=0.01$).

Figure 16: Chemical Structure of Epidiolex (cannabidiol)



Source: PubChem

- **Posttraumatic Stress Disorder (PTSD)** can occur after someone goes through a traumatic event like combat, assault, or disaster. Most people have some stress reactions after a trauma. Individuals with posttraumatic stress disorder (PTSD) are at heightened risk for marijuana use. There are no controlled studies that have not been conducted to evaluate the safety or effectiveness of medical marijuana for PTSD. Posttraumatic stress disorder is one of the approved conditions for medicinal marijuana in some U.S. states. As noted by a review by Yarnell (*Prim Care Companion CNS Disord.* 2015 May 7;17(3)), the literature to date is suggestive of a potential decrease in PTSD symptomatology with the use of medicinal marijuana, however, there is a notable lack of large-scale trials, making any final conclusions difficult to confirm at this time. Based on another study (*Wilkinson et al J Clin Psychiatry.* 2015 Sep;76(9):1174-80) conducted from 1992 to 2011, veterans with DSM-III/-IV PTSD ($n = 2,276$) were admitted to specialized Veterans Affairs treatment programs, subjects were classified into 4 groups according to marijuana use: those with no use at admission or after discharge ("never-users"), those who used at admission but not after discharge ("stoppers"), those who used at admission and after discharge ("continuing users"), and those using after discharge but not at admission ("starters"). In this observational study, initiating marijuana use after treatment was associated with worse PTSD symptoms, more violent behavior, and alcohol use. Marijuana may actually worsen PTSD symptoms or nullify the benefits of specialized, intensive treatment.

The First Health Canada Approved Marijuana Clinical Trial

The first Health Canada-approved trial for medical marijuana (Cannabinoid PRofile Investigation, "CAPRI") was launched on June 23, 2015. This on-going study is a year-long, randomized, double-blind, placebo-controlled, proof-of-concept crossover trial to test five varieties of single-dose vaporized cannabis on adults with primary

osteoarthritis of the knee. The study is designed to recruit a total of 40 men and women with age over 50 at pain clinics in Montreal and Halifax. A formal screening process would be conducted to exclude current marijuana users and people with pre-existing knee problems or trauma. Subjects on the active arms would receive a single vaporized dose of medical marijuana once every week. The study is expected to end in May 2016 with results published in scientific paper soon after. This study is being funded by CanniMed, a wholly owned subsidiary of Prairie Plant Systems, a Saskatoon-based plant biotech company that has been growing medical marijuana for Health Canada at two locations in Saskatchewan since 2000.

Average Dose per Day of Medical Marijuana

A study (*Hazekamp A, et al. Eur. J. Clin. Pharmacol. 2013*) was published in the Netherlands tracking MMJ average dose per day obtained from the Dutch medical cannabis program over the years 2003-2010. The study reported that in a population of over 5,000 Dutch patients using cannabis for medical purposes, the average daily dose of dried marijuana (various potencies) used was 0.68 g/day (range: 0.65 - 0.82 grams per day). In addition, information from Israel's medical marijuana program suggests that the average daily amount used by patients was approximately 1.5 grams of dried marijuana per day in 2011-2012 (data obtained from Health Canada). Our industry sources have indicated that some veterans use 5-10 grams per day of medical marijuana.

Patient Acquisition Strategies

Unlike the U.S., in Canada, companies are not allowed to do direct to consumer (DTC) marketing for pharmaceuticals including medical marijuana. Canadian companies playing in the medical marijuana space have been acquiring patients via various routes: paying medical clinics for patient referrals, paying or acquiring medical support clinics/groups that are focused on specific patient populations such as pain treatment or veteran groups, targeting social media, promoting directly to physicians, promoting in medical journals and/or medical conferences.

No Reimbursement Policy in Place for Medical Marijuana

There is no policy in place for Canadians to be reimbursed by insurance companies when using medical marijuana. Medical marijuana producers have a key hurdle to overcome before insurers could begin routinely funding the drug – cannabis currently doesn't have a drug identification number (DIN). To obtain a DIN, the new form of medical marijuana would need to go through the full Health Canada approval process like any new drug. Medical marijuana is regulated under the Marihuana for Medical Purposes Regulations (MMPR) whereas typical prescription drugs are regulated under the Food and Drug Act. If an individual is prescribed medication in Canada, private medical and/or provincial health insurance will routinely cover the majority of the costs. If that same person has a “medical document” and orders medical marijuana from one of Canada’s federally licensed and regulated producers, they are currently expected to pay for himself/herself. Based on our discussions with Canadian marijuana producers, we are not aware of any companies that will pursue that path. The first patient to be reimbursed was a student, he was able to make the case that his medical marijuana constituted a ‘prescription’ to the Waterloo University Health and Dental Plan Committee. It is possible that insurance companies may reimburse patients for using medical marijuana via corporate health plans in the future.

Drug Enforcement Administration (DEA) - Drug Schedules

Investors should understand that marijuana is not legal in most countries in the world due to its addictive properties and potential for abuse. In the U.S., according to DEA, drugs, substances, and certain chemicals used to make drugs are classified into five distinct categories or schedules depending upon the drug’s acceptable medical use and the drug’s abuse or dependency potential. The abuse rate is a determinate factor in the scheduling of the drug; for example, Schedule I drugs are considered the most dangerous class of drugs with a high potential for abuse and potentially severe psychological and/or physical dependence. As the drug schedule changes – Schedule II, Schedule III, etc., so does the abuse potential – Schedule V drugs represents the least potential for abuse. A substance need not be listed as a controlled substance to be treated as a Schedule I substance for criminal prosecution.

Schedule I drugs, substances, or chemicals are defined as drugs with no currently accepted medical use and a high potential for abuse. Schedule I drugs are the most dangerous drugs of all the drug schedules with potentially severe psychological or physical dependence. Marijuana is currently listed under this category.

Figure 17: Drug Enforcement Administration (DEA) Drug Schedules

Schedule I	Schedule II	Schedule III	Schedule IV	Schedule V
<p>Description: Schedule I drugs, substances, or chemicals are defined as drugs with no currently accepted medical use and a high potential for abuse. Schedule I drugs are the most dangerous drugs of all the drug schedules with potentially severe psychological or physical dependence.</p>	<p>Description: Schedule II drugs, substances, or chemicals are defined as drugs with a high potential for abuse, with use potentially leading to severe psychological or physical dependence. These drugs are also considered dangerous.</p>	<p>Description: Schedule III drugs, substances, or chemicals are defined as drugs with a moderate to low potential for physical and psychological dependence. Schedule III drugs abuse potential is less than Schedule I and Schedule II drugs but more than Schedule IV.</p>	<p>Description: Schedule IV drugs, substances, or chemicals are defined as drugs with a low potential for abuse and low risk of dependence.</p>	<p>Description: Schedule V drugs, substances, or chemicals are defined as drugs with lower potential for abuse than Schedule IV and consist of preparations containing limited quantities of certain narcotics. Schedule V drugs are generally used for antidiarrheal, antitussive, and analgesic purposes.</p>
<p>Examples: heroin, lysergic acid diethylamide (LSD), marijuana (cannabis), 3,4-methylenedioxymethamphetamine (ecstasy), methaqualone, and peyote</p>	<p>Examples: combination products with less than 15 milligrams of hydrocodone per dosage unit (Vicodin), cocaine, methamphetamine, methadone, hydromorphone (Dilaudid), meperidine (Demerol), oxycodone (OxyContin), fentanyl, Dexedrine, Adderall, and Ritalin</p>	<p>Examples: products containing less than 90 milligrams of codeine per dosage unit (Tylenol with codeine), ketamine, anabolic steroids, testosterone</p>	<p>Examples: Xanax, Soma, Darvon, Darvocet, Valium, Ativan, Talwin, Ambien, Tramadol</p>	<p>Examples: cough preparations with less than 200 milligrams of codeine or per 100 milliliters (Robitussin AC), Lomotil, Motofen, Lyrica, Parepectolin</p>

Source: DEA and adapted by MRCC

As High As The Rockies – MRCC Canadian Medical Marijuana Market Size Estimates

We estimated the Canadian medical marijuana market total size as if it were a pharmaceutical. We have assumed that the Canadian market would follow the same growth and market penetration trends as occurred in Colorado and Oregon. Even if investors assume that our estimates are too high and assume our numbers are 50% lower than modelled estimates, the market potential is significant. The biggest problem for LPs is the loss of market share to the black market from illegal dispensaries. At this point, the Federal government has not implemented any plans to permanently close dispensaries.

Estimating the Total Number of Registered Medical Marijuana Clients

We derive our estimate of the total number of Canadian registered clients from the trends observed in the Colorado and Oregon medical marijuana programs. Colorado and Oregon started their official medical marijuana programs in 2000 and 1998, respectively. By 2015, the percentage of legal medical marijuana patients as a percentage of the total state population in the two states was 2.0% and 1.9%, respectively. We have assumed the maximum total number of registered clients in Canada would follow the same trend in Colorado and Oregon, reaching 2% of the total Canadian population in 2020 (715,000 by using 2015 population). Health Canada provides the data of the total number of registered clients at the end of each quarter from Q1 FY14 to Q2 FY15 (Please note Health Canada uses fiscal year ended on March 31). We assume the year-over-year (YoY) growth rate from FY15 to FY20 at 150%, 120%, 100%, 90%, 80%, and 3%, respectively, and convert to calendar year presentation. Therefore, the total number of registered clients from CY2015 to CY2020 is estimated at 38,863, 85,498, 178,178, 341,084, 619,041, and 715,000 (peak number), respectively.

Figure 18: Total number of registered clients

	CY2015E	CY2016E	CY2017E	CY2018E	CY2019E	CY2020E
Total number of registered clients	38,863	85,498	178,178	341,084	619,041	715,000
% Change	150%	120%	108%	91%	81%	16%

Source: MRCC

Estimating the amount of medical marijuana sold to clients

The actual quarterly amount (kg) of dried medical marijuana sold to registered clients from Q1 FY14 to Q2 FY15 (fiscal year) is provided by Health Canada. Following the trend implied in the Health Canada data, we have modeled the YoY growth rate from FY15 to FY20 to be 192%, 114%, 110%, 80%, 60%, and 25%, respectively, and have converted to calendar year presentation simply by adding the number of the fourth quarter of last fiscal year to the numbers of the first three quarters of current fiscal year. Thus the amount of the dried medical marijuana sold from CY2015 to CY2020 is 6,432 kg, 14,419 kg, 32,841 kg, 58,219 kg, 94,970 kg, and 124,443 kg, respectively.

Figure 19: Total amount of dried medical marijuana sold to registered clients (kg)

	CY2015E	CY2016E	CY2017E	CY2018E	CY2019E	CY2020E
Amount of MMJ sold to clients (kg)	6,432	14,419	32,841	58,219	94,970	124,443
<i>% Change</i>	205%	124%	128%	77%	63%	31%

Source: MRCC

Estimating the number of registered clients actually on medical marijuana

Medical marijuana companies have had poor disclosure for investors, in that companies have not been disclosing how many patients are actually being treated with medical marijuana (which is less than the number of patients registered). We assume each Canadian client would consume 0.68 g dried marijuana per day for medical uses (248 g/year), the same amount as shown in a Dutch study (as disclosed by the Bureau of Medical Cannabis in the Netherlands) estimates that the average daily dosage of medical marijuana in that country is about 0.68 grams per patient. By dividing the modeled amount of dried medical marijuana sold each year by 248 g/year, we get the number of clients actually using dried marijuana for medical purpose each year from CY2015 to CY2020: 8,901, 58,096, 132,317, 234,564, 382,633, and 501,381, respectively. We have further calculated the annualized implied market penetration rate (calendar year format) based on our modeled total number of registered clients and number of clients actually on dried medical marijuana. The formula we used is expressed as (number of clients actually on dried medical marijuana x 4)/(total number of registered clients) x 100%. We multiplied by 4 in the formula, as the number of clients actually on dried medical marijuana is reported quarterly (Q3 FY15 ended on Dec. 31, 2015). Therefore, the implied annualized market penetration rate is calculated as 92%, 68%, 74%, 69%, 62%, and 70%, respectively. Investors should note that the decrease of market penetration rate suggests faster growth of the total number of the registered clients than the growth of the number of clients actually on medical marijuana. We should also note that we use this same penetration rate calculation for pharmaceutical modelling.

Figure 20: Total number of registered clients, number of clients on dried marijuana, and implied market penetration rate

	CY2015E	CY2016E	CY2017E	CY2018E	CY2019E	CY2020E
Total number of registered clients	38,863	85,498	178,178	341,084	619,041	715,000
Number of clients actually on dried medical marijuana	8,901	58,096	132,317	234,564	382,633	501,381
<i>Implied market penetration rate</i>	92%	68%	74%	69%	62%	70%

Source: MRCC

Just Like The Rockies - Estimating the market split between dried marijuana and extracts/oil (volume)

In terms of conversion from dried marijuana to extracts/oil, we have done due diligence on Colorado market, finding that 45% of dried marijuana users would eventually convert to marijuana extracts/oil. We expect the Canadian market to follow a similar trend as Colorado, and we assume the market would gradually reach an approximate 45% conversion rate by 2018. By using our modeled number of clients actually on dried medical marijuana, we estimate the number of clients on dried marijuana/extracts (oil) from CY2015 to CY2020 at 25,737/178, 50,120/7,976, 99,238/33,079, 166,028/68,537, 267,843/114,790, and 350,967/150,414,, respectively. According to Health Canada, the approximate percent of the active ingredient in dried marijuana is 15.5%. We assume the yield from dried marijuana is 80%. By multiplying 15.5% by 80%, and by 0.68 g/day (the amount of dried marijuana for medical uses per day shown in the Dutch study), we obtained the per day per person consumption of extracts/oil at 0.08 g. Therefore, we estimate the annual amount of dried marijuana/ extracts (oil) for medical uses sold from CY2015 to CY2020 at 6,388/44 kg, 12,440/1,980 kg, 24,631/8,210 kg, 41,208/17,011 kg, 66,749/28,491 kg, and 87,110/37,333 kg, respectively.

Figure 21: Split between Dried Marijuana and Extracts/Oil (Volume)

	CY2015E	CY2016E	CY2017E	CY2018E	CY2019E	CY2020E
Dried marijuana (kg)	6,388	12,440	24,631	41,208	66,479	87,110
Extracts/oil (L)*	284	12,727	52,780	109,356	183,156	239,998
*Equivalent amount (kg) of dried marijuana (Equivalent factor: 6.4 ml/g)	44	1,980	8,210	17,011	28,491	37,333

Source: MRCC

Estimate of Canadian Marijuana Market Size After Full Legalization (Medical and Recreational Uses)

We have assumed that the Canadian marijuana market would follow a similar trend as the Colorado market after full legalization. Colorado had its first marijuana retail store in early 2014. Colorado market data has shown that the sales of dried marijuana for recreational uses did not cannibalize the medical market, and at the end of 2014, the recreational market constituted 36% of the total market. In Colorado for 2014, compared to the dried marijuana market, sales of marijuana extracts (oil), was derived mainly through retail stores, which was comprised of 33.3% medical and 66.7% recreational part in Colorado 2014. Since the uncertainty of the time when marijuana would be fully legalized in Canada, we assume three scenarios: full legalization in 2018, 2019, and 2020, respectively. In each scenario, we assume the recreational part would constitute 30% and 67% of the total dried marijuana and extracts/oil market, respectively, at the end of the first year of full legalization, leaving the medical part at 70% and 33%, respectively. The modeled amount of dried marijuana and extracts/oil sold after full legalization is summarized in the table below:

Figure 22: The amount of dried marijuana and extracts/oil sold after full legalization in each scenario

	CY2015E	CY2016E	CY2017E	CY2018E	CY2019E	CY2020E
Scenario 1: Full legalization in 2018						
Dried marijuana (kg)	6,388	12,440	24,631	55,945	101,015	142,832
Extracts/oil (L)*	284	12,727	52,780	301,699	569,373	769,094
*Equivalent amount (kg) of dried marijuana (Equivalent factor: 6.4 ml/g)	44	1,980	8,210	46,931	88,569	119,636
Scenario 2: Full legalization in 2019						
Dried marijuana (kg)	6,388	12,440	24,631	41,208	86,827	123,366
Extracts/oil (L)*	284	12,727	52,780	109,356	464,658	701,631
*Equivalent amount (kg) of dried marijuana (Equivalent factor: 6.4 ml/g)	44	1,980	8,210	17,011	72,280	109,142
Scenario 3: Full legalization in 2020						
Dried marijuana (kg)	6,388	12,440	24,631	41,208	66,479	110,034
Extracts/oil (L)*	284	12,727	52,780	109,356	183,156	562,613
*Equivalent amount (kg) of dried marijuana (Equivalent factor: 6.4 ml/g)	44	1,980	8,210	17,011	28,491	87,517

Source: MRCC Estimates

Estimate of Price (C\$) and Total Market Size (sales, C\$,'M)

First, we assume there would be no full legalization of marijuana. Being conservative and considering the uncertainty of future price, we estimate the price of dried marijuana at \$7.5/g and extracts/oil for medical uses at \$2.60/mL (or \$16.71g). By multiplying our modeled annual amount of dried medical marijuana and medical extracts/oil (without full legalization), we obtained our annual sales of medical marijuana from CY2015 to CY2020 as summarized in the table below. We should note that, for this calculation we kept the price of dried marijuana the same at \$7.50/g but for the oil we dropped the price 5% annually and for 2020 we dropped the price 10% annually. Our sensitivity analysis with different marijuana prices is seen in Figure 25.

Figure 23: Market size of marijuana from CY2015 to CY2020 assuming no full legalization

	CY2015E	CY2016E	CY2017E	CY2018E	CY2019E	CY2020E
	<i>Dec31/2015</i>	<i>Dec31/2016</i>	<i>Dec31/2017</i>	<i>Dec31/2018</i>	<i>Dec31/2019</i>	<i>Dec31/2020</i>
Dried marijuana (C\$, 'M)	\$48	\$93	\$185	\$309	\$499	\$653
Extracts/oil (C\$, 'M)	\$1	\$33	\$132	\$258	\$412	\$493
Total Market Size (C\$, 'M)	\$49	\$126	\$316	\$567	\$911	\$1,146
<i>% Change</i>		<i>160%</i>	<i>150%</i>	<i>79%</i>	<i>60%</i>	<i>26%</i>

Source: MRCC Estimates

We have also done a scenario analysis (depending on the year it would be approved) if marijuana would be fully legalized for recreational uses. Following the price trends observed in the Colorado marijuana market, we conservatively estimate the price for recreational uses would be 10% higher than for medical uses in Canada, that is, \$8.3/g for dried marijuana and \$2.90/mL (or \$18.30/g) for extracts/oil. Under this scenario, we modeled in no price decline for the dried and a 5% annual decline for the oil price with the exception of 2020 where we assume a 10% decline (for the oil price). By using our modeled amount of dried marijuana and extracts/oil sold in each of the three scenarios, we have obtained a total marijuana market size estimate in each launch scenario, respectively. Our sales estimate results are summarized in the table below:

Figure 24: Market size of marijuana from CY2015 to CY2020 assuming full legalization

Full Legalization in 2018	CY2015E	CY2016E	CY2017E	CY2018E	CY2019E	CY2020E
	<i>Dec31/2015</i>	<i>Dec31/2016</i>	<i>Dec31/2017</i>	<i>Dec31/2018</i>	<i>Dec31/2019</i>	<i>Dec31/2020</i>
Dried marijuana (C\$, 'M)	\$48	\$93	\$185	\$431	\$784	\$1,113
Extracts/oil (C\$, 'M)	\$1	\$33	\$132	\$755	\$1,367	\$1,687
Total Market Size (C\$, 'M)	\$49	\$126	\$316	\$1,186	\$2,151	\$2,800
<i>% Change</i>		<i>160%</i>	<i>150%</i>	<i>275%</i>	<i>81%</i>	<i>30%</i>

Full Legalization in 2019	CY2015E	CY2016E	CY2017E	CY2018E	CY2019E	CY2020E
	<i>Dec31/2015</i>	<i>Dec31/2016</i>	<i>Dec31/2017</i>	<i>Dec31/2018</i>	<i>Dec31/2019</i>	<i>Dec31/2020</i>
Dried marijuana (C\$, 'M)	\$48	\$93	\$185	\$309	\$666	\$952
Extracts/oil (C\$, 'M)	\$1	\$33	\$132	\$258	\$1,102	\$1,535
Total Market Size (C\$, 'M)	\$49	\$126	\$316	\$567	\$1,769	\$2,487
<i>% Change</i>		<i>160%</i>	<i>150%</i>	<i>79%</i>	<i>212%</i>	<i>41%</i>

Full Legalization in 2020	CY2015E	CY2016E	CY2017E	CY2018E	CY2019E	CY2020E
	<i>Dec31/2015</i>	<i>Dec31/2016</i>	<i>Dec31/2017</i>	<i>Dec31/2018</i>	<i>Dec31/2019</i>	<i>Dec31/2020</i>
Dried marijuana (C\$, 'M)	\$48	\$93	\$185	\$309	\$499	\$842
Extracts/oil (C\$, 'M)	\$1	\$33	\$132	\$258	\$412	\$1,205
Total Market Size (C\$, 'M)	\$49	\$126	\$316	\$567	\$911	\$2,047
<i>% Change</i>		<i>160%</i>	<i>150%</i>	<i>79%</i>	<i>60%</i>	<i>125%</i>

Source: MRCC Estimates

Price Sensitivity Study

We have also done a price sensitivity study to test the effect of other four different prices of dried medical marijuana (\$7.50/g, \$6.0/g, \$5.0/g, and \$4.0/g) on the total marijuana market size. We also have assumed price for oil (extracts) to decline by the same percentage as the four dried prices from CY2015 to CY2020. Our results are summarized in the tables below:

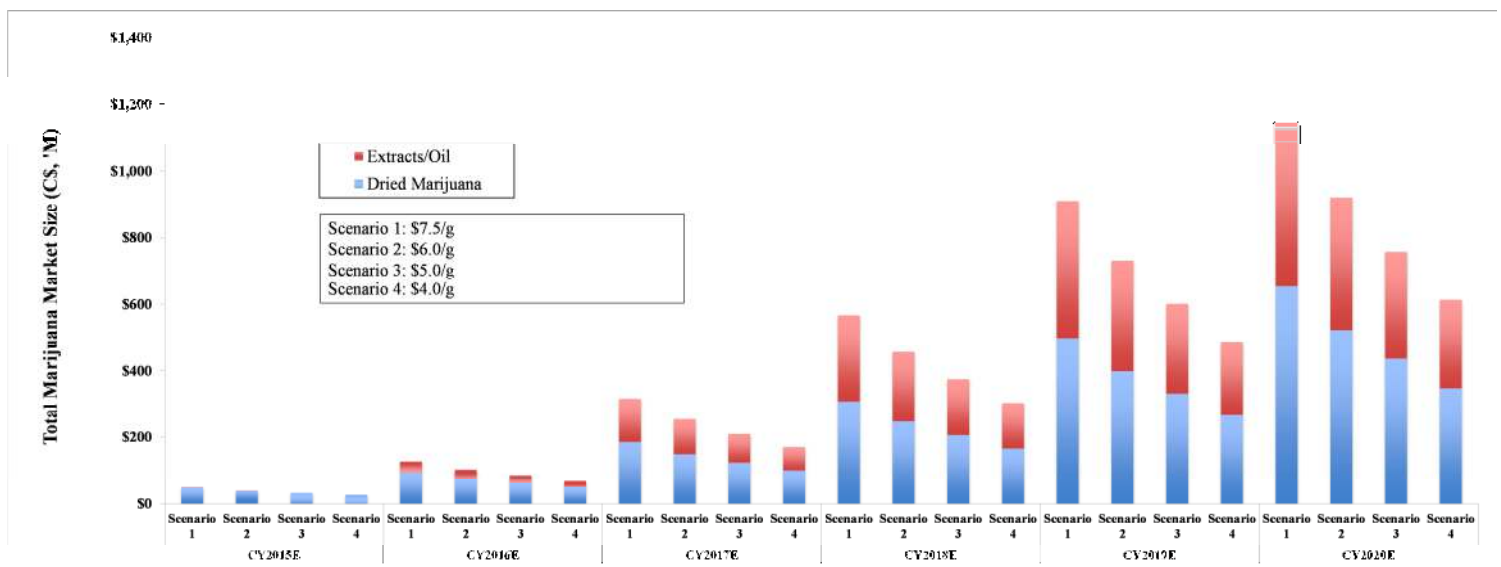
Figure 25: Marijuana Price Sensitivity Analysis

Total Marijuana Market Size (C\$, 'M)	CY2015E	CY2016E	CY2017E	CY2018E	CY2019E	CY2020E
	Dec 31/2015	Dec 31/2016	Dec 31/2017	Dec 31/2018	Dec 31/2019	Dec 31/2020
Assuming no full legalization						
Scenario 1: \$7.5/g for dried marijuana, \$2.6/ml for oil/extract	\$49	\$126	\$316	\$567	\$911	\$1,146
Scenario 2: \$6.0/g for dried marijuana, \$2.1/ml for oil/extract	\$39	\$101	\$254	\$456	\$732	\$921
Scenario 3: \$5.0/g for dried marijuana, \$1.7/ml for oil/extract	\$32	\$84	\$209	\$375	\$602	\$758
Scenario 4: \$4.0/g for dried marijuana, \$1.4/ml for oil/extract	\$26	\$68	\$169	\$304	\$488	\$614
Assuming full legalization in FY18						
Scenario 1: \$7.5/g for dried marijuana, \$2.6/ml for oil/extract	\$49	\$126	\$316	\$1,186	\$2,151	\$2,800
Scenario 2: \$6.0/g for dried marijuana, \$2.1/ml for oil/extract	\$39	\$101	\$254	\$954	\$1,731	\$2,253
Scenario 3: \$5.0/g for dried marijuana, \$1.7/ml for oil/extract	\$32	\$84	\$209	\$781	\$1,416	\$1,845
Scenario 4: \$4.0/g for dried marijuana, \$1.4/ml for oil/extract	\$26	\$68	\$169	\$636	\$1,154	\$1,502
Assuming full legalization in FY19						
Scenario 1: \$7.5/g for dried marijuana, \$2.6/ml for oil/extract	\$49	\$126	\$316	\$567	\$1,769	\$2,487
Scenario 2: \$6.0/g for dried marijuana, \$2.1/ml for oil/extract	\$39	\$101	\$254	\$456	\$1,423	\$2,001
Scenario 3: \$5.0/g for dried marijuana, \$1.7/ml for oil/extract	\$32	\$84	\$209	\$375	\$1,165	\$1,638
Scenario 4: \$4.0/g for dried marijuana, \$1.4/ml for oil/extract	\$26	\$68	\$169	\$304	\$949	\$1,334
Assuming full legalization in FY20						
Scenario 1: \$7.5/g for dried marijuana, \$2.6/ml for oil/extract	\$49	\$126	\$316	\$567	\$911	\$2,047
Scenario 2: \$6.0/g for dried marijuana, \$2.1/ml for oil/extract	\$39	\$101	\$254	\$456	\$732	\$1,647
Scenario 3: \$5.0/g for dried marijuana, \$1.7/ml for oil/extract	\$32	\$84	\$209	\$375	\$602	\$1,349
Scenario 4: \$4.0/g for dried marijuana, \$1.4/ml for oil/extract	\$26	\$68	\$169	\$304	\$488	\$1,098

Source: MRCC estimates

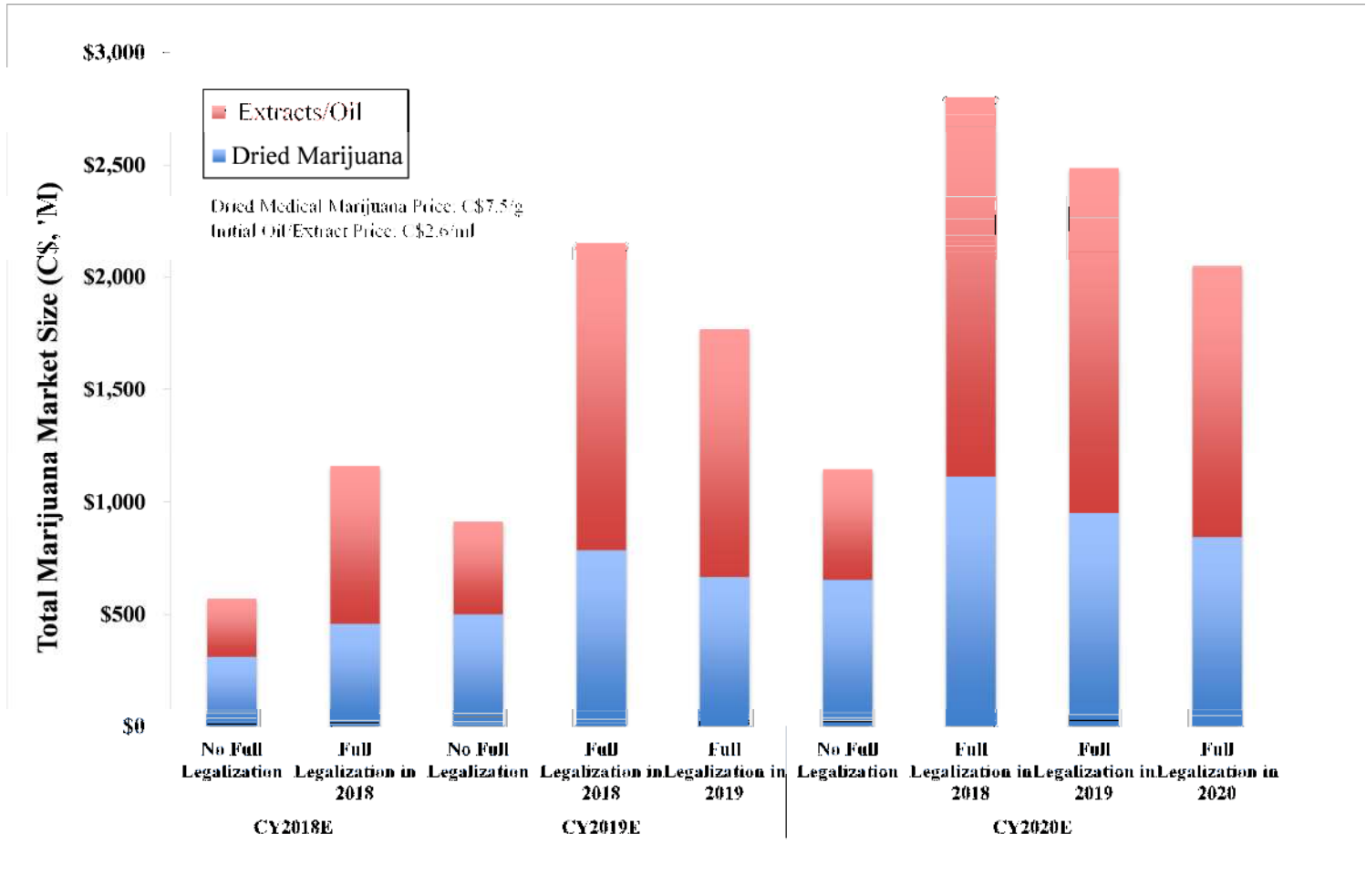
Note oil pricing drops by the same percentage as the dried.

Figure 26: Looking at the Medical Marijuana Market Based On Price (Assuming No Full Legalization)



Source: MRCC estimates

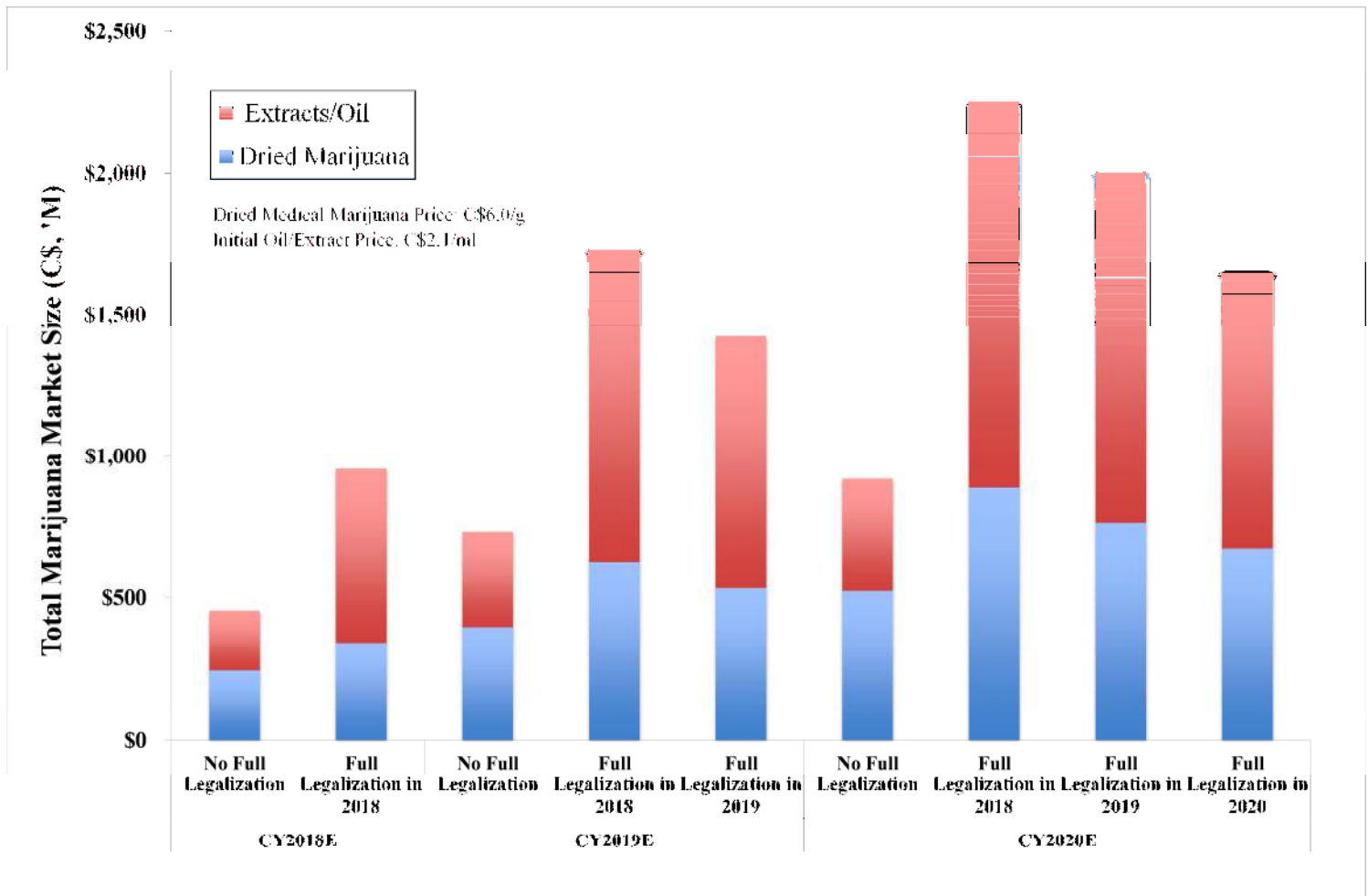
Figure 27: Marijuana Market Size (Medical and Recreational) – Scenarios Depending on Which Year Full Legalization Occurs Assuming \$7.5/g for Dried Medical Marijuana



Source: MRCC estimates

Note: The market size is represented in each calendar year based on the year marijuana becomes legal. eg. market size in calendar 2019 if it became legal in 2018 is represented by “Full legalization in 2018”

Figure 28: Marijuana Market Size (Medical and Recreational) – Scenarios Depending on Which Year Full Legalization Occurs Assuming \$6.0/g for Dried Medical Marijuana



Source: MRCC estimates

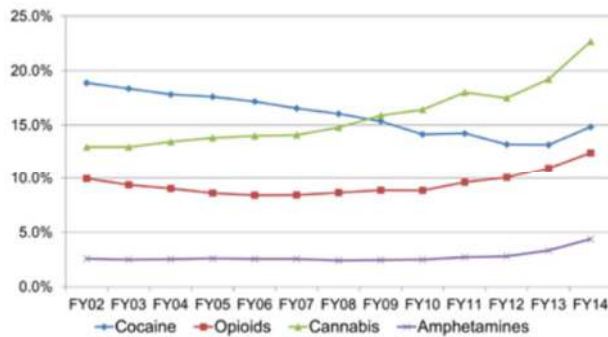
Note: Market size is represented in each calendar year based on the year it becomes legal. eg. market size in calendar 2019 if it became legal in 2018 is represented by “Full legalization in 2018”

Veteran Market for Medical Marijuana

In our model, we assumed that veterans who are on medical marijuana are inclusive of the total marijuana patient population which makes our model more conservative. Most veterans are heavy prescribers of medical marijuana as it is utilized for treating post traumatic stress disorder and pain. According to our industry sources, the average dose consumed by veterans ranges between 5 to 10 grams per day. According to Veterans Canada, the Canadian Military Veteran population is approximately 700,000. Included in the veteran members are the following groups: Royal Canadian Mounted Police, the Canadian Forces, Police Officers, Correctional Services, Firefighters, Coast Guard, Paramedics and Peace Officers. The average age of retirement of Canadian Force members is 46 years of age. The Canadian forces veteran population is approximately 558,000 with many under the age of 70 (Source: Veterans Canada).

In the U.S., the use of medical marijuana has increased substantially for treating post traumatic stress disorder (PTSD) and substance use disorders (SUD). To our knowledge, there has been no study of marijuana use in the overall veteran population. As noted in Figure 29, when considering the subset of U.S. veterans seen in U.S. Department of Veteran Affairs’ health care system with co-occurring PTSD and substance use disorders (SUD), cannabis use disorders has been the most diagnosed SUD since 2009. When considering the subset of veterans seen in the U.S. Department of Veteran Affairs health care with co-occurring PTSD and substance use disorders (SUD), cannabis use disorder has been the most diagnosed SUD since 2009.

Figure 29: U.S. Trends in Rates of SUD Diagnosis by Drug Category among Veterans with PTSD and SU



Source: Veterans Health Administration, 2015

Having a Closer Look at Historical Marijuana Use in Ontario

According to the CAMH report, population surveys in Ontario indicate that 14% of adults and 23% of high school students used cannabis in 2013. As shown in Figure 30, men are nearly 50% more likely to be past-year users than women. Cannabis use is most common among adolescents and young adults, but half of the province’s users are age 30 or older.

Figure 30: Historical Cannabis Use in Ontario - Percentage of the Population

	1997	2001	2005	2009	2013
General population (age 18+)	9.1	11.2	14.4	13.3	14.1
By gender					
• Men	11.4	15.4	18.8	17.4	17.6
• Women	7.0	7.3	10.3	9.5	10.8
By age					
• Grades 7-12	28.0*	28.6	26.5	25.6	23.0
• Age 18-29	21.4	26.8	38.2	35.8	40.4
• Age 30-39	9.8	15.8	16.9	12.9	17.3
• Age 40-49	4.3	7.2	10.8	11.7	8.4
• Age 50+	1.7	3.3	2.6	4.7	5.9

* figure from 1999

Source: CAMH October, 2014 report

Advice for the CMPA for Canadian Physicians Prescribing Medical Marijuana

This information was sourced directly (word for word) from the CMPA (Canadian Medical Protective Association) website. The CMPA is a not-for-profit association, incorporated by an Act of Parliament. Founded in 1901, the CMPA emerged from a need for physicians to work together to support their physician colleagues.

The guidelines and policies issued to date by most Colleges consistently state that more information is required on the medical risks and therapeutic benefits of marijuana. Most Colleges suggest that physicians should only sign the medical marijuana document when they have the necessary clinical knowledge to engage in a meaningful consent discussion with patients.

Each province has different guidelines for prescribing medical marijuana:

- The College of Physicians and Surgeons of British Columbia's Professional Standards and Guidelines on Marijuana for Medical Purposes (July 2015) state that physicians completing a medical document should write in the medical record that conventional therapies were attempted but were unsuccessful. The College also requires physicians to assess patients' risk of addiction using a validated addiction risk tool and retain a copy of that assessment in the medical record. Doctors must also "review the patient's PharmaNet information prior to issuing an authorization for marijuana for medical purposes and in any reassessment of patients receiving marijuana for medical purposes."
- The College of Physicians and Surgeons of Alberta's (CPSA) Standard of Practice on Marijuana for Medical Purposes (April 2014) states that doctors who choose to complete a medical document must register with the College. Once the patient has stabilized, they must be evaluated in person at least every three months.
- The Yukon Medical Council adopted the CPSA's Standard of Practice on Marijuana for Medical Purposes in September 2015.
- Physicians practising in the Northwest Territories or Nunavut should watch for new information or policies that may be provided by their medical regulatory bodies, or contact them directly to enquire about specific practices that must be followed when issuing a medical document under the Marijuana for Medical Purposes Regulations (MMPR).
- The College of Physicians and Surgeons of Saskatchewan revised its Regulatory Bylaws (August 2015) to require physicians to obtain a signed, written treatment agreement from patients setting out the patients' obligations, including using the marijuana as prescribed and not giving or selling it to anyone else. Physicians must also keep a separate record containing the names, quantity of marijuana authorized and duration of authorization, medical condition, and licensed producer (if known) for all relevant patients.
- The College of Physicians and Surgeons of Manitoba's Statement on Marijuana (Cannabis) for Medical Purposes (March 2014) indicates that physicians must remain at arm's length from licensed producers and be the treating physician for the condition for which marijuana is authorized. Physicians must keep a separate log of all authorizations and make the log available for inspection by the College.
- The College of Physicians and Surgeons of Ontario's Policy Statement on Marijuana for Medical Purposes (March 2015) states that "physicians must weigh the available evidence in support of dried marijuana against other available treatment options," and must not sign medical documents for marijuana for patients under the age of 25 unless all other conventional treatment has been attempted and failed to alleviate the patient's symptoms. Doctors must also "advise patients about the material risks and benefits of dried marijuana." The College recommends that physicians who prescribe dried marijuana first require patients to sign a written treatment agreement.
- Québec has a unique approach. The Collège des médecins du Québec states in its Guidelines concerning the prescription of dried cannabis for medical purposes (May 2015) that based on a provision in the province's Code of ethics of physicians, physicians in Québec should not provide patients with a medical document to access medical marijuana except as part of a recognized research project and only for specified conditions. A provincial research project on dried cannabis was announced in May 2015, and patients wishing to obtain medical marijuana may now register to participate in the study.
- In New Brunswick, the College's Guidelines on Medical Marijuana (April 2014) require physicians who provide a medical document to warn the patient about obtaining marijuana from an unauthorized source and about redirecting the drug to another individual. The patient must also be advised to maintain the marijuana in a secure place and about the circumstances under which the marijuana could be discontinued. The College recommends that these issues be documented in a treatment agreement with the patient.

- The College of Physicians and Surgeons of Nova Scotia's Policy Regarding the Authorization of Marijuana for Medical Purposes (June 2014) indicates "physicians may only authorize the use of marijuana for medical purposes when in direct, in-person contact with their patients." The College also prohibits physicians from billing patients directly for services related to the authorization of marijuana for medical purposes.
- The College of Physicians and Surgeons of Prince Edward Island's revised Policy on Prescribing of Medical Marijuana (September 2014) states that any doctors contemplating providing a patient with a medical document must first make themselves aware of the CMPA and CMA's positions on this matter. The College also states that physicians cannot provide the medical document via telehealth. Further, physicians must obtain written patient consent to notify the College of patients' names and other specified relevant details (a template form is provided by the College), and must tell patients that this information will be provided to the College, which will report any irregularities to the prescribing physician and legal authorities.
- The College of Physicians and Surgeons of Newfoundland and Labrador (CPSNL) issued an advisory and interim guideline (March 2014) outlining eight conditions that must be met before a physician considers completing the medical document. Similar to the College in British Columbia, the CPSNL requires physicians to assess the patient for risk of addiction using a standardized addiction risk tool. Doctors are also expected to establish an individualized written protocol for periodic reassessment of those patients receiving marijuana and can only issue the medical document if they are the primary treating physician.

Guidance for Family Physicians

In September 2014, the College of Family Physicians of Canada (CFPC) published Preliminary Guidance on authorizing dried cannabis for chronic pain or anxiety. Among the CFPC's recommendations it is noted that authorizations should only be considered for patients with neuropathic pain that has failed to respond to standard treatments and not as a therapy for anxiety or insomnia. Physicians should assess and monitor all patients on cannabis therapy for potential misuse or abuse. The CFPC also notes that the authorizing physician, if not the patient's most responsible health provider, should communicate regularly with the patient's family physician. Further, it is recommended physicians should specify the percentage of tetrahydrocannabinol (THC) on the medical document. The CFPC also states physicians should follow the regulations of their provincial medical regulators (Colleges).

Other Prescribing Considerations

Physicians are reminded of the importance of having the necessary clinical knowledge to engage in meaningful discussions with patients about medical marijuana. They should also document all consent discussions in patients' medical records.

Physicians should not feel obligated to complete the medical document for medical marijuana when they are unfamiliar with its use or management, or when they feel it is medically inappropriate for a patient. Physicians who choose to complete a medical document should rely on sound medical judgment and comply with their College's relevant guideline or policy. Members may also call the CMPA for advice.

Under the MMPR, licensed producers are required to provide a College, upon request, with "any factual information that has been obtained about a healthcare practitioner." The MMPR also amended the Narcotic Control Regulations to require the Minister of Health to report physicians to their College if the Minister has reasonable grounds to believe a physician contravened a College rule of conduct, the Narcotic Control Regulations or MMPR, or was found guilty of a designated drug offence or of contravening either the Narcotic Control Regulations or MMPR.

The regulations state that only licensed producers are authorized to sell or provide medical marijuana. Supplying a patient with marijuana is different from a physician agreeing to assist in transferring it to the patient, as discussed above. Suppliers or producers of medical marijuana must be licensed and must meet strict quality control, safety, and security requirements. Some Colleges specifically prohibit physicians from applying to become licensed producers, such as the Colleges in Alberta, Yukon, Manitoba, Saskatchewan, Québec, and Newfoundland and Labrador. Physicians in other jurisdictions thinking about applying to be a licensed producer should consider, among other things, the risk that it might be perceived to be a conflict of interest for a doctor to both complete medical documents for patients to access medical marijuana and also to be a licensed producer or supplier.

As a result of a 2015 Supreme Court of Canada decision (*R. v. Smith*), licensed producers are now allowed to sell marijuana for medical purposes in three basic forms: fresh, dried, and oil. There is no change to the role of healthcare professionals in authorizing medical marijuana, nor is there any change to the medical document. Under the exemption, licensed producers are required to develop a conversion method between dried marijuana and cannabis oil and fresh marijuana, and to post that information on their website.

Finally, when considering whether or not to provide patients with access to medical marijuana, physicians must be aware of the regulations governing the drug and of their College's policies or guidelines. They must also determine if their clinical knowledge of the drug is sufficient and if it is appropriate for the specific patient.

Risk Factors of the Medical Marijuana Industry

Regulatory Reliance. Health Canada's licenses must be renewed each year and there is no guarantee that Health Canada will extend or renew a license for a given producer. In addition, should a company fail to comply with any requirements the license could be cancelled, which would impact the financial results of a producer.

Changes in Regulatory Environment. If Health Canada were to make further modifications to the MMPR program or introduce any other changes that could affect the medical marijuana industry it would have an impact on producers, either positively or negatively depending on the nature of the change.

Limited Operating History - Manufacturing Risks. The companies operating in this industry have a limited operating history. Some these risks could include crop failures, inability to scale production to full capacity or access to financial resources, among other risks typical of early-stage companies.

Dispensaries - The Black Market. Marijuana dispensaries have been operating illegally in Canada. Market share gains for LPs could continue to be cannibalized by dispensaries.

Legalization. While there was a campaign promise by the Liberals to legalize marijuana there is no guarantee the Federal government would be able to maneuver around the three international treaties which implement criminalizing possession and production of non-medical marijuana.

The Economics of Patient Population, Production and Pricing (Supply vs. Demand). Patient demand growth may be higher or lower than our estimates which may affect the overall market. If demand were to be significantly lower than forecast, the market may experience an over-supply situation, creating pricing pressure for producers. Conversely, if demand were to exceed expectations, the market may be constrained which could have a positive impact on prices. Over production by all LPs could result in lower prices as well under production could result in higher prices.

Lack of Significant Medical Marijuana Differentiation. Medical marijuana is largely perceived as a commodity product, currently, there is initially little to differentiate the different products in terms of unique features or benefits. Companies are competing aggressively in terms of product quality, variety and price. In additions, companies are also maintaining a focus on client services to retain a solid and sustainable patient base as well as a position in the market

Medical marijuana is largely perceived as a commodity product, currently, there is initially little to differentiate the different products in terms of unique features or benefits. Companies are competing aggressively in terms of product quality, variety and price. In additions, companies are also maintaining a focus on client services to retain a solid and sustainable patient base as well as a position in the market.

Pesticides Use. In the U.S., the marijuana industry has had major contamination issue due to pesticide (chemicals) used to control bugs and mold. Canada has strictly regulated pesticide use. As of May 12, 2015, there are seven registered pesticides approved by the Pest Management Regulatory Agency for use on cannabis (marijuana) that is produced commercially indoors: MilStop Foliar Fungicide, Actinovate SP Fungicide, Opal Insecticidal Soap, Neudosan Commercial, Kopa Insecticidal Soap, Rootshield HC Biological Fungicide Wettable Powder and Rootshield WP Biological Fungicide.

RISKS TO TARGET

No companies are discussed in this report.

RELEVANT DISCLOSURES APPLICABLE TO THIS RESEARCH REPORT

1. Yue Ma, M.Sc. an Intern Associate of Mackie Research Capital Corporation, was also involved in the preparation of this research report.
2. No relevant disclosures required for this research report as no companies are discussed.

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