

## SUBMISSION TO SENATE'S REVIEW INTO LEGALISED MEDICINAL CANNABIS

March 8th 2015

### INTRODUCTION

Mention the words cannabis or marijuana to most people and they immediately think of pot smoking hippies. This is the unfortunate connotation that has been cast on this amazing plant, Cannabis sativa, since the mid 20<sup>th</sup> century when the US Government's propaganda war against it was initiated; it was demonised in fact.

Industrial hemp and marijuana are both members of the Cannabis sativa family but contain different amounts of Tetrahydrocannabinol, THC, the psychoactive ingredient. The former has an allowable level of no more than 0.035% here in Australia whereas marijuana has a much higher proportion.

Prior to the US campaign, hemp had been grown safely for millennia; both for fibre, food, and pharmaceuticals.

Thankfully there is now a worldwide revival of interest in this plant and the possibilities of an amazing array of value-adding products. Among these are of course the pharmaceutical benefits of medicinal cannabis.

It is critical to note when debating whether or not to legalise the use of medicinal cannabis that neither **MARIJUANA, CANNABIS, nor HEMP HAVE EVER BEEN THE DIRECT CAUSE OF DEATH**. Compare that to the numerous instances of death from a whole variety of other drugs, alcohol or cigarettes. See Appendix One for full details

#### **The efficacy and safety of natural botanical medicinal cannabis flower and extracted cannabinoids for medical purposes**

Research into its benefits has been severely constrained due to the US Marijuana Tax Act of 1937 and the declaration of cannabis as a Schedule I narcotic drug. This classification asserts that cannabis is equally as dangerous to the public as heroin, which is ridiculous as **no one has died from cannabis** and yet cocaine and methamphetamine which can be fatal are classified as Schedule II. Despite this it has been proved to be a safe and effective treatment for many illnesses and **has never been the direct cause of death**. Whereas death from opiates does occur; take the example recently here in Tasmania when a foolish person died after drinking a tea made from poppies. Results from recent research can be obtained from the following website <http://norml.org/component/zoo/category/recent-research-on-medical-marijuana> Article is printed in full in Appendix 2. More in-depth information on individual scientific reports and published papers can be obtained from <http://www.ncbi.nlm.nih.gov/pubmed>

The Cannabis sativa plant contains over a hundred different compounds but the main ones used as medicines are Tetrahydrocannabinol, THC and Cannabidiol, CBD. It has been found that a combination of these two is more efficacious than using either one alone. There are countless combinations depending on the ratio between these two and this is where research can play a vital part.

Research has been carried out in USA by University of California's Centre for Medical Cannabis Research (CMCR) here is a link to their 24 page report

[http://cmcr.ucsd.edu/images/pdfs/cmcr\\_report\\_feb17.pdf](http://cmcr.ucsd.edu/images/pdfs/cmcr_report_feb17.pdf)

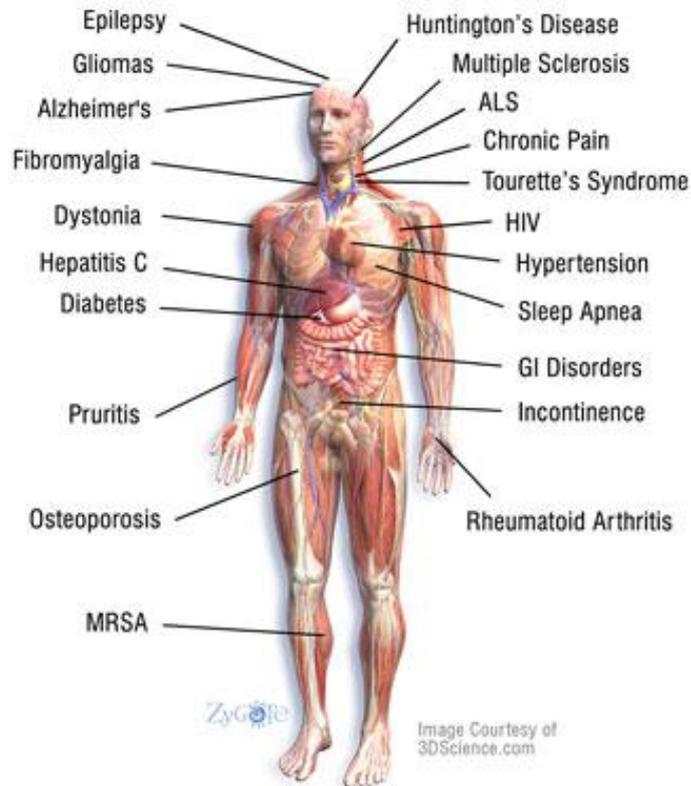
The human body already contains its own endocannabinoids which control areas such as movement, mood, memory, appetite and pain so cannabinoids from Cannabis sativa can naturally interact with these that is why they are so efficient as medicines in controlling a variety of illnesses and why they are safe to use. An extract from the following article explains in depth the endocannabinoid system (ECS)

[http://www.safeaccessnow.org/medical\\_cannabis\\_research\\_what\\_does\\_the\\_evidence\\_say](http://www.safeaccessnow.org/medical_cannabis_research_what_does_the_evidence_say)

*Dr Ethan Russo, a leading cannabinoid researcher states:*

- *The analgesic and palliative effects of the cannabis and cannabinoid preparation have been amply reported over the past generation.... In essence, the effects result from a combination of receptor and non-receptor mediated mechanisms. THC and other cannabinoids exert many actions through cannabinoid receptors, G-protein coupled membrane receptors that are extremely densely represented in central, spinal, and peripheral nociceptive pathways. Endogenous cannabinoids (endocannabinoids) even regulate integrative pain structures such as the periaqueductal gray matter. The endocannabinoid system also interacts in numerous ways with the endogenous opioid and vanilloid systems that that can modulate analgesia and with a myriad of other neurotransmitter systems such as the serotonergic, dopaminergic, glutamatergic, etc, pertinent to pain. Research has shown that the addition of cannabinoid agonists to opiates enhances analgesic efficacy markedly in experimental animals, helps diminish the likelihood of the development of opiate tolerance, and prevents opiate withdrawal. The current author has suggested that a clinical endocannabinoid deficiency may underlie the pathogenesis of migraine, fibromyalgia, idiopathic bowel syndrome, and numerous other painful conditions that defy modern pathophysiological explanation or adequate treatment.<sup>9</sup>*

Here is an example of the parts of the body aided by Medical Cannabis, courtesy of 3DScience.com mentioned in this link <http://norml.org/component/zoo/category/recent-research-on-medical-marijuana>



### **Potential Therapeutic Uses of Medical Marijuana**

From the same website further information can be found by clicking on each area as follows

[Alzheimer's Disease](#)

[ALS](#)

[Chronic Pain](#)

[Diabetes Mellitus](#)

[Dystonia](#)

[Epilepsy](#)

[Fibromyalgia](#)

[GI Disorders](#)

[Gliomas/Cancer](#)

[Hepatitis C](#)

[HIV](#)

[Huntington's Disease](#)

[Hypertension](#)

[Incontinence](#)

[MRSA](#)

[Multiple Sclerosis](#)

[Osteoporosis](#)

[Pruritis](#)

[Rheumatoid Arthritis](#)

[Sleep Apnea](#)

[Tourette's Syndrome](#)

A copy of the general information on medicinal cannabis taken from the same website appears as Appendix 2

Another very informative article from *Americans for Safe Access* discusses uses of medicinal cannabis under the following headings: see Appendix 3

- Endocannabinoid System
- Therapeutic potential of Cannabis
- Cannabis and Cancer
- Combating chemotherapy
- Cancer-fighting cannabinoids
- Cannabinoids and tumour reduction
- Cannabis, HIV/AIDS and Hepatitis C

#### Clinical Trials

- Neuropathic pain
- Hepatitis-C Virus
- Chronic Pain
- Multiple Sclerosis
- Other movements disorders
- Arthritis
- Alzheimer's Disease

We already have clear evidence here in Tasmania that medicinal cannabis does what no other drug has been able to do, namely decrease the amount of seizures that a young girl was experiencing. See <http://www.abc.net.au/news/2014-07-14/mother-of-ill-girl-wants-medical-cannabis-decision-reversed/5596152>

The following article <http://www.mpp.org/assets/documents/low-or-no-thc-high-cbd.html> gives an in-depth account by Dr Sanjay Gupta, a correspondent for a US TV company, who did a report on medicinal cannabis. He was a sceptic at first then came to realise just how efficacious medicinal cannabis could be. See Appendix IV

The following link

<http://medicalmarijuana.procon.org/view.resource.php?resourceID=000145> gives an account of the safety of medicinal cannabis compared to many other drugs. **The result: there has never been a death from the former but many from the latter.** Proof that medicinal cannabis is very safe to use. See Appendix 1

From the Testimony before the Crime Subcommittee of the Judiciary Committee in the US House of Representatives, October 1, 1997 by Prof Grinspoon a Professor of Psychiatry: see <http://medicalmarijuana.procon.org/view.source.php?sourceID=000156>

- . *"Cannabis is remarkably safe. Although not harmless, it is surely less toxic than most of the conventional medicines it could replace if it were legally available. Despite its use by millions of people over thousands of years, **cannabis has never caused an overdose death.**"*

<http://www.youtube.com/watch?v=tEtpxPWjcrw> this is a short video of Prof Grinspoon talking about how his son's nausea, while undergoing chemotherapy, was curtailed immediately after using cannabis

### **If and how natural botanical medicinal cannabis flowers and extracted cannabinoids could and/or should be supplied for medical use**

Generally medicinal cannabis is administered as drops of oil, or smoked, used as a cream as an anti-inflammatory and anti-bacterial agent, or as in recent research using a vapour inhaler. The latter has the benefit of the drug being rapidly absorbed by the body.

At present there are synthetic forms of cannabis available; Dronabinol (Marinol) used to limit nausea following chemotherapy and to stimulate appetite in weight loss from HIV sufferers and Nabilone (Cesamet) also an antiemetic. However research in the UK has shown that far better results are obtained from using natural plant extracts rather than synthetics.

Sativex® an oral/mucosal spray (containing equal parts of THC and CBD) from GW Pharmaceuticals is already available in Canada, UK, Spain, New Zealand and Germany. It has also been approved for distribution in the Czech Republic and Denmark and pending approval in Italy, Sweden and Austria and is in final stages of clinical trials in US. See Appendix V for media release from the company

To deny patients the therapeutic effects of cannabis and yet readily prescribe morphine is an anomaly. The former has never killed anyone--opiates have, therefore medicinal cannabis should be made available on prescription here in Australia as soon as possible

All the above information in this section is taken from  
[http://www.safeaccessnow.org/medical\\_cannabis\\_research\\_what\\_does\\_the\\_evidence\\_say](http://www.safeaccessnow.org/medical_cannabis_research_what_does_the_evidence_say)

There is an excellent report, see Appendix 3, which gives in- depth detail into various illnesses and how their symptoms can be alleviated in many cases by cannabinoids.  
[http://www.safeaccessnow.org/medical\\_cannabis\\_research\\_what\\_does\\_the\\_evidence\\_say](http://www.safeaccessnow.org/medical_cannabis_research_what_does_the_evidence_say)

### **The legal implications and barriers to the medicinal use of natural botanical medicinal, cannabis flower and extracted cannabinoids in Australia**

There are two worldwide Laws regarding narcotic drugs:

- The Single Convention on Narcotic Drugs 1961
- 1971 Convention on Psychotropic Substances

Cannabis appears both as Schedule I and the more severe Schedule IV

It would help if the Federal Government were to reduce it from a Schedule I drug to Schedule II as explained earlier. According to the article on link

<http://norml.org/component/zoo/category/recent-research-on-medical-marijuana.....>

- *there exists little if any scientific basis to justify the federal government's present prohibitive stance and there is ample scientific and empirical evidence to rebut it.*

And again from

[http://www.safeaccessnow.org/medical\\_cannabis\\_research\\_what\\_does\\_the\\_evidence\\_say](http://www.safeaccessnow.org/medical_cannabis_research_what_does_the_evidence_say)

- *A federal policy that prohibits physicians from alleviating suffering by prescribing marijuana to seriously ill patients is misguided, heavy-handed, and inhumane.... It is also hypocritical to forbid physicians to prescribe marijuana while permitting them to prescribe morphine and meperidine to relieve extreme dyspnea and pain... [because] there is no risk of death from smoking marijuana.*

There should be no obstacles to the use of medicinal cannabis in Australia. It should be available on prescription the same as any other drug.

### **The legal implications and barriers to the growing and commercialisation of cannabis flower and extracted cannabinoids in Australia**

Rules and regulations regarding growing of varieties of Cannabis sativa in Australia for medicinal purposes should be no more onerous than that for the poppy industry here in Tasmania.. After all we have successfully grown the latter for decades and as already mentioned cannabis sativa is far less hazardous than poppies.

Any private company who wishes to partake in medicinal marijuana processing would presumably have to undertake the same methods and abide by the same rules and regulations as in the poppy industry.

Information from a 60 minutes TV program on the legal growing of medicinal cannabis in Colorado should allay the fears of people who are concerned re the safety issues of growing the plant in Australia <http://sixtyminutes.ninemsn.com.au//stories/8883772/green-rush-the-push-to-legalise-medical-marijuana-for-aussie-children>

It is **not** grown in open paddocks; rather it is grown in glasshouses under strictly controlled conditions, each plant in its separate container has its own bar code and any interference is therefore easily monitored by state officials.....seed to sale tracking in fact.

There should therefore be no safety or security concerns when growing medicinal cannabis here in Australia.

Incidentally the variety of crop shown in the video is called Charlotte's Web after a little girl called Charlotte Figi who was suffering up to 300 seizures a week. These stopped immediately upon using this variety of medicinal cannabis. It is low in THC (the

psychoactive compound in cannabis) and high in CBD (the non psychoactive compound), therefore it could be termed as a variety of hemp rather than marijuana.

### **The potential impact on agricultural or other sectors in Australia**

It would be a welcome addition to the agricultural sector, providing yet another string to a farmer's bow. Scientific research, the manufacturing and processing of the crop would supply much needed jobs and a boost to the economy, plus the drug could ease the suffering of Australians with severe illnesses whose relief can only be obtained by using medicinal cannabis.

### **SUMMARY**

Medicinal Cannabis has been used safely for millennia and there is ample evidence worldwide of its therapeutic value. **No one has died from using medicinal cannabis whereas other drugs have proved lethal at times.**

Research should be encouraged to enable different varieties to be grown. Medical practitioners should be encouraged to attend information sessions on the different species and information on the various ailments which can be treated (see the appendix items). No one should be denied the opportunity to use medicinal cannabis for medical purposes and this should be made legal.

It would create jobs in agriculture, manufacturing and scientific research, at the same time alleviating the distressing symptoms of many illnesses

**I therefore urge the Federal Government to allow the use of medicinal cannabis without delay.**

Sincerely Estelle Ross

## APPENDIX 1

### MEDICAL MARIJUANA PROS AND CONS

#### Deaths from Marijuana v. 17 FDA-Approved Drugs

*(Jan. 1, 1997 to June 30, 2005)*

- I. [Background](#)
- II. [Cause of Death Categories & Definitions](#)
- III. [FDA Disclaimer of Information](#)
- IV. [Summary of Deaths by Drug Classification](#)
- V. [Deaths from Marijuana & 17 FDA-Approved Drugs](#)
- VI. [Sources & Disagreement on Marijuana Deaths](#)
- VII. [Full Text of All 17 FDA "Adverse Event" Reports](#)

#### **I. Background**

Much of the medical marijuana discussion has focused on the safety of marijuana compared to the safety of FDA-approved drugs. On June 24, 2005 ProCon.org sent a [Freedom of Information Act \(FOIA\) request](#) to the US [Food and Drug Administration](#) (FDA) to find the number of deaths caused by marijuana compared to the number of deaths caused by 17 FDA-approved drugs. Twelve of these FDA-approved drugs were chosen because they are commonly prescribed in place of medical marijuana, while the remaining five FDA-approved drugs were randomly selected because they are widely used and recognized by the general public.

We chose Jan. 1, 1997 as our starting date as it is the beginning of the first year following the Nov. 1996 approval of the first state medical marijuana laws (such as [California's Proposition 215](#)). The FDA reports we read from Sep. 13, 2005 to Oct. 14, 2005 included drug deaths "to present", which was the date each report was compiled for our request. We cut off the counting as of June 30, 2005 to provide a uniform end-date to the various reports.

On Aug. 25, 2005 the FDA sent us 12 CDs and five printed reports containing copies of their Adverse Event Reporting System (AERS) report on each drug requested. These reports included all adverse events reported to the FDA, only a portion of which included deaths. We manually counted the number of deaths reported on each drug from the FDA-supplied information.

A review of the FDA Adverse Events reports also revealed some deaths where marijuana was at least a concomitant drug (a drug also used at the time of death) in some cases. On Oct. 14, 2005 we used the Freedom of Information Act to request a copy of the adverse events reported deaths for marijuana, cannabis, and cannabinoids. We received those reports on Aug. 3, 2006 in the form of three additional CDs. The FDA listed over 150 deaths on more than one report (aka double counted them), however, to ensure accuracy, we removed duplicates from our final count. All the FDA adverse events reports that we received can be seen in full at the bottom of this page.

#### **II. Cause of Death Categories & Definitions**

The FDA AERS reports rely on health professionals to detect an "adverse event" and attribute that event to the drug, and then to voluntarily report that effect to either the FDA or the drug manufacturer. The drug firm, by law, must report that event to the FDA. The FDA states "ninety percent of the FDA's reports are received from drug manufacturers" on page one of its "[Adverse Event Reporting System \(AERS\) Brief Description with Caveats of System](#)."  (PDF 2.7 MB)

Select instructions on how to report adverse events, as per the FDA's [AERS Form Instructions](#)  (PDF 65 KB), are provided below:

- **Adverse Event:** Any incident where the use of a medication (drug or biologic, including HCT/P), at any dose, a medical device (including in vitro diagnostics) or a special nutritional product (e.g., dietary supplement, infant formula or medical food) is suspected to have resulted in an adverse outcome in a patient.
  - **Death:** Check only if you suspect that the death was an outcome of the adverse event, and include the date if known. Do not check if:
    - The patient died while using a medical product, but there was no suspected association between the death and
    - A foetus is aborted because of a congenital anomaly (birth defect), or is miscarried
- A. **Suspect Product(s):** A suspect product is one that you suspect is associated with the adverse event.

Up to two (2) suspect products may be reported on one form (#1=first suspect product, #2=second suspect product). Attach an additional form if there were more than two suspect products associated with the reported adverse event.

- B. **To report:** it is not necessary to be certain of a cause/effect relationship between the adverse event and the use of the medical product(s) in question. Suspicion of an association is sufficient reason to report. Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

### III. FDA Disclaimer of Information

#### III. FDA Disclaimer of Information

Included in the 15 CDs and five printed reports from the FDA was the following disclosure:

*"The information contained in the reports has not been scientifically or otherwise verified. For any given report there is no certainty that the suspected drug caused the reaction. This is because physicians are encouraged to report suspected reactions. The event may have been related to the underlying disease for which the drug was given to concurrent drugs being taken or may have occurred by chance at the same time the suspected drug was taken.*

*Numbers from these data must be carefully interpreted as reported rates and not occurrence rates. True incidence rates cannot be determined from this database. Comparisons of drugs cannot be made from these data."*

-- July 18, 20/05 - FDA Office of Pharmacoepidemiology and Statistical Science, "Adverse Event Reporting System (AERS) Brief Description with Caveats of System"

**[Editor's Note - ProCon.org makes no claim that the data below reflects occurrence rates. The information is presented for our readers' benefit who may feel that the relative comparisons have value. ProCon.org attempted to find the total number of users of each of these drugs by contacting the FDA, pharmaceutical trade organizations, and the actual drug manufacturers. We either did not receive a response or were told the information was proprietary or otherwise unavailable]**

#### IV. Summary of Deaths by Drug Classification

DRUG CLASSIFICATION	Specific Drugs per Category	Primary Suspect of the Death	Secondary Suspect (Contributing to death)	Total Deaths Reported 1/1/97 - 6/30/05
<b>A. MARIJUANA</b> <i>also known as: Cannabis sativa L</i>	<a href="#">Marijuana</a> <a href="#">Cannabis</a> <a href="#">Cannabinoids</a>	<b>0</b>	<b>279</b>	<b>279</b>
<b>B. ANTI-EMETICS</b> <i>(used to treat vomiting)</i>	<a href="#">Compazine</a> <a href="#">Reglan</a> <a href="#">Marinol</a> <a href="#">Zofran</a> <a href="#">Anzemet</a> <a href="#">Kytril</a> <a href="#">Tigan</a>	<b>196</b>	429	<b>625</b>
<b>C. ANTI-SPASMODICS</b> <i>(used to treat muscle spasms)</i>	<a href="#">Baclofen</a> <a href="#">Zanaflex</a>	<b>118</b>	56	<b>174</b>
<b>D. ANTI-PSYCHOTICS</b> <i>(used to treat psychosis)</i>	<a href="#">Haldol</a> <a href="#">Lithium</a> <a href="#">Neurontin</a>	<b>1,593</b>	702	<b>2,295</b>
<b>E. OTHER POPULAR DRUGS</b> <i>(used to treat various conditions including ADD, depression, narcolepsy, erectile dysfunction, and pain)</i>	<a href="#">Ritalin</a> <a href="#">Wellbutrin</a> <a href="#">Adderall</a> <a href="#">Viagra</a> <a href="#">Vioxx*</a>	<b>8,101</b>	492	<b>8,593</b>
<b>F. TOTALS of A-E</b>	<b>Number of Drugs in Total</b>	<b>Primary Suspect of the Death</b>	<b>Secondary Suspect (Contributing to death)</b>	<b>Total Deaths Reported 1/1/97 - 6/30/05</b>
• <b>TOTAL DEATHS FROM MARIJUANA</b>	<b>1</b>	<b>0</b>	<b>279</b>	<b>279</b>
• <b>TOTAL DEATHS FROM 17 FDA-APPROVED DRUGS</b>	<b>17</b>	<b>10,008</b>	<b>1,679</b>	<b>11,687</b>

#### V. Chart of Deaths from Marijuana and 17 FDA-Approved Drugs

<b>A. Marijuana</b>
---------------------

<b>DRUG</b> (Year Approved)	<b>Primary Suspect of the Death</b>	<b>Secondary Suspect (Contributing to death)</b>	<b>Total Deaths Reported</b> 1/1/97 - 6/30/05
1. <b>Marijuana</b> (not approved) <i>also known as: Cannabis sativa L</i>	<b>0</b>	109	<b>109</b>
2. <b>Cannabis</b> (not approved) <i>also known as: Cannabis sativa L</i>	<b>0</b>	78	<b>78</b>
3. <b>Cannabinoids</b> <i>(unclear if these mentions include non-plant cannabinoids)</i>	<b>0</b>	92	<b>92</b>
<b>Sub-Total - Anti-Emetics</b>	<b>0</b>	279	<b>279</b>

<b>FDA-Approved Drugs Prescribed in Place of Medical Marijuana</b>			
<b>B. Anti-Emetics</b>			
<b>DRUG</b> (Year Approved)	<b>Primary Suspect of the Death</b>	<b>Secondary Suspect (Contributing to death)</b>	<b>Total Deaths Reported</b> 1/1/97 - 6/30/05
1. <b>Compazine</b> (1980) <i>also known as: Phenothiazine, prochlorperazine</i>	<b>15</b>	30	<b>45</b>
2. <b>Reglan</b> (1980) <i>also known as: Metaclopramide, Paspertin, Primperan</i>	<b>37</b>	278	<b>315</b>
3. <b>Marinol</b> (1985) <i>also known as: Dronabinol</i>	<b>4</b>	1	<b>5</b>
4. <b>Zofran</b> (1991) <i>also known as: Ondansetron hydrochloride</i>	<b>79</b>	76	<b>155</b>
5. <b>Anzemet</b> (1997) <i>also known as: Dolasetron mesylate</i>	<b>22</b>	5	<b>27</b>
6. <b>Kytril</b> (1999) <i>also known as: Granisetron hydrochloride</i>	<b>36</b>	24	<b>60</b>
7. <b>Tigan</b> (2001) <i>also known as: Trimethobenzamide</i>	<b>3</b>	15	<b>18</b>

<b>Sub-Total - Anti-Emetics</b>		<b>196</b>	<b>429</b>	<b>625</b>
<b>C. Anti-Spasmodics</b>				
<b>DRUG (Year Approved)</b>		<b>Primary Suspect of the Death</b>	<b>Secondary Suspect (Contributing to death)</b>	<b>Total Deaths Reported 1/1/97 - 6/30/05</b>
1.	<b>Baclofen (1967)</b> <i>also known as: Lioresal, 4-amino-3-(4-chlorophenyl)-butanoic acid</i>	<b>72</b>	33	<b>105</b>
2.	<b>Zanaflex (1996)</b> <i>also known as: Tizanidine hydrochloride, Sirdalud, Ternelin</i>	<b>46</b>	23	<b>69</b>
<b>Sub-Total - Anti-Spasmodics</b>		<b>118</b>	56	<b>174</b>
<b>D. Anti-Psychotics</b>				
<b>DRUG (Year Approved)</b>		<b>Primary Suspect of the Death</b>	<b>Secondary Suspect (Contributing to death)</b>	<b>Total Deaths Reported 1/1/97 - 6/30/05</b>
1.	<b>Haldol (1967)</b> <i>also known as: Haloperidol, Haldol Decanoate, Serenace, Halomonth</i>	<b>450</b>	267	<b>717</b>
2.	<b>Lithium (1970)</b> <i>also known as: Lithium Carbonate, Eskalith, Lithobid, Lithonate, Teralithe, Lithane, Hypnorex, Limas, Lithionit, Quilonum</i>	<b>175</b>	133	<b>308</b>
3.	<b>Neurontin (1994)</b> <i>also known as: Gabapentin</i>	<b>968</b>	302	<b>1,270</b>
<b>Sub-Total - Anti-Psychotics</b>		<b>1,593</b>	702	<b>2,295</b>
<b>E. Other Well-Known and Randomly Selected FDA-Approved Drugs</b>				
<b>DRUG (Year Approved)</b>		<b>Primary Suspect of the Death</b>	<b>Secondary Suspect (Contributing to death)</b>	<b>Total Deaths Reported 1/1/97 - 6/30/05</b>
1.	<b>Ritalin (1955)</b> <i>also known as: Methylphenidate, Concerta, Medadate, Ritaline (used to treat ADD and ADHD)</i>	<b>121</b>	53	<b>174</b>

2.	<b>Wellbutrin</b> (1997) <i>also known as: Bupropion Hydrochloride, Zyban, Zyntabac, Amfebutamone</i> (used to treat depression & anxiety)	<b>1,132</b>	220	<b>1,352</b>
3.	<b>Adderall</b> (1966) <i>also known as: Dextroamphetamine Saccharate, Amphetamine Aspartate, Dextroamphetamine Sulfate USP, Amphetamine Sulfate USP</i> (used to treat narcolepsy or to control hyperactivity in children)	<b>54</b>	12	<b>66</b>
4.	<b>Viagra</b> (1998) <i>also known as: Sildenafil Citrate</i> (used to treat erectile dysfunction)	<b>2,254</b>	40	<b>2,294</b>
5.	<b>Vioxx*</b> (1999) <i>also known as: Rofecoxib, Arofexx</i> (used to treat osteoarthritis and pain)	<b>4,540</b>	167	<b>4,707</b>
<b>Sub-Total - Other Popular Drugs</b>		<b>8,101</b>	492	<b>8,593</b>
<b>F. TOTALS of A-E</b>		<b>Primary Suspect</b>	<b>Secondary Suspect (Contributing to death)</b>	<b>Total Deaths Reported 1/1/97 - 6/30/05</b>
• <b>TOTAL DEATHS FROM MARIJUANA</b>		<b>0</b>	279	<b>279</b>
• <b>TOTAL DEATHS FROM 17 FDA-APPROVED DRUGS</b>		<b>10,008</b>	1,679	<b>11,687</b>

\*[**Editor's Note:** Merck, the maker of Vioxx, publicly announced its voluntary withdrawal of Vioxx from the global market on September 30, 2004. In 2005, advisory panels in both the US and Canada encouraged the return of Vioxx to the market, stating that Vioxx's benefits outweighed the risks for some patients. The FDA advisory panel voted 17-15 to allow the drug to return to the market despite being found to increase heart risk. The vote in Canada was 12-1, and the Canadian panel noted that the cardiovascular risks from Vioxx seemed to be no worse than those from ibuprofen. Notwithstanding these recommendations, Merck has not returned Vioxx to the market as of July 8, 2009.]

---

## VI. Sources & Disagreement on Marijuana Deaths

<b>Has marijuana caused any deaths?</b>	
<b>General Reference</b> (not clearly pro or con)	
<p>The Substance Abuse and Mental Health Services Administration's (SAMHSA) 2003 report <a href="#">Mortality Data from the Drug Abuse Warning Network, 2001</a> (1.5 MB)  stated:</p> <p><i>"Marijuana is rarely the only drug involved in a drug abuse death. Thus ... the proportion of marijuana-induced cases labelled as 'One drug' (i.e., marijuana only) will be zero or nearly zero."</i></p> <p>2003 - <a href="#">Substance Abuse and Mental Health Services Administration</a> ★</p>	
PRO (Yes)	CON (No)
<p>Thomas Geller, MD, Associate Professor of Child Neurology at the Saint Louis University Health Sciences Centre, et al., wrote the following in their Apr. 4, 2004 article titled "Cerebellar Infarction in Adolescent Males Associated with Acute Marijuana Use," published in the journal <i>Paediatrics</i>:</p> <p><i>"Each of the 3 cannabis-associated cases of cerebellar infarction was confirmed by biopsy (1 case) or necropsy (2 cases)... Brainstem compromise caused by cerebellar and cerebral oedema led to death in the 2 fatal cases."</i></p> <p>Apr. 4, 2004 - <a href="#">Thomas Geller, MD</a> ★★★★★</p> <p>Liliana Bachs, MD, Senior Medical Officer at the Norwegian Institute of Public Health, et al., wrote the following in their Dec. 27, 2001 article titled "Acute Cardiovascular Fatalities Following Cannabis Use," published in the journal <i>Forensic Science International</i>:</p> <p><i>"Cannabis is generally considered to be a drug with very low toxicity. In this paper, we report six cases where recent cannabis intake was associated with sudden and unexpected death. An acute cardiovascular event was the probable cause of death. In all cases, cannabis intake was documented by blood analysis... Further investigation of clinical, toxicological and epidemiological aspects is needed to enlighten causality between cannabis intake and acute cardiovascular events."</i></p> <p>Dec. 27, 2001 - <a href="#">Liliana Bachs, MD</a> ★★★★★</p> <p><b>[Editor's Note:</b> Dr. Bachs clarified the findings from her Dec. 27, 2001 study reported above in a Nov. 28, 2005 email to ProCon.org, as quoted below.</p>	<p>Stephen Sidney, MD, Associate Director for Clinical Research at Kaiser Permanente, wrote the following in his Sep. 20, 2003 article titled "Comparing Cannabis with Tobacco -- Again," published in the <i>British Medical Journal</i>:</p> <p><i>"No acute lethal overdoses of cannabis are known, in contrast to several of its illegal (for example, cocaine) and legal (for example, alcohol, aspirin, acetaminophen) counterparts..."</i></p> <p><i>Although the use of cannabis is not harmless, the current knowledge base does not support the assertion that it has any notable adverse public health impact in relation to mortality."</i></p> <p>Sep. 20, 2003 - <a href="#">Stephen Sidney, MD</a> ★★★★★</p> <p>Joycelyn Elders, MD, former US Surgeon General, wrote the following in her Mar. 26, 2004 editorial published in the <i>Providence Journal</i>:</p> <p><i>"Unlike many of the drugs we prescribe every day, marijuana has never been proven to cause a fatal overdose."</i></p> <p>Mar. 26, 2004 - <a href="#">Joycelyn Elders, MD</a> ★★★★★</p>

"Causality is a difficult assessment in forensic toxicology. It is often an 'exclusion diagnosis,' and so it is in our cases. I'm therefore not sure about how to classify those deaths.

At the time I published that study I would probably not classify [the cannabis] as primary causation because it was not broadly accepted that [a death from cannabis] could occur at all. Today I see reports coming all the time that acknowledge cannabis cardiovascular risks, and the situation may be different."

## VII. Full Text of All 20 FDA "Adverse Event" Reports

[Please note that some of these PDF files exceed 5 megabytes and may take several minutes to load]

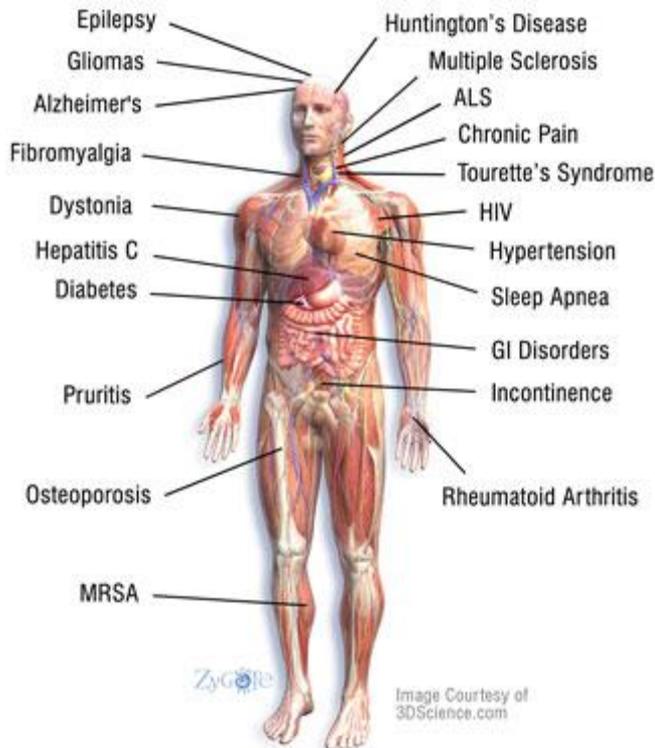
1. [Adderall \(PDF 495 KB\)](#)
2. [Anzemet \(PDF 1.5 MB\)](#)
3. [Baclofen \(PDF 755 KB\)](#)
4. [Cannabinoids \(PDF 65 KB\)](#)
5. [Cannabis \(PDF 330 KB\)](#)
6. [Compazine \(PDF 1.6 MB\)](#)
7. [Haldol \(PDF 1.5 MB\)](#)
8. [Kytrel \(PDF 2.2 MB\)](#)
9. [Lithium \(PDF 2.4 MB\)](#)
10. [Marijuana \(PDF 220 KB\)](#)
11. [Marinol \(PDF 535 KB\)](#)
12. [Neurontin \(PDF 6.3 MB\)](#)
13. [Ritalin \(PDF 1.6 MB\)](#)
14. [Reglan \(PDF 1.5 MB\)](#)
15. [Tigan \(PDF 2.4 MB\)](#)
16. [Viagra \(PDF 7.6 MB\)](#)
17. [Vioxx \(PDF 31.5 MB\)](#)
18. [Wellbutrin \(PDF 8.3 MB\)](#)
19. [Zanaflex \(PDF 6556 KB\)](#)
20. [Zofran \(PDF 1 MB\)](#)

©ProCon.org, a 501(c)(3) nonprofit  
All rights reserved  
233 Wilshire Blvd., Suite 200, Santa Monica, CA 90401  
Tel: 310-451-9596 Fax: 310-393-2471

## APPENDIX 2

### ● **Recent Research on Medical Marijuana**

- **PDF**
- **Emerging Clinical Applications For Cannabis & Cannabinoids**  
A Review of the Recent Scientific Literature, 2000 — 2013



### ● **Potential Therapeutic Uses of Medical Marijuana**

- [Foreword](#)
- [Endocannabinoid System](#)
- [Why Medical Cannabis](#)
- [Alzheimer's Disease](#)
- [ALS](#)
- [Chronic Pain](#)
- [Diabetes Mellitus](#)
- [Dystonia](#)
- [Epilepsy](#)
- [Fibromyalgia](#)
- [GI Disorders](#)
- [Gliomas/Cancer](#)
- [Hepatitis C](#)
- [HIV](#)
- [Huntington's Disease](#)
- [Hypertension](#)
- [Incontinence](#)
- [MRSA](#)
- [Multiple Sclerosis](#)
- [Osteoporosis](#)
- [Pruritus](#)
- [Rheumatoid Arthritis](#)
- [Sleep Apnea](#)
- [Tourette's Syndrome](#)

- Humans have cultivated and consumed the flowering tops of the female cannabis plant, colloquially known as [marijuana](#), since virtually the beginning of recorded history. Cannabis-based textiles dating to 7,000 B.C.E have been recovered in northern China, and the plant's use as a medicinal and mood altering agent date back nearly as far. In 2008, archaeologists in Central Asia discovered over two-pounds of cannabis in the 2,700-year-old grave of an ancient shaman. After scientists conducted extensive testing on the material's potency, they affirmed, "[T]he most probable conclusion ... is that [ancient] culture[s] cultivated cannabis for pharmaceutical, psychoactive, and divinatory purposes."
- Modern cultures continue to indulge in the consumption of cannabis for these same purposes, despite a present-day, virtual worldwide ban on the plant's cultivation and use. In the United States, federal prohibitions outlawing cannabis' recreational, industrial, and therapeutic use were first imposed by Congress under the Marihuana Tax Act of 1937 and then later reaffirmed by federal lawmakers' decision to classify marijuana -- as well as all of the plant's organic compounds (known as cannabinoids) -- as a Schedule I substance under the Controlled Substances Act of 1970. This classification, which asserts by statute that cannabis is equally as dangerous to the public as is heroin, defines cannabis and its dozens of distinct cannabinoids as possessing 'a high potential for abuse, ... no currently accepted medical use, ... [and] a lack of accepted safety for the use of the drug ... under medical supervision.' (By contrast, cocaine and methamphetamine -- which remain illicit for recreational use but may be consumed under a doctor's supervision -- are classified as Schedule II drugs; examples of Schedule III and IV substances include anabolic steroids and Valium respectively, while codeine-containing analgesics are defined by a law as Schedule V drugs, the federal government's most lenient classification.) In July 2011, the Obama Administration [rebuffed](#) an administrative inquiry seeking to reassess cannabis' Schedule I status, and federal lawmakers continue to cite the drug's dubious categorization as the primary rationale for the government's ongoing criminalization of the plant and those who use it. A three-judge panel for the US Court of Appeals for the District of Columbia [affirmed](#) the Administration's position in 2013, arguing that a judicial review of cannabis' federally prohibited status was not warranted at this time.
- Nevertheless, there exists little if any scientific basis to justify the federal government's present prohibitive stance and there is ample scientific and empirical evidence to rebut it. Despite the US government's nearly century-long prohibition of the plant, cannabis is nonetheless one of the most investigated therapeutically active substances in history. To date, there are over 20,000 published studies or reviews in the scientific literature referencing the cannabis plant and its cannabinoids, nearly half of which were published within the last five years according to a key word search on the search engine PubMed Central, the US government repository for peer-reviewed scientific research. While much of the renewed interest in cannabinoid therapeutics is a result of the discovery of the [endocannabinoid regulatory system](#) (which is [described](#) in detail later in this booklet), some of this increased attention is also due to the growing body of testimonials from medical cannabis patients and their physicians.
- The scientific conclusions of the overwhelmingly majority of modern research directly conflicts with the federal government's stance that cannabis is a highly dangerous substance worthy of absolute criminalization.
- For example, in February 2010 investigators at the [University of California Center for Medicinal Cannabis Research](#) publicly announced the [findings](#) of a series of randomized, placebo-controlled clinical trials on the medical utility of inhaled cannabis. The studies, which utilized the so-called 'gold standard' FDA clinical trial

design, concluded that marijuana ought to be a "first line treatment" for patients with neuropathy and other serious illnesses.

- Several of studies conducted by the Center assessed smoked marijuana's ability to alleviate neuropathic pain, a notoriously difficult to treat type of nerve pain associated with cancer, diabetes, HIV/AIDS, spinal cord injury and many other debilitating conditions. Each of the trials found that cannabis consistently reduced patients' pain levels to a degree that was as good or better than currently available medications.
- Another study conducted by the Center's investigators assessed the use of marijuana as a treatment for patients suffering from multiple sclerosis. That study determined that "smoked cannabis was superior to placebo in reducing spasticity and pain in patients with MS, and provided some benefit beyond currently prescribed treatments."
- A [summary](#) of the Center's clinical trials, published in 2012 in the *Open Neurology Journal*, concluded: "Evidence is accumulating that cannabinoids may be useful medicine for certain indications. ... The classification of marijuana as a Schedule I drug as well as the continuing controversy as to whether or not cannabis is of medical value are obstacles to medical progress in this area. Based on evidence currently available the Schedule I classification is not tenable; it is not accurate that cannabis has no medical value, or that information on safety is lacking."
- Around the globe, similarly controlled trials are also taking place. A 2010 [review](#) by researchers in Germany reports that since 2005 there have been 37 controlled studies assessing the safety and efficacy of marijuana and its naturally occurring compounds in a total of 2,563 subjects. By contrast, many FDA-approved drugs go through far fewer trials involving far fewer subjects.
- As clinical research into the therapeutic value of cannabinoids has proliferated so too has investigators' understanding of cannabis' remarkable capability to combat disease. Whereas researchers in the 1970s, 80s, and 90s primarily assessed cannabis' ability to temporarily alleviate various disease symptoms -- such as the [nausea](#) associated with cancer chemotherapy -- scientists today are exploring the potential role of cannabinoids to [modify disease](#).
- Of particular interest, scientists are investigating cannabinoids' capacity to moderate autoimmune disorders such as [multiple sclerosis](#), [rheumatoid arthritis](#), and [inflammatory bowel disease](#), as well as their role in the treatment of neurological disorders such as [Alzheimer's disease](#) and [amyotrophic lateral sclerosis](#) (a.k.a. Lou Gehrig's disease.) In 2009, the American Medical Association (AMA) [resolved](#) for the first time in the organization's history "that marijuana's status as a federal Schedule I controlled substance be reviewed with the goal of facilitating the conduct of clinical research and development of cannabinoid-based medicines."
- Investigators are also studying the [anti-cancer](#) activities of cannabis, as a growing body of preclinical and clinical data concludes that cannabinoids can reduce the spread of specific cancer cells via apoptosis (programmed cell death) and by the inhibition of angiogenesis (the formation of new blood vessels). Arguably, these latter findings represent far broader and more significant applications for cannabinoid therapeutics than researchers could have imagined some thirty or even twenty years ago.
- **THE SAFETY PROFILE OF MEDICAL CANNABIS**
- Cannabinoids have a remarkable safety record, particularly when compared to other therapeutically active substances. Most significantly, the consumption of marijuana -- regardless of quantity or potency -- cannot induce a fatal overdose. According to a 1995 [review](#) prepared for the World Health Organization, "There are no recorded cases of overdose fatalities attributed to cannabis, and the estimated lethal dose for

humans extrapolated from animal studies is so high that it cannot be achieved by ... users."

- In 2008, investigators at McGill University Health Centre and McGill University in Montreal and the University of British Columbia in Vancouver [reviewed](#) 23 clinical investigations of medical cannabinoid drugs (typically oral THC or [liquid cannabis extracts](#)) and eight observational studies conducted between 1966 and 2007. Investigators "did not find a higher incidence rate of serious adverse events associated with medical cannabinoid use" compared to non-using controls over these four decades.
- That said, cannabis should not necessarily be viewed as a 'harmless' substance. Its active constituents may produce a variety of physiological and euphoric effects. As a result, there may be some populations that are susceptible to increased risks from the use of cannabis, such as [adolescents](#), [pregnant or nursing mothers](#), and patients who have a family history of [mental illness](#). Patients with decreased lung function (such as chronic obstructive pulmonary disease) or those who have a history of heart disease or [stroke](#) may also be at a greater risk of experiencing adverse side effects from marijuana. As with any medication, patients should consult thoroughly with their physician before deciding whether the medical use of cannabis is safe and appropriate.
- **HOW TO USE THIS REPORT**
- As states continue to approve legislation enabling the physician-supervised use of medical marijuana, more patients with varying disease types are exploring the use of therapeutic cannabis. Many of these patients and their physicians are now discussing this issue for the first time and are seeking guidance on whether the therapeutic use of cannabis may or may not be advisable. This report seeks to provide this guidance by summarizing the most recently published scientific research (2000-2013) on the therapeutic use of cannabis and cannabinoids for 20 clinical indications.
- In some of these cases, modern science is now affirming longtime anecdotal reports of medical cannabis users (e.g., the use of cannabis to alleviate [GI disorders](#)). In other cases, this research is highlighting entirely new potential clinical utilities for cannabinoids (e.g., the use of cannabinoids to modify the progression of [diabetes](#).)
- The conditions profiled in this report were chosen because patients frequently inquire about the therapeutic use of cannabis to treat these disorders. In addition, many of the indications included in this report may be moderated by cannabis therapy. In several cases, preclinical data and clinical data indicate that cannabinoids may halt the advancement of these diseases in a more efficacious manner than available pharmaceuticals.
- For patients and their physicians, this report can serve as a primer for those who are considering using or recommending medical cannabis. For others, this report can serve as an introduction to the broad range of emerging clinical applications for cannabis and its various compounds.
- Paul Armentano  
Deputy Director  
NORML | NORML Foundation  
Washington, DC  
January 7, 2014
- \* The author would like to acknowledge Drs. [Dale Gieringer](#), Estelle Goldstein, Dustin Sulak, Gregory Carter, Steven Karch, and [Mitch Earleywine](#), as well as Bernard Ellis, MPH, former NORML interns

- John Lucy, Christopher Rasmussen, and Rita Bowles, for providing research assistance for this report. The NORML Foundation would also like to acknowledge Dale Gieringer, [Paul Kuhn](#), and [Richard Wolfe](#) for their financial contributions toward the publication of this report.
  - \*\* Important and timely publications such as this are only made possible when concerned citizens become involved with NORML. For more information on joining NORML or making a donation, please visit: <http://www.norml.org/join>. Tax-deductible donations in support of NORML's public education campaigns should be made payable to the [NORML Foundation](#).
-

## **APPENDIX 3**

### **From**

[http://www.safeaccessnow.org/medical\\_cannabis\\_research\\_what\\_does\\_the\\_evidence\\_say](http://www.safeaccessnow.org/medical_cannabis_research_what_does_the_evidence_say)

### Medical Cannabis Research What the Science Says

It can be difficult to locate information about the safety and therapeutic value of cannabis. An unfortunate result of the federal prohibition of cannabis has been limited clinical research to investigate the safety and efficacy of cannabis to control symptoms of serious and chronic illness. Many scientists have noted research is “hindered by a complicated federal approval process, limited availability of research grade marijuana, and the debate over legalization.”<sup>1</sup>

Nonetheless, the documented use of cannabis as a safe and effective therapeutic botanical dates to 2700 BC. Between 1840 and 1900, European and American journals of medicine published more than 100 articles on the therapeutic use of cannabis. In fact, cannabis was part of the American pharmacopoeia until 1942, and is currently available by prescription in Canada, the Netherlands, Israel, and Germany.

The political interference with cannabis research and its use as a medicine originated with the Marihuana Tax Act of 1937. Over the objections of the American Medical Association,<sup>2</sup> the United States Congress passed the first federal law restricting access to cannabis, even for medical and research purposes. Since then, numerous reviews by local, federal and international commissions have confirmed the relative safety and efficacy of cannabis as a medicine. And in recent decades, research studies have further shown cannabis has the potential to treat a variety of debilitating conditions for which conventional treatments are lacking. Yet the use of cannabis remains completely prohibited by federal law—even for medical purposes.

#### **Content:**

1. [The Endocannabinoid System](#)
2. [Emerging Clinical Data](#)
3. [The Clinical Trials](#)
4. [Cannabis-based Medicines](#)
5. [Investigative Roadblocks](#)
6. [Government Studies and Programs](#)

### **The Endocannabinoid System (ECS)**

Humans have used drugs derived from the opium poppy for thousands of years to lessen pain and produce euphoria. In 1973, scientists discovered the brain receptors that interact with these opiates, which include opium, morphine, and heroin. In 1975, the first of the brain's natural chemicals that bind with these receptors was identified. The similarity of this chemical, enkephalin, to morphine suggested opiate drugs work primarily by mimicking natural opiate-like molecules. These discoveries helped explain the effects of opiate drugs and opened the door to the development of powerful new therapeutic drugs that revolutionized pain management.

Similarly, humans have used the cannabis plant for thousands of years to reduce pain, control nausea, stimulate appetite, control anxiety, and produce feelings of euphoria. Since 1964 when the first cannabinoid was identified, researchers have made new discoveries that help us better understand not just why and how cannabis works so well for so many people but its full therapeutic potential.

The therapeutic benefits of cannabis are derived from the interactions of cannabinoids and the human body's own endocannabinoid system, first identified in 1988. The endocannabinoid system (ECS) is a sophisticated group of neuromodulators, their receptors, and signaling pathways involved in regulating a variety of physiological processes including movement, mood, memory, appetite, and pain.

One of the leading modern cannabinoid researchers, Dr. Ethan Russo, offers this comprehensive description of the ECS and its importance to a variety of physiological functions:

The analgesic and palliative effects of the cannabis and cannabinoid preparation have been amply reported over the past generation.... In essence, the effects result from a combination of receptor and non-receptor mediated mechanisms. THC and other cannabinoids exert many actions through cannabinoid receptors, G-protein coupled membrane receptors that are extremely densely represented in central, spinal, and peripheral nociceptive pathways. Endogenous cannabinoids (endocannabinoids) even regulate integrative pain structures such as the periaqueductal gray matter. The endocannabinoid system also interacts in numerous ways with the endogenous opioid and vanilloid systems that can modulate analgesia and with a myriad of other neurotransmitter systems such as the serotonergic, dopaminergic, glutamatergic, etc, pertinent to pain. Research has shown that the addition of cannabinoid agonists to opiates enhances analgesic efficacy markedly in experimental animals, helps diminish the likelihood of the development of opiate tolerance, and prevents opiate withdrawal. The current author has suggested that a clinical endocannabinoid deficiency may underlie the pathogenesis of migraine, fibromyalgia, idiopathic bowel syndrome, and numerous other painful conditions that defy modern pathophysiological explanation or adequate treatment.<sup>9</sup>

In the little more than 20 years since researchers began developing an understanding of the ECS, two types of cannabinoid receptors, CB1 and CB2, have been identified, setting the stage for discoveries that have dramatically increased our understanding of how cannabis and its many constituent cannabinoids affect the human body.<sup>10-11</sup>

CB1 receptors are found in the central nervous system, particularly the brain, and in other organs and tissues such as the eyes, lungs, kidneys, liver and digestive tract. In fact, the brain's receptors for cannabinoids far outnumber its opiate receptors, perhaps by as much as ten to one. The relative safety of cannabis is explained by the fact that cannabinoid receptors are virtually absent from those regions at the base of the brain that are responsible for such vital functions as breathing and heart control. CB2 receptors are primarily located in tissues associated with immune function, such as the spleen, thymus, tonsils, bone marrow, and white blood cells.

Research is helping scientists and physicians understand the role of the endocannabinoid system in regulating a variety of bodily functions. As noted by the researcher who first identified THC, Raphael Mechoulam, the discovery of the endocannabinoid system has

generated a great deal of interest in identifying opportunities for the development of a wide variety of cannabis-based and other cannabinoid therapeutic drugs.<sup>12</sup>

In the meantime, physicians are developing protocols for treating patients with cannabis medicines. Doctors at the University of California Center for Medicinal Cannabis Research, which has completed a series of randomized clinical trials with patients, recently published guidelines for medical care. They note that the decision to use cannabis therapeutics, like other treatment modes, should be based on careful assessment of the patient's condition with consideration for other possible treatments. They propose a possible treatment decision-tree for physicians, using neuropathic pain as an example, as reproduced below.

This is similar to the guidelines established by the California Medical Board for doctors. They indicate that physicians recommending medical cannabis should:

1. Take a history and conduct a good faith examination of the patient;
2. Develop a treatment plan with objectives;
3. Provide informed consent, including discussion of side effects;
4. Periodically review the treatment's efficacy;
5. Obtain consultations, as necessary; and
6. Keep proper records supporting the decision to recommend the use of medical marijuana.

## **Emerging Clinical Data**

### **The Therapeutic Potential of Cannabis**

While research in the United States has been sharply restricted by the federal prohibition on cannabis in the past, recent discoveries have increased interest among scientists in the more than 100 different cannabinoids so far identified in the cannabis plant. The International Cannabinoid Research Society (ICRS) was formally incorporated as a scientific research organization in 1991, and since its incorporation the membership has more than tripled. The International Association for Cannabis as Medicine (IACM), founded in 2000, publishes a bi-weekly newsletter and holds a bi-annual symposium to highlight emerging clinical research concerning cannabis therapeutics. The University of California established the Center for Medical Cannabis Research (CMCR) in 2001 to conduct scientific studies to ascertain the general medical safety and efficacy of cannabis products and examine alternative forms of cannabis administration. In 2010, the CMCR issued a report on the 14 clinical studies it has conducted, most of which were FDA-approved, double-blind, placebo-controlled clinical studies that have demonstrated that cannabis can control pain, in some cases better than the available alternatives.<sup>13</sup>

To date, more than 15,000 modern peer-reviewed scientific articles on the chemistry and pharmacology of cannabis and cannabinoids have been published, as well as more than 2,000 articles on the body's natural endocannabinoids. In recent years, more placebo-controlled human trials have also been conducted.

A 2009 review of clinical studies conducted over a 38-year period, found that “nearly all of the 33 published controlled clinical trials conducted in the United States have shown significant and measurable benefits in subjects receiving the treatment.”<sup>14</sup> The review's authors note that cannabinoids have the capacity for analgesia through neuromodulation in

ascending and descending pain pathways, neuroprotection, and anti-inflammatory mechanisms—all of which indicates that the cannabinoids found in cannabis have applications in managing chronic pain, muscle spasticity, cachexia, and other debilitating conditions.

Currently, cannabis is most often recommended as complementary or adjunct medicine. But there is a substantial consensus among experts in the relevant disciplines, including the American College of Physicians, that cannabis and cannabis-based medicines have therapeutic properties that could potentially treat a variety of serious and chronic illness. What follows is a brief, annotated compilation of the emerging clinical data that support the therapeutic use of cannabis.

### **Cannabis and Cancer**

People with cancer who must undergo radiation and chemotherapy frequently stop treatments rather than suffer the nausea, pain, and other unpleasant side effects. Years before any state had authorized the medical use of cannabis, a 1991 Harvard Medical School study revealed that nearly half (44%) of U.S. oncologists were recommending cannabis to their patients as a way of mitigating the side effects of cancer treatments.<sup>15</sup>

In its 1999 review, the Institute of Medicine concluded that cannabis could be a valid alternative for many people living with cancer. Specifically, the IOM notes, “In patients already experiencing severe nausea or vomiting, pills are generally ineffective, because of the difficulty in swallowing or keeping a pill down, and slow onset of the drug effect.”<sup>16</sup>

Since the release of the IOM report, new research has been published which supports the use of cannabis to curb the debilitating effects of cancer treatment. In 2001, a review of clinical studies conducted in several states during the past two decades revealed that, in 768 individuals with cancer, cannabis was a highly effective anti-emetic in chemotherapy.<sup>17</sup> Other studies have concluded that the active components in cannabis produce palliative effects in cancer patients by preventing nausea, vomiting and pain and by stimulating appetite.

The tumor-fighting properties of cannabinoids have also been demonstrated in numerous laboratory studies, though not yet in human clinical trials. Researchers have observed that “these compounds have been shown to inhibit the growth of tumor cells in culture and animal models by modulating key cell-signaling pathways. Cannabinoids are usually well tolerated, and do not produce the generalized toxic effects of conventional chemotherapies.”<sup>18</sup>

### **Combating Chemotherapy**

Cannabis is used most often to combat nausea induced by chemotherapy agents and pain caused by various cancers. More than 30 human clinical trials have examined the effects of cannabis or synthetic cannabinoids on nausea, not including several U.S. state trials that took place between 1978 and 1986.<sup>19-20</sup> In reviewing this literature, scientists have concluded that, “THC is superior to placebo, and equivalent in effectiveness to other widely-used anti-emetic drugs, in its capacity to reduce the nausea and vomiting caused by some chemotherapy regimens in some cancer patients.”<sup>21</sup>

A 1998 review by the British House of Lords Science & Technology Select Committee concluded that “cannabinoids are undoubtedly effective as anti-emetic agents in vomiting induced by anti-cancer drugs. Some users of both find cannabis itself more effective.”<sup>22</sup> The House of Lords review builds upon data provided in a 1997 inquiry by the British Medical Association that determined cannabis is, in some cases, more effective than Marinol.<sup>23</sup>

### **Cancer-fighting Cannabinoids**

Recent scientific advances in the study of cannabinoid receptors and endocannabinoids have produced exciting new leads in the search for anti-cancer treatments. In the past decade, scores of studies, both in vivo and in vitro, have demonstrated that various cannabinoids have a significant effect fighting cancer cells. To date, studies have shown that cannabinoids arrest many kinds of cancer growths through promotion of apoptosis (programmed cell death) in tumors and by arresting angiogenesis (increased blood vessel production). Cannabinoids have also been shown to halt the proliferation or spread of cancer cells in a wide variety of cancer types. Unlike conventional chemotherapy treatments that work by creating a toxic environment in the body that frequently compromises overall health, cannabinoids have been shown to selectively target tumor cells.

### **Cannabinoids and Tumour Reduction**

The direct anti-tumor and anti-proliferation activity of cannabinoids, specifically CB1 and CB2 agonists, has now been demonstrated in dozens of studies across a range of cancer types, including brain (gliomas), breast, liver, leukemic, melanoma, pheochromocytoma, cervical, pituitary, prostate and bowel.<sup>24-40</sup> The anti-tumor activity has led in laboratory animals and in-vitro human tissues to regression of tumors, reductions in vascularisation (blood supply) and metastases (secondary tumors), as well as the direct destruction of cancer cells (apoptosis).<sup>41-45</sup> A 2009 review of recent studies on the role of cannabinoids and cannabinoid receptors in the treatment of breast cancer notes that research on the complex interactions of endogenous cannabinoids and receptors is leading to greater scientific understanding of the basic mechanisms by which cancers develop.<sup>46</sup>

Cannabinoids have been shown to inhibit tumor growth in laboratory animals in multiple studies.<sup>47-52</sup> In one study, injections of synthetic THC eradicated malignant brain tumors in one-third of treated rats, and prolonged life in another third by as long as six weeks.<sup>53</sup> Other research on pituitary cancers suggests that cannabinoids may be the key to regulating human pituitary hormone secretion.<sup>54-57</sup>

Research published in 2009 found that the non-psychoactive cannabinoid cannabidiol (CBD) inhibits the invasion of both human cervical cancer and human lung cancer cells. By manipulating cannabidiol's up-regulation of a tissue inhibitor, researchers may have revealed the mechanism of CBD's tumor-fighting effect. A further in vivo study demonstrated “a significant inhibition” of lung cancer metastasis in mice treated with CBD.<sup>58</sup> The mechanism of the anti-cancer activity of CBD and other cannabinoids has also been repeatedly demonstrated with breast cancers.<sup>59-63</sup>

Scientists have also demonstrated the anti-tumor effects of the cannabinoid THC on cholangiocarcinoma cells, an often-fatal type of cancer that attacks the liver's bile ducts. A 2009 study found that “THC inhibited cell proliferation, migration and invasion, and induced cell apoptosis.” At low levels, THC reduced the migration and invasion of cancer cells, while

at high concentrations, THC triggered cell-death in tumors. In short, THC reduced the activity and number of cancer cells.<sup>64</sup> This dose-dependent action of cannabinoids on tumors has also been demonstrated in animal studies.

Research on cannabinoids and gliomas, a type of aggressive brain cancer for which there is no cure, holds promise for future treatments for this disease. A study that examined both animal and human glioblastoma multiforme (GBM) tumors, the most common and aggressive form of brain cancer, describes how cannabinoids controlled glioma growth by regulating the blood vessels that supply the tumors.<sup>65</sup> In another study, researchers demonstrated that the administration of the non-psychoactive cannabinoid cannabidiol (CBD) significantly inhibited the growth of subcutaneously implanted U87 human glioma cells in mice. The authors of the study noted that “CBD was able to produce a significant antitumor activity both in vitro and in vivo, thus suggesting a possible application of CBD as an antineoplastic agent.”<sup>66</sup>

The targeted effects of cannabinoids on GBM were further demonstrated in 2005 by researchers who showed that the cannabinoid THC both selectively inhibited the proliferation of malignant cells and induced them to die off, while leaving healthy cells unaffected.<sup>67</sup> While CBD and THC have each been demonstrated to have tumor-fighting properties in isolation, research published in 2010 shows that they work better in combination, as CBD enhances the inhibitory effects of THC on GBM cell proliferation and survival.<sup>68</sup>

Similarly, researchers reported in 2010 that the way cannabinoid and cannabinoid-like receptors in brain cells “regulate these cells' differentiation, functions and viability” suggests cannabinoids and other drugs that target cannabinoid receptors can “manage neuroinflammation and eradicate malignant astrocytomas,” a type of glial cancer.<sup>69</sup> These recent studies confirm the findings of multiple studies that indicated the effectiveness of cannabinoids in fighting gliomas, some of the deadliest forms of brain cancer.<sup>70-77</sup>

Indications of the remarkable potential of cannabinoids to fight cancer in humans have also been seen in three recent large-scale population studies. The studies were designed to find correlations between smoking cannabis and cancers of the lung, throat, head and neck. Instead, the researchers discovered that the cancer rates of cannabis smokers were at worst no greater than those who smoked nothing at all or even significantly better.<sup>78</sup> One study found that 10-20 years of cannabis use reduced the incidence of head, neck and throat cancers by 62%.<sup>79</sup> Researchers suggest that cannabinoids may produce a prophylactic effect against cancer development, as seen in the anti-proliferation effect that has been demonstrated in vitro and in vivo.

### **Cannabis, HIV/AIDS and Hepatitis-C**

Cannabis helps to improve the lives of many people living with HIV/AIDS. Its effects help manage appetite loss, wasting, nausea, vomiting, pain, anxiety, stress, depression and other symptoms of both the disease and the anti-retroviral regimes used to treat it. As many as one in four people living with HIV/AIDS use cannabis for medical purposes.<sup>80</sup>

An international group of nursing researchers has determined from a longitudinal, multi-country, multi-site, randomized-control clinical trial that cannabis is frequently used to manage the six common symptoms of HIV/AIDS. The 2009 study found that a significant percentage of those with HIV/AIDS find cannabis effective for anxiety, depression, fatigue,

diarrhea, nausea, and peripheral neuropathy. Researchers note that “those who did use marijuana rate it as effective as prescribed or over the counter medicines for the majority of common symptoms....”<sup>81</sup>

In addition to symptoms of the disease, cannabis has proven to be effective in controlling unpleasant effects of the drugs used to treat HIV/AIDS. People living with HIV/AIDS who use cannabis to combat the side-effects of HAART therapy are approximately three times more likely to remain on their prescribed drug therapies than those who do not use cannabis, according to a 2007 study.<sup>82</sup>

In the 1970s, a series of human clinical trials established that cannabis stimulates food intake and weight gain in healthy volunteers, a finding confirmed by numerous subsequent studies. In a randomized trial in people living with AIDS, THC significantly improved appetite and nausea in comparison with placebo. There were also trends towards improved mood and weight gain. Unwanted effects—dry mouth, drowsiness and anxiety—were generally mild or moderate in intensity.<sup>83-85</sup>

The Institute of Medicine’s comprehensive review in *Marijuana and Medicine* concluded, “For patients such as those with AIDS or who are undergoing chemotherapy and who suffer simultaneously from severe pain, nausea, and appetite loss, cannabinoid drugs might offer broad-spectrum relief not found in any other single medication.”

An FDA-approved preliminary safety trial of smoked cannabis, conducted in 2003 at the University of California at San Francisco, concluded that neither synthetic THC nor inhaled cannabis had any significant effect on the immune system or viral load. Moreover, the researchers noted that study participants who used cannabis gained weight.<sup>86</sup>

Cannabinoids may also inhibit the spread of the HIV virus within the body by acting on CD4+ T cells, which are critical to immune function and a target of the virus. A 2012 study found that a cannabinoid that activates CB2 receptors produced a dose-specific reduction of HIV infection of up to 50%, leading the researchers to suggest that the therapeutic use of cannabinoids may help fight the spread of the virus to uninfected T cells in late stages of HIV-1 infection.<sup>87</sup>

Previous research has shown that the use of cannabinoid drugs in patients with HIV is associated with an increase in CD4+ T cell number and has been shown to reduce viral load in an animal model of HIV.

## **The Clinical Trials**

### **Neuropathic Pain**

More than one-third of people living with HIV/AIDS suffer from excruciating nerve pain in the hands or feet, frequently in response to the antiretroviral therapies that constitute the first line of treatment for HIV/AIDS. This neuropathic pain is extremely difficult to treat, and as a result, many individuals reduce or discontinue their HIV/AIDS therapy because they cannot tolerate or get adequate relief from the debilitating side effects of the antiretroviral medications.

The effectiveness of cannabis and cannabinoids in relieving neuropathic pain has been demonstrated in more than three dozen preclinical and clinical trials. A 2009 review noted that “a large number of research articles have demonstrated the efficacy of cannabinoids” and concluded that “cannabinoids show promise for treatment of neuropathic pain.”<sup>88</sup>

A series of double-blind, placebo-controlled studies of people living with HIV/AIDS have demonstrated that cannabis can reduce neuropathic pain and promote weight gain without immunological compromise.<sup>89</sup> One randomized, placebo-controlled clinical trial of 50 people who had experienced neuropathic pain for an average of six years showed that smoked cannabis was well-tolerated and effectively relieved chronic neuropathic pain from HIV-associated sensory neuropathy, according to researchers at the University of California, San Francisco.<sup>90</sup> Other double-blind, placebo-controlled clinical trials with people living with HIV who experience neuropathy pain not adequately controlled by other pain-relievers, including opiates, found that cannabis provided pain relief.<sup>91</sup>

More recent randomized clinical trials conducted by the University of California Center for Medicinal Cannabis Research (CMCR) also demonstrated that smoked cannabis is effective in treating neuropathic pain.<sup>92</sup> Researchers found that over half of patients with painful HIV peripheral neuropathy experienced pain reduction of more than 30% when treated with cannabis, a level of relief pain researchers correlate with improved life quality. That improvement occurred in two CMCR trials of patients with HIV peripheral neuropathy and in a separate trial of patients with mixed neuropathic pain due to peripheral or central dysfunction of the nervous system.<sup>93,94</sup>

Additional double-blind, placebo-controlled clinical trials indicate cannabis medicines may improve neuropathic pain associated with multiple sclerosis and mixed neuropathies resulting from herpes, trauma and vascular problems.<sup>95,96</sup> This research is also important for people with cancer, as many of them also experience neuropathic pain.

While at least one study found that the effectiveness of cannabis as an analgesic was dose specific, with lower doses decreasing pain and higher doses increasing pain,<sup>97</sup> other studies have indicated that low- and high-dose cannabis produced similar levels of pain relief, reducing both the intensity and unpleasantness of unbearable nerve pain.

Researchers have found that cannabinoids such as THC work in concert with opiate-based painkillers to increase their effectiveness, particularly in neuropathic pain, allowing patients to reduce their opiate dosage.<sup>98-99</sup> That synergistic or entourage effect extends to cannabinoids, with multiple studies finding isolated synthetic cannabinoids such as THC (dronabinol) did not provide the same degree of efficacy as a whole-plant preparation of cannabis.<sup>100</sup>

### **Hepatitis-C Virus**

Cannabis may improve the effectiveness of drug therapy for the hepatitis C virus (HCV), a potentially deadly viral infection that affects more than 3 million Americans. Treatment for Hepatitis-C virus (HCV) involves months of therapy with two powerful drugs, interferon and ribavirin, both of which have severe side effects, including extreme fatigue, nausea, muscle aches, loss of appetite and depression. Due to these side effects, people often do not finish treatment, which worsens their symptoms and can promote harm to the liver.

Researchers from the University of California, San Francisco medical school and the Organization to Achieve Solutions in Substance-Abuse (OASIS) found that “modest cannabis use may offer symptomatic and virological benefit to some patients undergoing HCV treatment by helping them maintain adherence to the challenging medication regimen.”<sup>101</sup> Other research found that people combating HCV who used cannabis while undergoing combination ribavirin and interferon treatment were about three times more likely to complete their conventional medical treatment than those participants who did not use cannabis.

While cannabis may have a positive biomedical effect on the immune system similar to that demonstrated with HIV, these studies indicate that for people fighting HCV it improves appetite and offers psychological benefits such as reduced depression that help them tolerate the treatment's unpleasant side effects.

### **Chronic Pain**

According to the American Academy of Pain, nearly 50 million Americans suffer from persistent pain. Unfortunately, it is estimated that four out of every ten people living with moderate-to-severe pain have yet to experience relief. After reviewing a series of trials in 1997, the U.S. Society for Neuroscience concluded that “substances similar to or derived from marijuana could benefit the more than 97 million Americans who experience some form of pain each year.”<sup>102</sup>

Although a wide variety of prescription analgesic drugs are available to treat pain—from aspirin to oxycontin—none of these drugs are completely adequate and many cause severe side-effects with continued use. Opiate painkillers are notorious for causing severe nausea, disorientation and drowsiness, while prolonged use can increase tolerance and, in some cases, result in severe dependence or addiction. Even milder analgesics can pose serious risk. Drugs such as aspirin can cause stomach irritation and in some cases ulceration. Prolonged use of acetaminophen can result in liver damage. Ibuprofen can cause kidney failure. Each of these analgesics can produce fatal overdose.

By contrast, the safety record of cannabis is remarkable, and its centuries of use as an analgesic well documented.<sup>103,104</sup> In their meta-analysis of the available data, the Institute of Medicine acknowledged the wide use of cannabis for pain, noting that “after nausea and vomiting, chronic pain was the condition cited most often to the IOM study team as a medicinal use for marijuana.”<sup>105</sup> Currently, pain relief is by far the most common condition for which physicians recommend the use of cannabis.

Many well-designed, double-blind placebo-controlled clinical trials clearly demonstrate that cannabis can reduce neuropathic pain, as previously noted. Years of clinical studies confirm that the active ingredients in cannabis have powerful analgesic effects, sometimes equivalent to codeine or morphine.<sup>106-109</sup> A review of the body of scientific research concerning the analgesic effects of cannabis concluded that “[t]here is now unequivocal evidence that cannabinoids are antinociceptive [capable of blocking the transmission of pain] in animal models of acute pain.”<sup>105</sup>

Research shows that cannabinoids also produce an entourage effect that enhances the effectiveness of opiate painkillers. One animal study found morphine was 15 times more active with the addition of a small dose of THC. Codeine was enhanced on the order of 900

fold.<sup>106</sup> Human and animal studies have repeatedly shown that cannabinoids work synergistically with opioid drugs in relieving neuropathic pain. Researchers suggest that direct and indirect interactions between opioid and cannabinoid receptors not only enhance analgesia but also reduce the development of tolerance to opiates. These interactions hold promise for developing therapeutic strategies that provide better pain relief with fewer of the dangerous and debilitating side effects that patients reliant on opiate pain killers experience.<sup>107-111</sup>

Decades of research on cannabis' effectiveness in pain management include clinical human trials and volumes of anecdotal evidence, as well as new understanding of how activation of the cannabinoid system in the central nervous system reduces sensitivity to pain.<sup>112-118</sup> Some of the most encouraging clinical data on the effects of cannabinoids on pain involve the treatment of intractable cancer pain and hard-to-treat neuropathic pain. Somewhere between 25% and 45% of cancer patients experience neuropathic pain, a type of chronic nerve pain that resists conventional treatment.

The effectiveness of cannabis and cannabinoids in relieving neuropathic pain has been demonstrated in more than three dozen preclinical and clinical trials. A 2009 review notes that “a large number of research articles have demonstrated the efficacy of cannabinoids” for treating neuropathic pain and concludes that “cannabinoids show promise for treatment.”<sup>119</sup>

Multiple clinical trials have shown that a dosage-controlled whole-plant extract of cannabis (Sativex) relieves intractable cancer pain, and does so better than THC alone. A recent double blind, randomized, placebo-controlled trial of 360 cancer patients in 14 countries found that pain scores improved significantly with a cannabis extract. Researchers report that the combination of natural cannabinoids in Sativex “is an efficacious adjunctive treatment for cancer-related pain” for patients who do not get relief from opiate painkillers such as Oxycontin or Vicodin.<sup>120, 121</sup>

Pain from spinal injuries may also be treatable with cannabis. Several sets of researchers have recently published findings on the efficacy of cannabinoids in treating pain resulting from spinal cord injuries (SCI). A French team, noting that “very few pharmacological studies have dealt specifically with neuropathic pain related to SCI,” suggests that for “refractory central pain, cannabinoids may be proposed on the basis of positive results in other central pain conditions (e.g. multiple sclerosis).”<sup>122</sup> Researchers have demonstrated in an animal model of SCI pain that cannabinoids yield more consistent positive results than conventional analgesics such as opiates, which “decrease in efficacy with repeated treatment over time,” concluding that drugs targeting the body's cannabinoid receptors “hold promise for long-term use in alleviating chronic SCI pain.”<sup>123</sup>

Researchers have also determined that neuropathic pain may be treatable via bolstering the body's natural cannabinoids. A study that inhibited the two enzymes that break down the body's natural cannabinoids found that preserving them “reduces neuropathic pain through distinct receptor mechanisms of action” that “present viable targets” for developing new analgesic drugs.<sup>124</sup>

Drugs which can selective target CB2 cannabinoid receptors, which are almost completely absent from the central nervous system, have also been shown to have therapeutic potential for both inflammatory and neuropathic pain control. <sup>125</sup>

## Multiple Sclerosis

One survey of people living with multiple sclerosis reported that more than 40 percent of respondents used cannabis to relieve symptoms of the disease. Among them, nearly three quarters said that cannabis mitigated their muscle spasms, and more than half said it alleviated their pain. A similar survey found that 96% of Canadians living with MS believe cannabis is therapeutically useful for treating the disease. Of those who admitted using cannabis to treat symptoms of MS, the majority cited relief of chronic pain, spasticity, and depression.<sup>126</sup>

In addition, numerous studies have reported improvement in tremor, sexual dysfunction, bowel and bladder dysfunctions, vision dimness, dysfunctions of walking and balance (ataxia), and memory loss, as well as pain and spasticity.<sup>127-131</sup>

In fact, cannabinoids have been shown in animal models to not just measurably lessen MS symptoms but may also slow or halt the progression of the disease. Cannabinoids have demonstrated effects on immune function that may reduce the autoimmune neuroinflammatory response which drives relapsing neurological attacks and increasing disability.<sup>132-136</sup> Clues as to why may lie in research that discovered that persons with multiple sclerosis have increased levels of endocannabinoids in their blood, indicating that the endocannabinoid system “may be dynamically modulated depending on the subtype of the disease.”<sup>137</sup>

Previous studies of the pharmacology of cannabis have identified effects on motor systems of the central nervous system that have the potential of affecting tremor and spasticity. A controlled study of the efficacy of THC in the animal model of MS, experimental allergic encephalomyelitis (EAE), demonstrated significant amelioration of these two MS symptoms. A review of six randomized controlled trials of a cannabis extracts that combines delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) finds “a trend of reduced spasticity in treated patients” and “evidence that combined THC and CBD extracts may provide therapeutic benefit for MS spasticity symptoms.”<sup>138</sup>

One such dosage-controlled THC-CBD whole-plant extract—GW Pharmaceuticals' sublingual spray, Sativex®—has been shown in numerous clinical trials to ease pain, decrease spasm frequency, and improve bladder control and sleep. Clinical trials of Sativex® found that it “demonstrated a statistically significant and clinically relevant improvement in spasticity and was well tolerated in MS patients.”<sup>139</sup> As of June 2012, Sativex® is available by prescription in the UK, Spain, Germany and Denmark for the symptomatic relief of spasticity, neuropathic pain, or both in adults with multiple sclerosis. It has been approved for distribution in Italy, Sweden, Austria and the Czech Republic, with recommendations for approval in Belgium, Finland, Iceland, Ireland, Luxembourg, the Netherlands, Norway, Poland, Portugal and Slovakia.

MS patients frequently report cannabis helps with bladder control, and a review of studies on cannabinoid receptors in the bladder notes that non-psychoactive cannabinoids are effective, and psychotropic effects of THC can be mitigated by delivering cannabinoids directly into the bladder.<sup>140</sup>

The distribution of CB1 cannabinoid receptors in the brain suggests that they may play a role in movement control. Only recently have scientists identified EAE as an animal model for

MS, allowing testing for symptom suppression. While objective measures of spasticity in humans have not consistently shown benefit from cannabinoid treatment, a randomized clinical trial with 189 MS patients being treated with a cannabis extract showed 40% achieved a greater than 30% improvement.<sup>141</sup>

In addition to studying the potential role of cannabis and its derivatives in the treatment of MS-related symptoms, scientists are exploring the potential of cannabinoids to inhibit neurodegeneration. A 2003 study that the National MS Society called “interesting and potentially exciting” demonstrated that cannabinoids were able to slow the disease process in mice by offering neuroprotection against EAE.<sup>142</sup> Neurodegeneration is implicated in a host of debilitating conditions.

### **Other Movement Disorders**

Muscular spasticity is a common condition, affecting millions of people in the United States. It afflicts individuals who have suffered strokes, as well as those with multiple sclerosis, cerebral palsy, paraplegia, quadriplegia, and spinal cord injuries. Conventional medical therapy offers little relief for spasticity. Phenobarbital and diazepam (Valium) are commonly prescribed, but they rarely provide complete relief, and many patients develop a tolerance, become addicted, or complain of heavy sedation. These drugs also cause weakness, drowsiness and other side-effects that people find intolerable.

The therapeutic use of cannabis for treating muscle problems and movement disorders has been known to western medicine for nearly two centuries. In 1839, Dr. William B. O'Shaughnessy noted the plant's muscle relaxant and anti-convulsant properties, writing that doctors had “gained an anti-convulsive remedy of the greatest value.”<sup>143</sup> Contemporary animal and human clinical studies reveal that cannabis and its constituent cannabinoids may effectively treat movement disorders affecting older patients, such as tremors and spasticity, because cannabis has antispasticity, analgesic, antitremor, and antiataxia actions.<sup>144-155</sup>

As mentioned, the contemporary understanding of the actions of cannabis was advanced by the discovery of an endogenous cannabinoid system in the human body. This system appears to be intricately involved in regulating normal physiology.<sup>156-158</sup> Central cannabinoid receptors are densely located in the basal ganglia, the area of the brain that controls body movement. Endogenous cannabinoids also appear to play a role in the manipulation of other transmitter systems within the basal ganglia--increasing transmission of certain chemicals, inhibiting the release of others, and affecting how still others are absorbed. Most movement disorders are caused by a dysfunction of the chemical loops in this part of the brain. Research suggests that an endogenous cannabinoid “tone” participates in the control of movements.<sup>160-161</sup>

Endocannabinoids have modulating effects on the nervous system: Sometimes they block neuronal excitability and other times they augment it. As scientists are developing a better understanding of the physiological role of endocannabinoids, it is becoming clear that these chemicals may be involved in the pathology of several neurological diseases. This means researchers are identifying an array of potential therapeutic targets within the human nervous system. They have determined that various cannabinoids found in the cannabis plant interrupt the synthesis, uptake, or metabolism of the endocannabinoids that drive the progression of Huntington's disease, Parkinson's disease, and tremor.<sup>162</sup>

The neuroprotective qualities of cannabis mean it has enormous potential for protecting the brain and central nervous system from the damage from disease or injury that creates various disorders. Researchers have found that cannabinoids fight the effects of strokes, brain trauma, and spinal cord injury, as well as multiple sclerosis and neurodegenerative diseases. More than 100 research articles have been published on how cannabinoids act as neuroprotective agents that slow the progression of Huntington's, Alzheimer's, and particularly Parkinson's, a condition that affects more than 52% of people over the age of 85.<sup>163-165</sup>

### **Arthritis**

According to the Arthritis Foundation, arthritis is one of the most prevalent chronic health problems and the nation's leading cause of disability among Americans over age 15. A 2006 report estimated that 46 million Americans-nearly 1 in 5 adults-live with chronic joint pain and arthritis.

The use of cannabis as a treatment for musculoskeletal pain in western medicine dates to the 1700s.<sup>166</sup> Modern research confirms that cannabis and related therapies can relieve the pain associated with arthritis and the other rheumatic and degenerative hip, joint and connective tissue disorders. Not only is cannabis an effective pain reliever and anti-inflammatory in its own right, it also has the potential to enhance the efficacy of opiate painkillers, allowing for better pain relief at reduced dosages. In their 1999 meta-analysis of the data then available, the Institutes of Medicine specifically noted that the anti-inflammatory properties of cannabinoids could have therapeutic application in preventing or reducing pain caused by swelling (such as arthritis).<sup>167</sup>

Research has shown that cannabis and its constituent cannabinoids have powerful immunomodulation and anti-inflammatory properties that may treat chronic inflammatory diseases directly.<sup>168-170</sup> Many patients and doctors report cannabis has proven an effective treatment for rheumatoid arthritis, and it is one of the recognized conditions for which many states permit medical use. Specifically, cannabis has a demonstrated ability to improve mobility and reduce morning stiffness and inflammation, and research suggests that individuals can reduce their use of potentially harmful Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) when using cannabis as an adjunct therapy.<sup>171,172</sup>

One of the non-psychoactive cannabinoid components of cannabis, cannibidol (CBD), has also been shown to have numerous medical applications as an anti-inflammatory and neuroprotective agent, including as a treatment for rheumatoid arthritis.<sup>173-175</sup> Research indicates that CBD suppresses the immune response in mice and rats that is responsible for a disease resembling arthritis, protecting them from severe damage to their joints, and markedly improving their condition.<sup>176,177</sup>

### **Alzheimer's Disease**

Alzheimer's disease is a neurodegenerative condition for which cannabis and cannabinoid therapies show promise, both for treating the symptoms and the underlying disease.

Agitation is the most common behavioral management problem in people with Alzheimer's and affects an estimated 75 percent of people with the disease. It can include symptoms ranging from physical or verbal abusive behavior to pacing and restlessness, as well as disruptive behaviors such as screaming and repetitive requests for attention. Clinical research

involving THC indicates that the cannabinoid reduced the agitation common to Alzheimer's sufferers.<sup>178,179</sup> THC is also proven effective in combating anorexia or wasting syndrome, a common problem for people with Alzheimer's disease.<sup>180</sup>

Alzheimer's disease is widely held to be associated with oxidative stress due, in part, to the membrane action of beta-amyloid peptide aggregates. Recent studies have indicated that one of the cannabis plant's primary components, cannabidiol (CBD), combats that problem through a combination of neuroprotective, anti-oxidative and anti-apoptotic effects by inhibiting the release of the toxic beta-amyloid peptide.<sup>181,182</sup>

This new research, coupled with the extensive work done on other neuroprotective qualities of cannabis and its components, indicates that cannabis or cannabis-based therapy may become the source of the most effective treatments for battling the Central Nervous System diseases that afflict millions of elderly Americans.<sup>183-186</sup>

## **Cannabis-based Medicines**

### **The 'Pharmaceuticalization' of Cannabis**

Dr. Lester Grinspoon, a professor emeritus at Harvard Medical School and author of several books on the medical use of cannabis, has defined the “pharmaceuticalization of cannabis” as the development of isolated individual cannabinoids, synthetic cannabinoids, and cannabinoid analogs. While this process is characteristic of medical research, it also represents what Dr. Grinspoon describes as the U.S. federal government's desire to introduce a cannabis-like pill to replace natural cannabis use.<sup>187</sup> The first efforts to “pharmaceuticalize” cannabis came to fruition in 1985 when a synthetic form of THC known as dronabinol (or Marinol) was approved by the FDA.

### **Dronabinol (Marinol)**

Dronabinol (Marinol) is an encapsulated synthetic preparation of delta-9-tetrahydrocannabinol, the primary psychoactive cannabinoid found in the cannabis plant, suspended in sesame oil. Designed and marketed by Solvay Pharmaceuticals and its subsidiary Unimed, Marinol was first indicated for treatment of nausea and vomiting associated with cancer chemotherapy in people who failed to respond adequately to conventional antiemetic treatments; it was later made available for the treatment of anorexia associated with weight loss for people living with HIV/AIDS.

When first approved for medical use, dronabinol was tightly controlled as a Schedule II drug under the Controlled Substances Act, meaning it was classified as a drug with a “high potential for abuse” that could “lead to severe psychological or physical dependence.” In 1999, in response to a rescheduling request by Unimed to make dronabinol more widely available, it was moved by administrative rule to Schedule III, meaning it was now classified as having a lower potential for abuse and only a low or moderate likelihood of physical dependency. Currently Marinol is available in three dosage strengths: 2.5, 5, and 10mg. Despite the well-documented therapeutic value of THC, dronabinol has enjoyed only moderate success.

Marinol's oral route of administration hampers its effectiveness because of slow absorption and difficulty in controlling dosing. In their review of Marinol, the Institute of Medicine

specifically noted that only about 10-20% of an oral dose is absorbed by the human body, and onset of action is not obtained until two and four hours after dosing. By contrast, inhalation yields very rapid onset of therapeutic effects, allowing for both more immediate relief and control over dosage. People prescribed dronabinol for severe nausea and vomiting also frequently report difficulty keeping the pills down, a problem not shared by inhalation delivery methods.

### **Nabilone (Cesamet)**

Nabilone (Cesamet) is a synthetic derivative of THC with a slightly modified molecular structure from dronabinol. Currently available for medical use in Canada, United Kingdom, and Mexico, it was approved by the FDA in 1985 for treatment of chemotherapy-induced nausea and vomiting that has not responded to conventional medication. Although nabilone was approved more than twenty years ago, it has only been marketed in the United States since 2006 as a treatment of nausea and vomiting caused by cancer chemotherapy.

### **Cannabis Extract Oral-mucosal Spray (Sativex®)**

THC or delta-9-tetrahydrocannabinol is the most familiar cannabinoid, and its therapeutic effects have been well established. However, at least 100 other cannabinoids have been identified in cannabis, including CBD, which not only offset the psychoactive effect of THC, but may contain therapeutic benefits of their own. In fact, research suggests that the therapeutic effect of cannabis might be linked to what researchers call an “entourage effect,” the synergistic relationship between multiple cannabinoids which may make them more therapeutically beneficial in combination than they are individually.

Researchers affiliated with GW Pharmaceuticals, a company founded in the United Kingdom in 1998 to develop cannabis-based medicines, have noted that in practice medicines or extracts derived from the cannabis plant provide greater relief of pain than the equivalent amount of synthetic cannabinoid given as a single chemical entity like dronabinol.

Sativex® is GW Pharmaceuticals' lead cannabinoid product, and in 2005 became the world's first prescription medicine derived from extracts of the cannabis plant. Specifically, Sativex® is a cannabis extract containing equal amounts of dronabinol (THC) and cannabidiol (CBD), which is administered as an oral spray absorbed in the patient's mouth.

Sativex® is available by prescription for varying conditions in Canada, the UK, Spain, New Zealand, and Germany. It has been approved for distribution in the Czech Republic and Denmark, and regulatory approval is pending in Italy, Sweden and Austria. It is currently undergoing late stage clinical trials in the United States. Upon approval in the United States, Sativex will be marketed by Otsuka Pharmaceuticals.

The primary indication for which Sativex® has been approved is for the treatment of spasticity due to multiple sclerosis. In Canada, it is also approved for symptomatic relief of neuropathic pain in multiple sclerosis and as adjunctive analgesic treatment in people with advanced cancer who experience moderate to severe pain during the highest tolerated dose of strong opioid therapy for persistent background pain.

According to Dr. Grinspoon's theory, the “pharmaceuticalization” of cannabis will only succeed if the pharmaceutical derivatives and extracts displace cannabis as medicine.

Although a few individuals will prefer dose-consistent pharmaceutical alternatives, it seems unlikely that these drugs will completely replace the use of organic cannabis, especially given the plant's negligible toxicity, easy availability, and low cost of production relative to pharmaceuticals. New vaporization devices that replace smoking as an easy and rapid delivery method that allows better dosage control than oral ingestion of pills or oralmucosal sprays such as Sativex® are expanding the plant's remarkable medical versatility.

## **Investigative Roadblocks**

### **The U.S. Research Experience**

Over the past three decades, there has been an explosion of international research on the therapeutic applications of cannabis and cannabinoids. But restrictions on cannabis research in the U.S. have resulted in very few clinical trials conducted domestically. Meanwhile, scientific teams in Great Britain, Spain, Italy, Israel, and elsewhere have confirmed-through case studies, basic research, pre-clinical and clinical investigations-the medical value of cannabis for treating a wide variety of conditions. Equally important, numerous studies have provided strong indications of the potential for more targeted drugs, whole-plant cannabis derivatives and synthetic cannabinoids. The current research challenge is to conduct controlled human clinical trials that can establish protocols for cannabis-based treatments of specific medical conditions.

That challenge was identified in Marijuana and Medicine, the Institute of Medicine's 1999 report, but there has been no additional U.S. government effort to fully implement the IOM's recommendations or review the vast amount of research conducted since then. Worse, the federal prohibition of cannabis continues to limit clinical research that could investigate the safety and efficacy of cannabis to treat serious and chronic conditions or control their symptoms. In the United States research is stalled, and in some cases blocked, by a complicated federal approval process and restricted access to research-grade cannabis, despite the order of a federal administrative law judge to allow other production sites to meet research demands.

### **A Movement in Public Health**

Despite barriers to research, a growing body of clinical data supports the use of cannabis for medical purposes, as it has been for millennia. While there is still much to learn, the medical value of cannabis is indisputable. As a result, a growing number of public health organizations have endorsed the therapeutic use of cannabis and programs that advance medical and scientific research. Here are some of the more prominent ones.

In 1994 the Federation of American Scientists recommended that the President instruct the National Institutes of Health and the FDA to reopen Investigational New Drug (IND) protocols that would provide federal research cannabis to seriously ill patients who physicians believed would be helped by it. The following year, the American Public Health Association passed a resolution that encourages vigorous research and “urges the Administration and Congress to move expeditiously to make cannabis available as a legal medicine.”

In 1996 the American Academy of Family Physicians offered their support for using medical cannabis to treat specific conditions under the supervision of a licensed medical professional.

And, in 1997, two years prior to the publication of the Institute of Medicine's report, the New England Journal of Medicine, one of the world's leading medical publications, published an editorial that said:

A federal policy that prohibits physicians from alleviating suffering by prescribing marijuana to seriously ill patients is misguided, heavy-handed, and inhumane.... It is also hypocritical to forbid physicians to prescribe marijuana while permitting them to prescribe morphine and meperidine to relieve extreme dyspnea and pain... [because] there is no risk of death from smoking marijuana.

Citing the 1999 Institute of Medicine report and studies published since which indicate that the use of cannabis can alleviate the debilitating symptoms of cancer chemotherapy and wasting, the Lymphoma Foundation of America passed a resolution urging Congress and the President to enact legislation to reschedule cannabis to allow doctors to prescribe cannabis for their patients in accordance with need. The Leukemia & Lymphoma Society also “supports legislation to remove criminal and civil sanctions for the doctor-advised, medical use of marijuana by patients with serious physical medical conditions” and has encouraged “the federal government to authorize the Drug Enforcement Administration to license privately funded production facilities that meet all regulatory requirements to produce pharmaceutical-grade marijuana for use exclusively in federally approved research.”

Following the lead of several state nurses organizations, the American Nurses Association passed a resolution in support of health care providers who recommend the use of cannabis and further acknowledged that “the right of patients to have safe access to therapeutic cannabis.” The ANA specifically called for more research and urged the removal of cannabis from the list of Schedule I controlled substances.

Recently, the Assembly of the American Psychiatric Association unanimously approved a strongly worded statement championing legal protections for individuals using cannabis in accordance with a physician's recommendation. The American Psychiatric Association is the main professional organization for psychiatrists in the United States, representing 40,000 members and 16 allied organizations (including the American Academy of Psychiatry and the Law, American Academy of Child and Adolescent Psychiatry, American Association for Social Psychiatry, American Academy of Addiction Psychiatry, and the American Association of Emergency Psychiatrists).

In 2008, the American College of Physicians (ACP) published a position paper underscoring the therapeutic value of cannabis and specifically recommending the federal government consider “reclassification [of cannabis] into a more appropriate schedule, given the scientific evidence regarding marijuana's safety and efficacy in some clinical conditions.” The ACP is the second largest physician group in the United States with 124,000 members and publishes the the most widely-cited medical specialty journal in the world.

Regarding the growing support by public health organization, former Surgeon General Dr. Jocelyn Elders observed that “large medical associations are by their nature slow and cautious creatures that move only when the evidence is overwhelming.” She continued, “The evidence is indeed overwhelming that, as ACP put it, there is 'a clear discord' between what research tells us and what our laws say about medical marijuana.”

Other professional health organizations that have endorsed the medical use of cannabis include the American Medical Association, American Public Health Association, the American Academy of Family Physicians, the National Association of Boards of Pharmacy, the California Medical Association, the American Preventive Medical Association, the American Society of Addiction Medicine, the Iowa Board of Pharmacy, and many more.

The current acceptance of cannabis as medicine in the US is further evidenced by the thousands of American doctors who have recommended its use to their patients, the tens of thousands of individuals who are using it safely and effectively, and millions of American voters and many state legislatures—representing more than 1/3 of the U.S. population—that have approved its legal use as medicine.

## **Government Studies and Programs**

### **LaGuardia Report (1944)**

The 1937 Marihuana Tax Act may have ended safe and legal access, but it did not end the debate about cannabis policy. In 1939, New York Mayor Fiorello LaGuardia appointed a blue-ribbon panel of renowned physicians, psychiatrists, clinical psychologists, pharmacologists, chemists and other researchers from the New York Academy of Medicine to review claims that smoking cannabis resulted in criminal behavior and a deterioration of physical and mental health.

A summary of the preliminary findings published in 1942 by the American Journal of Psychiatry concluded that “prolonged use of marihuana does not lead to physical, mental or moral degeneration, nor have we observed any permanent deleterious effects from its continued use. Quite the contrary, marihuana and its derivatives and allied synthetics have potentially valuable therapeutic applications which merit further investigation.”<sup>3</sup> The final LaGuardia report expanded on those findings, noting that cannabis is not addictive, does not provide a gateway to other drugs of abuse, and is not associated with increased criminal behavior or juvenile delinquency.

### **The National Commission on Marihuana and Drug Abuse (1972)**

The Comprehensive Drug Abuse Prevention and Control Act of 1970 included a provision to study the abuse of cannabis in the United States. President Richard Nixon appointed Pennsylvania Governor Raymond Shafer to chair the National Commission on Marihuana and Drug Abuse. On March 22, 1972, the commission presented to Congress its report, “Marihuana: A Signal of Misunderstanding.”

The Shafer report, like the LaGuardia report before it, concluded that cannabis use does not jeopardize health, lead to experimentation with other drugs, or cause criminal activity. It recommended the decriminalization of cannabis for personal use. President Nixon rejected the Shafer report because it conflicted with many of the provisions of both the Comprehensive Drug Abuse Prevention and Control Act and the Controlled Substances Act. Instead of accepting the findings of scientists and doctors, Nixon declared a “War on Drugs.”

### **Investigational New Drug Compassionate Access (1978)**

In 1975, shortly after discovering that smoking cannabis could relieve symptoms of his severe glaucoma, Washington, DC resident Robert Randall was arrested for cultivating cannabis in his home. Randall successfully used the common law “Doctrine of Necessity” to fight the charges. In November 1976, Judge James Washington ruled that “[w]hile blindness was shown by competent medical testimony to be the otherwise inevitable result of the defendant's disease, no adverse effects from the smoking of marijuana have been demonstrated. Medical evidence suggests that the medical prohibition is not well-founded.”

Randall petitioned the federal government to provide him with access to medical cannabis in accordance with his medical necessity and shortly thereafter became the first American to receive a government-supplied source of cannabis. When Randall went public with his victory, the federal government retaliated with threats to withdraw his access to cannabis. In 1978, Randall filed suit, and federal agencies settled immediately by agreeing to provide free cannabis through a local pharmacy. The Randall settlement helped create the FDA's Investigational New Drug (IND) Compassionate Access Program, which continues to supply a handful of individuals who suffer from severe or chronic illness with a free monthly supply of federally grown cannabis, up to nine pounds annually.

Though only 30 patients were ever enrolled in the program at any one time, in 1992 an overwhelming number of applications from people suffering the effects of AIDS led President George H.W. Bush to close the program to new applicants, citing concerns that the program undermined prohibition.

In 2002, a study of the remaining individuals in the federal IND program found cannabis to have long-term clinical effectiveness in treating chronic musculoskeletal pain, spasm and nausea, and spasticity associated with multiple sclerosis. Assessment of their physiological systems using MRI scans of the brain, pulmonary function tests, chest X-ray, neuropsychological tests, hormone and immunological assays, electroencephalography, **P300 testing and neurological clinical examinations found no functionally significant health problems after 11 to 27 years consuming up to 12 joints a day.**<sup>4</sup>

### **Institute of Medicine (1982, 1999)**

In 1982, the Institute of Medicine (IOM), a division of the National Academy of Sciences, published the report “Marijuana and Health.” The IOM noted that “[p]reliminary studies suggest that marijuana and its derivatives or analogues might be useful in the treatment of the raised intraocular pressure of glaucoma, in the control of the severe nausea and vomiting caused by cancer chemotherapy, and in the treatment of asthma.”<sup>5</sup>

More than a decade later, in response to new state laws that permitted the use of cannabis on the recommendation of a licensed physician, the White House Office of National Drug Control Policy commissioned another report from the IOM to assess the medical and scientific value of cannabis. In 1999 the IOM published *Marijuana as Medicine: Assessing the Science Base*, a comprehensive meta-analysis of existing research concerning the therapeutic value of cannabis.<sup>6</sup> In describing the findings of the IOM review, the Congressional Research Service observes that “[f]or the most part, the IOM Report straddled the fence and provided sound bites for both sides of the medical marijuana debate.”<sup>7</sup>

Both IOM reports conclude that there is a sound medical and scientific basis for using cannabis as treatment for a variety of serious or chronic medical conditions. Both reports

emphasize the need for continued research with a focus on well-designed clinical trials aimed at developing rapid-onset, reliable, and safe delivery systems. Congress and executive agencies have largely ignored these findings and have never convened a panel to oversee the full implementation of recommendations.

### **The House of Lords Select Committee on Science & Technology Report (1998)**

In 1998, the British House of Lords Select Committee on Science and Technology issued a comprehensive report on cannabis that includes testimony from people with serious illness, scientific researchers, and physicians. The report recommended immediately rescheduling cannabis so that doctors could prescribe cannabis to their patients and pharmacies could safely distribute cannabis. This recommendation was made in part because the committee acknowledged that individuals using cannabis for therapeutic purposes “are caught in the front line of the war against drug abuse. This makes criminals of people whose intentions are innocent, it adds to the burden on enforcement agencies, and it brings the law into disrepute. Legalizing medical use on prescription, in the way that we recommend, would create a clear separation between medical and recreational use, under control of the health care professions.”<sup>8</sup>

The report says further “that clinical trials of cannabis for the treatment of MS and chronic pain should be mounted as a matter of urgency.” Specifically, the committee recommended that research focus on alternative modes of administration that “would retain the benefit of rapid absorption offered by smoking, without the adverse effects.”

Since then, a variety of vaporizing systems have been developed and commercially marketed that allow for rapid-onset delivery of cannabis via inhalation without smoking. A sublingual cannabis spray is now also available from GW Pharmaceuticals and has been approved as of 2011 for use by prescription in the UK, Canada, Spain, Germany, Denmark, and the Czech Republic.

<http://www.advancedholistichealth.org/history.htm> A very long list of cannabis through the ages from 8000BC onwards includes lots of videos and a running total of drug enforcement costs in USA horrific!

## **APPENDIX IV**

<http://www.mpp.org/assets/documents/low-or-no-thc-high-cbd.html>

In August 2013, CNN correspondent Dr. Sanjay Gupta filed a report on medical marijuana explaining that he had a change of heart and announcing his support for using marijuana for medical purposes. While Dr. Gupta mentioned multiple patients suffering from a variety of ailments (neuropathic pain, PTSD, and nausea as a result of chemotherapy), one particular patient caught the nation's attention: Charlotte Figi.

Charlotte suffers from a rare and devastating paediatric seizure disorder. After trying numerous treatment options that did not work, her family found medical marijuana providers who developed a strain of marijuana that is high in cannabidiol (CBD) and low in THC. This strain, "Charlotte's Web," has been remarkably effective at calming Charlotte's seizures. She went from having 300 seizures a week to suffering from two or three per month. Dozens of families from across the country have uprooted themselves and moved to Colorado to give their children the same chance.

Charlotte's story and the concern for other young patients have led some lawmakers to consider passing legislation that *only* allows patients to access marijuana oils that are high in CBD and that have little or no THC (tetrahydrocannabinol). While it is heartening to see lawmakers' concern for the plight of patients with catastrophic seizure disorders, these proposals unfortunately exclude the vast majority of those who can benefit from medical marijuana, some of whom also face life-threatening ailments.

### **Relative Rarity**

While cannabis preparations with significant amount of CBD appear to be particularly effective at treating seizures, the number of individuals treating seizure disorders through medical marijuana programs is relatively low. For example, only 2% of the registered patients in both Rhode Island and Colorado report seizures as their qualifying conditions. While it is imperative that these individuals be allowed to legally access medical marijuana – and the strain they need – it is just as important to remember that there are tens of thousands of other men and women and a small number of children who suffer from a variety of debilitating conditions whose symptoms are alleviated by medical marijuana. The vast majority of those patients have symptoms that benefit from strains of marijuana that include more than trace amounts of THC.

### **THC: Why It Matters**

Tetrahydrocannabinol, or THC, is just one of the roughly 85 cannabinoids found naturally in marijuana. Clinical trials and the experiences of hundreds of thousands of patients have shown that THC, and strains of marijuana that include THC, provide important medical benefits for individuals suffering from pain, multiple sclerosis, nausea, and wasting disease. THC is also the cannabinoid most responsible for marijuana's psychoactive effects. While THC does cause marijuana's "high," patients use marijuana for relief, not for euphoria. Patients who inhale marijuana can titrate their dosage precisely to use only as much as they need, reducing or eliminating the euphoria. Some use marijuana only before bed.

The federal government has officially recognized THC's medical properties since 1985, when the FDA approved a prescription drug that is made of synthetic THC — Marinol — for nausea. Yet, Marinol is not adequate for many patients who can benefit from marijuana. For nauseated patients, a pill can be impossible to keep down. Meanwhile, many patients benefit from the synergistic effect of THC and the other cannabinoids, such as CBD. Natural marijuana is less intoxicating than Marinol because patients can titrate their dosage and other cannabinoids moderate THC's psychoactive properties.

Studies have shown that marijuana that includes THC can alleviate a host of debilitating conditions, including:

- Nausea and appetite loss: Researchers have found THC and marijuana with THC are effective anti-emetics and appetite stimulants for individuals suffering from the side effects of cancer chemotherapy or AIDS treatments.
- Multiple sclerosis: Research has found that marijuana with THC can alleviate spasticity. In addition, Canada, the U.K., and several other countries approved an oral marijuana extract made of equal proportions of CBD and THC.
- Pain: Several studies have found that marijuana strains that include THC can alleviate neuropathic pain — a notoriously difficult-to-treat nerve pain commonly found in amputees, AIDS patients, and patients with multiple sclerosis.

Since the 1970's, the federal government has been providing a handful of individuals who suffer from various ailments with marijuana grown at the University of Mississippi as part of the Compassionate Investigational New Drug program. The four surviving patients still receiving federal marijuana receive a strain with almost no CBD that has been essential to managing their conditions — a rare bone spur disorder, multiple sclerosis, glaucoma, and a painful condition called nail patella syndrome, respectively. The marijuana these individuals have benefitted from would not be allowed under CBD-only proposals.

## **Conclusion**

Medical marijuana legislation should not be so restrictive as to leave behind around 98% of the individuals who can benefit from it. THC has proven medical benefits and individuals who can benefit from strains that include it should not be forgotten when legislators debate medical marijuana bills.

## **APPENDIX V**

### **GW announces UK launch of world's first prescription cannabis medicine**

**21 June 2010**

Porton Down, UK, 21 June 2010: GW Pharmaceuticals plc (GWP:AIM) today announces the UK launch of Sativex®, its Oromucosal Spray for the treatment of spasticity due to Multiple Sclerosis (MS). Sativex® is the world's first prescription cannabis medicine and the UK is the first country in the world to grant a full regulatory authorization for the product.

Sativex® contains two cannabinoids or active ingredients - THC (delta-9-tetrahydrocannabinol) and CBD (cannabidiol). It is the first cannabinoid medicine derived from whole plant extracts from the cannabis sativa plant.

Sativex®, available as a prescription only medicine, was developed by GW in specific response to calls from people with MS for a prescription cannabis-based medicine. Today's launch means that MS patients suffering the spasms and cramping associated with spasticity have access to a new treatment option which has been shown to improve their symptoms where current treatments have failed.

Sativex® is manufactured by GW under Home Office licence at an undisclosed location in the UK. The medicine is being marketed in the UK by GW's UK licensee, Bayer Schering Pharma.

Dr Geoffrey Guy, GW's Chairman, said: "The approval and launch of Sativex® in the UK is the world's first full approval of a cannabis-derived prescription medicine and the product of eleven year's research by GW into the cannabinoid system. GW was founded with the primary goal of developing a medicine to address the unmet needs of people with MS and today's launch of Sativex® represents a welcome advance in MS symptom treatment. This is also an historic moment for GW and marks the beginning of the company's transition from late stage development company to a commercial pharmaceutical business. Today's news validates our cannabinoid technology platform and enables us to progress the development of our pipeline across a range of therapeutic areas with increased confidence."

Under the terms of the agreement with Bayer, GW will receive a £10m milestone payment in respect of the UK approval of Sativex®.

Outside the UK, Sativex is expected to be approved in Spain shortly. Further submissions will be made in additional European countries during the second half of 2010 under the mutual recognition procedure. Almirall S.A. will market Sativex in Europe (ex-UK).

The full text of a statement issued today by Bayer Schering Pharma can be [downloaded here](#)