# A PETITION TO ADD 'TERMINAL ILLNESS' TO THE LIST OF QUALIFYING CONDITIONS FOR MEDICAL MARIJUANA

SUBMITTED TO OFFICE OF MEDICAL MARIJUANA 417 FEDERAL STREET - SUITE 130 - DOVER, DELAWARE 19901

3/21/2016

SUBMITTED BY RICHARD N. JESTER MBA, MMS

rj05008@gmail.com

1

### CONTENTS

PURPOSE
WHAT ABOUT BOB? (BOB'S STORY)
EXTENT TO WHICH THE CONDITION IS GENERALLY ACCEPTED AS A DEBILITATING MEDICAL CONDITION
EXTENT TO WHICH CONVENTIONAL TREATMENTS MAY ALLEVIATE SUFFERING
EXTENT TO WHICH CONVENTIONAL TREATMENTS that ARE GENERALLY ACCEPTED BY THE MEDICAL COMMUNITY ARE CAUSING OR ADDING TO A PATIENT'S SUFFERING
CITATION
EXTENT TO WHICH THE CONDITION OR TREATMENT SEVERELY IMPAIR THE PATIENT'S ABILITY TO CARRY ON ACTIVITIES OF DAILY LIVING
EVIDENCE THAT THE USE OF THE OF MARIJUANA ALLEVIATES SUFFERING CAUSED BY THE CONDITION OR TREATMENT
EXHIBIT A: The medical necessity for medicinal cannabis: prospective, observational study evaluating the treatment in cancer patients on supportive or palliative care (2013)
EXHIBIT B: Rebranding Cannabis: The Next Generation of Chronic Pain Medicine (2015)
EXHIBIT C: Assessment of hospice health professionals' knowledge, views, and experience with medical marijuana (2011)
EXHIBIT D: Medicinal Cannabis: A Survey Among Health Care Providers in Washington State (2015)
EXHIBIT E: Cannabis in palliative medicine: improving care and reducing opioid-related morbidity (2011)
EXHIBIT F: Prospectively surveying health-related quality of life and symptom relief in a lot-based sample of medical cannabis-using patients in urban Washington State reveals managed chronic illness and debility. (2013). 12
EXHIBIT G: Cannabinoids in chronic pain and palliative care (2008)12
EXHIBIT H: Use of cannabinoid receptor agonists in cancer therapy as palliative and curative agents (2009)
EXHIBIT I: Cannabinoids: their role in pain and palliation (2007)13
LETTERS OF SUPPORT FROM LICENSED MEDICAL PROFESSIONALS

#### PURPOSE

I would like to petition the State of Delaware to add "Terminal Illness" to the accepted list of qualifying conditions for Medical Marijuana on the grounds that 24 states allow medical cannabis and three states including Minnesota, New Hampshire and New Jersey have already "TERMINAL ILLNESSES" as qualifying conditions.

This petition is dedicated to the memory of my father, Robert Lee Jester. It is my hope that Bob's story will inspire our State and Local Leaders to expand access to medical cannabis for terminally ill patients with the goal of to improving end of life care in the State of Delaware.

For more information about Bob and his legacy, visit <u>http://www.stranofeeley.com/obituaries/Robert-Jester-3/#!/Obituary.</u>

#### WHAT ABOUT BOB? (BOB'S STORY)

Robert "Bob" Jester was diagnosed with Stage 3 Lung Cancer on his 62<sup>nd</sup> birthday in April 11, 2014.

After being subjected to over 20 rounds of chemo and radiation, Bob began to consider any option to remove the pain, nausea and lack of appetite that was symptomatic of the chemo and radiation treatments. On a recommendation from his oldest son, Bob began using medical cannabis to manage the negative symptoms of radiation & chemotherapy. Bob's daughter in law had been using cannabis for months to treat her fibromyalgia, chronic pain and chronic nausea and was actually awaiting the opening of the First State Compassion Center the following summer so she and her husband could procure her medicine more safely.

The cannabis oil was a game changer for Bob. Bob finally had the energy to get out of bed, play games and spending more time with his family. Bob discovered the nausea, exhaustion, pain, headaches, and vomiting was much more manageable with medical cannabis. Even though Bob felt depleted from the radiation and chemotherapy, the cannabis oil significantly improved Bob's quality of life. By January 2015, the tumor in Bob's lung had shrunk in size by almost a third.

Later that spring, Bob decided he wanted to do the legal thing now that a compassion center is opening. Bob went to his doctor and asked for his doctor's support in applying for medical Marijuana license. Bob had already seen the benefits of the cannabis oil and wanted to be up front with the oncologist. When Bob and his wife met with the "CANCER DOCTOR", the doctor became irate and threatened that if Bob mentioned the subject again, he would discontinue care and he would need to seek a new doctor for continuity of care. The doctor threatened that if any trace of marijuana came up on any blood test, he would discontinue treatment and report Bob to the authorities, making him ineligible for hospice care.

Although Bob had already experienced the positive benefits of medical cannabis and knew it could help improve his quality of life, Bob and his wife were terrified about starting the cancer process from scratch with a new doctor. Rather than take the risk of having to search for another oncologist, they chose to stop using the medical cannabis oil despite experiencing the positive benefits. After that day, Bob never used medical cannabis again.

In August 2015, Bob began palliative care at home with Delaware Hospice. Bob vowed never to go back to the hospital. After a few months of palliative care, the doctor decided that Bob no longer needed the Ativan (Generic- Lorazepam) that he had been taking for the past 30 years. The doctor did not renew Bob's prescription and Bob began withdrawal from the Lorazepam becoming irate, loud, difficult, and defiant.

The last time Bob's doctor had seen his patient was during his August 2015 stay at the hospital. Despite refusing to see his patient, Bob's sons, wife and hospice nurses continued to plead with the doctor to renew the Lorazepam, but the doctor refused. Bob's primary care provider was in the State of Maryland. Since Bob's primary care provider was an out of state doctor, Delaware Hospice still could not renew the prescription. The doctor discouraged the Hospice Doctors and Nurse Practitioners at Delaware Hospice from renewing the Lorazepam prescription. Bob was bedridden by this time and could not leave the house, so finding a new primary care provider in Delaware was not an option.

All the while, Bob's withdrawal symptoms continue to get worse, allowing him to fall into a deep depression. A few days before Thanksgiving, his withdrawal hit rock bottom when his 67-year-old sister had to wrestle a gun away from him. After the suicide attempt, Bob's family and nurses appealed successfully to another doctor at the same oncology practice as his main the doctor to finally renew Bob's prescription for Lorazepam. Within 24 hours of restarting the Lorazepam, Bob's withdrawal symptoms had completely subsided.

Bob continued a steady decline for the remainder of 2015. His life expectancy was unpredictable. Around mid-December 2015, Bob stopped eating. If terminal illnesses were a qualifying condition in Delaware, Bob could have gotten medical marijuana to stimulate his appetite and help make him comfortable. Bob never ate again. Bob did not eat for 28 days. Every day he would ask his wife and his sons to end his suffering and everyday they had to tell him they could do nothing.

By this time, Bob was taken off oral morphine and had reached the maximum amount of IV pain medication for his condition; he could not sit up in the bed anymore. He was incontinent, his family having to change him at least 2 or 3 times a day. His shaking had gotten so bad that he couldn't even hold a water glass on his own.

Shortly before New Year's Eve, the Hospice nurses told Bob's family he had at most 24 or 48 hours left. For the next two weeks, Bob's family watched and waited for Bob to die. Every day the family did what they could to make him comfortable. Despite not eating for 28 days, they still tried to get Bob to eat but Bob had lost all interest in food, which, as a professionally trained chef, had been his passion for most of his life. Every day Bob asked to die. Every day Bob asked for something, anything that would ease his pain and suffering. Every day Bob's family waited, never knowing which breath would be his last.

With his loving wife by his side, Bob finally found peace on January 7th, 2016. Bob was only 63 years old.

In the last few months of Bob's life, Bob kept telling his family "this wasn't the way things were supposed to end." Even though Bob's battle was finally over, his oldest son could not let go of his anger. Bob's son was angry with the "CANCER DOCTOR" for how he responded when his father tried to do the legal thing. Bob's son could not understand how someone who took the Hippocratic Oath could ever refuse a treatment option that could improve a patient's quality of life, or at least reduce suffering. Bob's son wanted the emotional pain his family and his father endured, to mean something. Most of all, Bob's son desperately wanted to spare future patients from the same pain that was so willfully inflicted upon them. One day, while voicing this frustration to his mother, Bob's son started crying. Bob's wife wiped the tears from her son's face and told him to either "let go of the pain or use it to do some good."

This petition started that day.

# EXTENT TO WHICH THE CONDITION IS GENERALLY ACCEPTED AS A DEBILITATING MEDICAL CONDITION

A terminal illness is a disease that cannot be cured or adequately treated and that is reasonably expected to result in the death of the patient within a short period of time. This term is more commonly used for progressive diseases such as cancer or advanced heart disease than for trauma. In popular use, it indicates a disease that eventually ends the life of the sufferer.

Often, a patient is considered terminally ill when their estimated life expectancy is six months or less, under the assumption that the disease will run its normal course. The six-month standard is arbitrary and best available estimates of longevity may be incorrect. However, this does not guarantee that the patient will not die unexpectedly early.

In general, physicians slightly overestimate the survival time of terminally ill cancer patients, so that, for example, a person who is expected to live for about six weeks would likely die around four weeks. If a condition is a terminal illness, there is no cure. Treatment focuses on providing patients with relief from the symptoms, pain, physical stress, and mental stress of a serious illness—whatever the diagnosis. The goal of such therapy is to improve quality of life for both the patient and the family.

#### EXTENT TO WHICH CONVENTIONAL TREATMENTS MAY ALLEVIATE SUFFERING

Terminal illness is, by definition, an illness that is going to result in death. By the time an illness is deemed terminal, it is incurable and not treatable with any hope of successfully prolonging life. Treatments for terminal illness are typically geared toward quality of life and comfort. Because many illnesses can become terminal and many more are terminal by nature, there are numerous and varied symptoms associated with terminal illness that may require treatment.

Some of the most common symptoms that caregivers seek to alleviate in patients with terminal illness are pain, depression, digestive discomfort, excretive discomfort, nausea and loss of appetite. While treating these symptoms will not cure terminal illness, it can make patients feel more comfortable.

Palliative care is normally offered to terminally ill patients, regardless of their overall disease management style, if it seems likely to help manage symptoms such as pain and improve quality of life. Hospice care, which can be provided at home or in a long-term care facility, additionally provides emotional and spiritual support for the patient and loved ones.

# EXTENT TO WHICH CONVENTIONAL TREATMENTS THAT ARE GENERALLY ACCEPTED BY THE MEDICAL COMMUNITY ARE CAUSING OR ADDING TO A PATIENT'S SUFFERING

By definition, there is no cure or adequate treatment for terminal illnesses. Many illnesses can become terminal and many more are terminal by nature, there are numerous and varied symptoms associated with terminal illness that may require treatment. As such, countless care and medicine options may assist in end of life treatment. Some of the most common symptoms that caregivers seek to alleviate in patients with terminal illness are pain, depression, digestive discomfort, excretive discomfort, nausea and loss of appetite.

Medications used for palliative patients are used differently from standard medications, based on established practices with varying degrees of evidence. Examples include the use of antipsychotic medications to treat nausea, anticonvulsants to treat pain, and morphine to treat dyspnea. Routes of administration may differ from acute or chronic care, as many patients lose the ability to swallow. Medications are often managed at home by family or nursing support.

Opioid therapy is the cornerstone of management of severe chronic pain in the field of palliative care medicine. Medical and societal philosophy evolved during the 1960s and 1970s to accept the use of opioids in the treatment of both malignant and nonmalignant pain. Though dosages are still kept within safe limits to avoid overdosing terminal patients, there is typically no holding back of medication at this point, due to the nature of terminal illness. In spite of the long established history of opioid therapy and its widespread use today, clinical problems in the proper use of opioid therapy remain prevalent. These problems can be divided into 2 main categories: (1) errors in prescribing opioids, and (2) opioid toxicity.

In regards to errors in prescribing opioids, the American Academy of Hospice and Palliative Medicine and Hospice and Palliative Nursing Association in January 2005, addressed this topic in a prospective study of 132 patients with cancer-related pain, 76% experienced errors in opioid dosing. That study divided these errors into categories: (1) errors in dosing strategy (which represented over 80% of all errors) uncovered a variety of problems, including under-treatment of pain, under-treatment of side effects, incorrect dosing intervals, and the use of multiple opioids simultaneously. Errors in opioid prescribing are especially common when dosing becomes as-needed for continuous pain, failing to treat breakthrough and incident pain, and using more than one opiate at a time.

The other major problem is opioid toxicity, the progression of neurologic and psychological toxicity from opioids as resulting in a continuum of symptoms including sedation, hallucinations, myoclonus, seizures, and cognitive dysfunction. Sedation, the most commonly seen symptom of toxicity, is considered the "tip of the iceberg" leading toward delirium. This is hard for the patient, but especially hard on the caregivers and loved ones who have to watch this transformation. Delirium can complicate opioid therapy. Disorientation with impaired memory and language develops with a subacute onset and fluctuating course. Hallucinations and delusions often occur early in opioid-related delirium.

Opioid-induced myoclonus is often a sign of evolving delirium. Risk factors include dehydration and other medications (e.g., selective serotonin reuptake inhibitors, dopamine antagonists, and nonsteroidal anti-inflammatory agents [NSAIDs]). NSAIDs are thought to produce mild renal insufficiency and decrease opioid and metabolite excretion. Treatments to consider are hydration, opioid rotation, and GABA agonists such as clonazepam and baclofen. Seizures are a rare complication except with meperidine (Demerol). They may result from hypoxia or respiratory depression.

When sedation occurs, opioid dose reduction or opioid rotation to an alternate drug or another route of administration is the next step. If sedation persists, or if there is reluctance to reduce the opioid dose, psychostimulants can be used to counteract the opioid-induced sedation. It should be noted that the use of these

medications in this manner is not approved by the US Food and Drug Administration, and is considered "off-label" prescribing. Methylphenidate (*Ritalin*) and dextroamphetamine (*Adderall*) block the reuptake of norepinephrine and dopamine in presynaptic nerve terminals to increase alertness. Modafinil (*Provigil*) may also be used, but it is expensive and its mechanism of action is unknown.

Though opioid dosages are still kept within safe limits to avoid overdosing terminal patients, there is typically no holding back of medication at this point, due to the nature of terminal illness. Medical marijuana has been shown to help with nearly all of the common symptoms that appear in terminal illness. There is evidence that it works with chronic pain, loss of appetite, nausea, vomiting and possibly even depression, as it can affect a patient's mood. It can also help terminally ill patients sleep.

### CITATION

- The Use of Opioids in Palliative Medicine, Gail Austin Cooney, MD, FAAHPM.
  - o <u>http://www.medscape.org/viewarticle/499455</u>.

# EXTENT TO WHICH THE CONDITION OR TREATMENT SEVERELY IMPAIR THE PATIENT'S ABILITY TO CARRY ON ACTIVITIES OF DAILY LIVING

Patients with Terminal illness often chose palliative care or hospice care. Hospice services and palliative care programs share similar goals of providing symptom relief and pain management. Palliative care services can be offered to any patient without restriction to disease or prognosis, and can be appropriate for anyone with a serious, complex illness, whether they are expected to recover fully, to live with chronic illness for an extended time, or to experience disease progression.

Hospice is a type of care involving palliation without curative intent. Usually, it is used for people with no further options for curing their disease or in people who have decided not to pursue further options that are arduous, likely to cause more symptoms, and not likely to succeed. Hospice care under the Medicare Hospice Benefit requires that two physicians certify that a patient has less than six months to live if the disease follows its usual course. This does not mean, though, that if a patient is still living after six months in hospice he or she will be discharged from the service. The philosophy and multi-disciplinary team approach are similar with hospice and palliative care, and indeed the training programs and many organizations provide both. The biggest difference between hospice and palliative care is the patient: where they are in their illness especially related to prognosis and their goals/wishes regarding curative treatment.

Although the concept of palliative care is not new, most physicians have traditionally concentrated on trying to cure patients. Treatments for the alleviation of symptoms were viewed as hazardous and seen as inviting addiction and other unwanted side effects.

Palliative care clinicians are often concerned about access to symptom controlling medications and therapies when it comes to relieving suffering. For example with opioids, you can hear clinicians advocate for access to these important medications, but also recognize the public health risk which comes from diversion and inappropriate/non-prescribed use.

# EVIDENCE THAT THE USE OF THE OF MARIJUANA ALLEVIATES SUFFERING CAUSED BY THE CONDITION OR TREATMENT

Medications and treatments are said to have a palliative effect if they relieve symptoms without having a curative effect on the underlying disease or cause. Marijuana has been documented to provide relief to patients in palliative and hospice care. The US National Library of Medicine for the National Institutes of Health provides evidence that the use of Marijuana alleviates suffering caused by the Terminal Illnesses and is generally accepted among the medical community and other experts. The following articles/studies provide evidence support the assertion that Medical Marijuana yields potential benefits for Terminally Ill patients.

### EXHIBIT A: THE MEDICAL NECESSITY FOR MEDICINAL CANNABIS: PROSPECTIVE, OBSERVATIONAL STUDY EVALUATING THE TREATMENT IN CANCER PATIENTS ON SUPPORTIVE OR PALLIATIVE CARE (2013)

- Bar-Sela G, Vorobeichik M, Drawsheh S, Omer A, Goldberg V, Muller E. The medical necessity for medicinal cannabis: prospective, observational study evaluating the treatment in cancer patients on supportive or palliative care. Evid Based Complement Alternate Med. 2013;2013:510392. doi: 10.1155/2013/510392. Epub 2013 Jul 16. PubMed PMID: 23956774; PubMed Central PMCID: PMC3730175.
- o <u>http://www.ncbi.nlm.nih.gov/pubmed/239556774</u>

"Results. Of the 211 patients who had a first interview, only 131 had the second interview, 25 of whom stopped treatment after less than a week. All cancer or anticancer treatmentrelated symptoms showed significant improvement (P < 0.001). No significant side effects except for memory lessening in patients with prolonged cannabis use (P = 0.002) were noted. Conclusion. The positive effects of cannabis on various cancer-related symptoms are tempered by reliance on self-reporting for many of the variables. Although studies with a control group are missing, the improvement in symptoms should push the use of cannabis in palliative treatment of oncology patients."

## EXHIBIT B: REBRANDING CANNABIS: THE NEXT GENERATION OF CHRONIC PAIN MEDICINE (2015)

- Carter GT, Javaher SP, Nguyen MH, Garret S, Carlini BH. Re-branding cannabis: the next generation of chronic pain medicine? Pain Manag. 2015;5(1):13-21. doi:10.2217/pmt.14.49. PubMed PMID: 25537695.
- o <u>http://www.ncbi.nlm.nih.gov/pubmed/25537695</u>

"The field of pain medicine is at a crossroads given the epidemic of addiction and overdose deaths from prescription opioids. Cannabis and its active ingredients, cannabinoids, are a much safer therapeutic option. Despite being slowed by legal restrictions and stigma, research continues to show that when used appropriately, cannabis is safe and effective for many forms of chronic pain and other conditions, and has no overdose levels. Current literature indicates many chronic pain patients could be treated with cannabis alone or with lower doses of opioids. To make progress, cannabis needs to be re-branded as a legitimate medicine and rescheduled to a more pharmacologically justifiable class of compounds."

EXHIBIT C: ASSESSMENT OF HOSPICE HEALTH PROFESSIONALS' KNOWLEDGE, VIEWS, AND EXPERIENCE WITH MEDICAL MARIJUANA (2011)

- Uritsky TJ, McPherson ML, Pradel F. Assessment of hospice health professionals' knowledge, views, and experience with medical marijuana. J Palliat Med. 2011 Dec;14(12):1291-5. doi: 10.1089/jpm.2011.0113. Epub 2011 Nov 11. PubMed. PMID: 22077541.
- o <u>http://www.ncbi.nlm.nih.gov/pubmed/22077541</u>

"Given its demonstrated efficacy in symptom management, marijuana has a potential role in palliative care. This study utilized a 16-item questionnaire to assess the knowledge, experience, and views of hospice professionals regarding the use of marijuana in terminally ill patients. The study results revealed that, like the general public, hospice health care providers are generally in favor of legalization of marijuana and, if legalized, would support its use in symptom management for their terminally ill patients."

## EXHIBIT D: MEDICINAL CANNABIS: A SURVEY AMONG HEALTH CARE PROVIDERS IN WASHINGTON STATE (2015)

- Carlini BH, Garrett SB, Carter GT. Medicinal Cannabis: A Survey Among Health Care Providers in Washington State. Am J Hosp Palliat Care. 2015 Sep 15. pii: 1049909115604669. [Epub ahead of print] PubMed PMID: 26377551.
- <u>http://www.ncbi.nlm.nih.gov/pubmed/26377551</u>

"Four hundred ninety-four health care providers responded to the survey. Approximately two-third were women, aged 30 to 60 years, and working in family or internal medicine. More than half of the respondents were legally allowed to write MC authorizations per Washington State law, and 27% of those had issued written MC authorizations. Overall, respondents reported low knowledge and comfort level related to recommending MC. Respondents rated MC knowledge as important and supported inclusion of MC training in medical/health provider curriculum. Most Washington State providers have not received education on scientific basis of MC or training on best clinical practices of MC. Clinicians who had issued MC authorizations were more likely to have received MC training than those who had not issued MC authorization."

### EXHIBIT E: CANNABIS IN PALLIATIVE MEDICINE: IMPROVING CARE AND REDUCING OPIOID-RELATED MORBIDITY (2011)

- Carter GT, Flanagan AM, Earleywine M, Abrams DI, Aggarwal SK, Grinspoon L. Cannabis in palliative medicine: improving care and reducing opioid-related morbidity. Am J Hosp Palliat Care. 2011 Aug;28(5):297-303. doi: 10.1177/1049909111402318. Epub 2011 Mar 28. Review. PubMed PMID: 21444324.
- o <u>http://www.ncbi.nlm.nih.gov/pubmed/21444324</u>

"Unlike hospice, long-term drug safety is an important issue in palliative medicine. Opioids may produce significant morbidity. Cannabis is a safer alternative with broad applicability for palliative care. Yet the Drug Enforcement Agency (DEA) classifies cannabis as Schedule I (dangerous, without medical uses). Dronabinol, a Schedule III prescription drug, is 100% tetrahydrocannabinol (THC), the most psychoactive ingredient in cannabis. Cannabis contains 20% THC or less but has other therapeutic cannabinoids, all working together to produce therapeutic effects. As palliative medicine grows, so does the need to reclassify cannabis. This article provides an evidence-based overview and comparison of cannabis and opioids. Using this foundation, an argument is made for reclassifying cannabis in the context of improving palliative care and reducing opioid-related morbidity."

### EXHIBIT F: PROSPECTIVELY SURVEYING HEALTH-RELATED QUALITY OF LIFE AND SYMPTOM RELIEF IN A LOT-BASED SAMPLE OF MEDICAL CANNABIS-USING PATIENTS IN URBAN WASHINGTON STATE REVEALS MANAGED CHRONIC ILLNESS AND DEBILITY. (2013)

- Aggarwal SK, Carter GT, Sullivan MD, Zumbrunnen C, Morrill R, Mayer JD. Prospectively surveying healthrelated quality of life and symptom relief in a lot-based sample of medical cannabis-using patients in urban Washington State reveals managed chronic illness and debility. Am J Hosp Palliat Care. 2013 Sep;30(6):523-31. Doi: 10.1177/1049909112454215. Epub 2012 Aug 10. PubMed PMID: 22887696.
- o <u>http://www.ncbi.nlm.nih.gov/pubmed/22887696</u>

"Patients reported using medical cannabis to treat a wide array of symptoms across multiple body systems with relief ratings consistently in the 7-10/10 range."

#### EXHIBIT G: CANNABINOIDS IN CHRONIC PAIN AND PALLIATIVE CARE (2008)

- Bonfá L, Vinagre RC, de Figueiredo NV. Cannabinoids in chronic pain and palliative care. Rev Bras Anestesiol. 2008 May-Jun;58(3):267-79. English, Portuguese. PubMed PMID: 19378523.
- o <u>http://www.ncbi.nlm.nih.gov/pubmed/19378523</u>

Pure delta-9-tetrahydrocannabinol (Delta9-THC) and its analogues have clinical applicability, being beneficial in selected individuals. The development of pure synthetic substances, in an attempt to attenuate undesirable psychoactive effects, indicates that perspectives for its use in the future are favorable. More detailed studies should be undertaken. Ample debates will be necessary to create standards for its formulation and clinical availability, since it is a substance that generates prejudice, due to its illegal commercialization and use, and also because its use has been attributed to mysticism.

# EXHIBIT H: USE OF CANNABINOID RECEPTOR AGONISTS IN CANCER THERAPY AS PALLIATIVE AND CURATIVE AGENTS (2009)

- Pisanti S, Malfitano AM, Grimaldi C, Santoro A, Gazzerro P, Laezza C, Bifulco M. Use of cannabinoid receptor agonists in cancer therapy as palliative and curative agents. Best Pract Res Clin Endocrinol Metab. 2009 Feb;23(1):117-31. doi: 10.1016/j.beem.2009.02.001. Review. PubMed PMID: 19285265.
- o <u>http://www.ncbi.nlm.nih.gov/pubmed/19285265</u>

Cannabinoids (the active components of Cannabis sativa) and their derivatives have received renewed interest in recent years due to their diverse pharmacological activities. In particular, cannabinoids offer potential applications as anti-tumour drugs, based on the ability of some members of this class of compounds to limit cell proliferation and to induce tumour-selective cell death. Although synthetic cannabinoids may have pro-tumour effects in vivo due to their immunosuppressive properties, predominantly inhibitory effects on tumour growth and migration, angiogenesis, metastasis, and also inflammation have been described. Emerging evidence suggests that agonists of cannabinoid receptors expressed by tumour cells may offer a novel strategy to treat cancer. In this chapter we review the more recent results generating interest in the field of cannabinoids and cancer, and provide novel suggestions for the development, exploration and use of cannabinoid agonists for cancer therapy, not only as palliative but also as curative drugs.

### EXHIBIT I: CANNABINOIDS: THEIR ROLE IN PAIN AND PALLIATION (2007)

- McCarberg BH. Cannabinoids: their role in pain and palliation. J Pain Palliat Care Pharmacother. 2007;21(3):19-28. Review. PubMed PMID: 18032352.
- o <u>http://www.ncbi.nlm.nih.gov/pubmed/18032352</u>

"Recent research has demonstrated the underlying mechanisms of cannabinoid analgesia via endocannabinoids, an endogenous system of retrograde neuromodulatory messengers that work in tandem with endogenous opioids. Additional receptor and non-receptor mechanisms of cannabinoid drugs have pertinent activity, including anti-carcinogenesis and neuroprotection that may be of key importance in aging and terminal patient populations. The results of clinical trials with synthetic and plant-based cannabinoids suggest that the role of formulation and delivery system is critical in optimizing the risk-benefit profile of cannabinoid products. Synergy between opioids and cannabinoids may produce opioid-sparing effects, as well as extend the duration of analgesia and reduce opioid tolerance and dependence. This article reviews the mechanism of action of cannabinoids, examines marketed agents and those in clinical trials, and addresses their role in treatment of chronic pain, cancer, neurodegenerative diseases, and HIV/ AIDS. The ability of cannabinoid medicines to treat pain, associated sleep disorders, appetite loss, muscle spasm and a wide variety of other symptoms suggests that such agents may in the future play an important role in palliative care."

#### LETTERS OF SUPPORT FROM LICENSED MEDICAL PROFESSIONALS

