1. Medical condition proposed:

Chronic traumatic encephalopathy

2. Provide justification for why this medical condition should be included as a qualifying debilitating medical condition for the use of medical marihuana. Be specific as to why medical marihuana should be used for this condition.

Connecticut has “damage to the nervous tissue of the spinal cord with objective neurological indication of intractable spasticity” as a qualifying condition in its medical marijuana program.

Illinois lists “Post-Concussion Syndrome”, “Spinal cord disease (including but not limited to arachnoiditis)”, “Spinal cord injury with damage to the nervous tissue of the spinal cord with objective neurological indication of intractable spasticity” and Traumatic Brain Injury as qualifying conditions in its medical marijuana program.

New Hampshire lists “spinal cord injury or disease” and traumatic brain injury as qualifying conditions in its medical marijuana program.

Ohio lists chronic traumatic encephalopathy, “spinal cord disease or injury” and traumatic brain injury as qualifying conditions in its medical marijuana program.

Pennsylvania lists “damage to the nervous tissue of the spinal cord with objective neurological indication of intractable spasticity” as a qualifying condition for its medical marijuana program.

Washington lists Traumatic brain injury as a qualifying condition for its medical marijuana program.

West Virginia lists “Damage to the nervous tissue of the spinal cord with objective neurological indication of intractable spasticity.” as a qualifying condition for its medical marijuana program.

Oregon has added “a degenerative or pervasive neurological condition” to its medical marijuana program qualifying conditions.

https://olis.leg.state.or.us/liz/2015R1/Downloads/MeasureDocument/SB844/Enrolled
http://medicalmarijuana.procon.org/view.resource.php?resourceID=000881
https://www.mpp.org/issues/medical-marijuana/state-by-state-medical-marijuana-laws/key-aspects-of-state-and-d-c-medical-marijuana-laws/
http://www.dhhr.wv.gov/bph/Pages/Medical-Cannabis-Program.aspx

The US Department Of Health And Human Services has determined through thorough medical research and analysis that the cannabinoids including THC and CBD specifically from the

marijuana plant can be used safely and effectively to treat neurological damage, including concussion and Traumatic Brain Injury.

> *The cannabinoids are found to have particular application as neuroprotectants, for example in limiting neurological damage following ischemic insults, such as stroke and trauma,* or in the treatment of neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease and HIV dementia.
>
> *The present invention is believed to be particularly beneficial in the treatment of oxidative associated diseases of the CNS*, because of the ability of the cannabinoids to cross the blood brain barrier and exert their antioxidant effects in the brain. In particular embodiments, *the pharmaceutical composition of the present invention is used for preventing, arresting, or treating* neurological damage in Parkinson's disease, Alzheimer's disease and HIV dementia; autoimmune neurodegeneration of the type that can occur in encephalitis, and hypoxic or anoxic neuronal damage that can result from apnea, respiratory arrest or cardiac arrest, and *anoxia caused by drowning, brain surgery or trauma (such as concussion or spinal cord shock).*
>
> As used herein, a “cannabinoid” is a chemical compound (such as cannabinol, THC or cannabidiol) that is found in the plant species Cannabis sativa (marijuana).

http://www.google.com/patents/US6630507

Concussions, including sustained through contact sports like football, hockey, soccer, rugby, boxing, wrestling, cause brain damage and permanent side effects until death. The US DHHS found marijuana to be useful in treating brain trauma such as concussion.

http://jamanetwork.com/journals/jama/article-abstract/2645104

Clinicopathological Evaluation of Chronic Traumatic Encephalopathy in Players of American Football:

> Dr. Ann McKee, a neuropathologist, has examined the brains of 202 deceased football players. A broad survey of her findings was published on Tuesday in The Journal of the American Medical Association.
>
> Of the 202 players, 111 of them played in the N.F.L. — and 110 of those were found to have chronic traumatic encephalopathy, or C.T.E., the degenerative disease believed to be caused by repeated blows to the head.
>
> C.T.E. causes myriad symptoms, including memory loss, confusion, depression and dementia. The problems can arise years after the blows to the head have stopped.

> The brains here are from players who died as young as 23 and as old as 89. And they are from every position on the field quarterbacks, running backs and linebackers, and even a place-kicker and a punter.
>
> The study found that the high school players had mild cases, while college and professional players showed more severe effects. But even those with mild cases exhibited cognitive, mood and behavioral symptoms.

https://www.nytimes.com/interactive/2017/07/25/sports/football/nfl-cte.html

Many UFC/MMA fighters utilize medical marijuana to treat symptoms of repeated blows to the head. UFC fighter Nick Diaz was banned for 5 years for failing a drug test because of his use of medical marijuana.

https://www.theguardian.com/sport/2015/sep/18/nick-diazs-five-year-ban-for-weed-is-master-stroke-of-outdated-thinking

The CDC has a website aimed at preventing kids from getting concussions.

https://www.cdc.gov/headsup/index.html

A concussion is a type of traumatic brain injury—or TBI—caused by a bump, blow, or jolt to the head or by a hit to the body that causes the head and brain to move quickly back and forth. This fast movement can cause the brain to bounce around or twist in the skull, creating chemical changes in the brain and sometimes stretching and damaging the brain cells.

https://www.cdc.gov/headsup/pdfs/youthsports/parent_athlete_info_sheet-a.pdf

'Concussion' Doctor: Letting Kids Play Football is 'Definition of Child Abuse'
The doctor credited with discovering chronic traumatic encephalopathy (CTE) likens children playing football to abuse and says there is nothing anyone can do to make the game safer.

https://www.si.com/nfl/2017/08/08/bennet-omalu-cte-football

> Even mild concussions should not be taken lightly. Neurosurgeons and other brain-injury experts emphasize that although some concussions are less serious than others, there is no such thing as a "minor concussion." In most cases, a single concussion should not cause permanent damage. A second concussion soon after the first one does not have to be very strong for its effects to be permanently disabling or deadly.
>
> According to the **University of Pittsburgh's Brain Trauma Research Center**, *more than 300,000 sports-related concussions occur annually in the U.S.*, and the likelihood of suffering a concussion while playing a contact sport is estimated to be as high as 19

percent per year of play. *More than 62,000 concussions are sustained each year in high school contact sports and, among college football players, 34 percent have had one concussion and 20 percent have endured multiple concussions. Estimates show that between four and 20 percent of college and high school football players will sustain a brain injury over the course of one season*. The risk of concussion in football is three to six times higher in players who have had a previous concussion.

A study conducted by McGill University in Montreal found that 60 percent of college soccer players reported symptoms of a concussion at least once during the season. The study also revealed that concussion rates in soccer players were comparable to those in football. According to this study, athletes who suffered a concussion were four to six times more likely to suffer a second concussion. Research such as this has led to greater interest in developing protective headgear for soccer participants but it is not clear that such headgear would actually reduce the risk of concussion.

During the 2014 World Cup, head injuries sustained by the participating soccer players reignited the debate over concussion management after one of Germany's players took a major hit to the head and continued to play, only to be helped away from the field shortly after. Major League Soccer created a concussion committee in 2010 and instituted a mandatory baseline neuropsychological testing for players. Now, players must be removed from a game immediately if they show signs of a head injury. If a series of cognitive tests are failed, the player must see a team specialist before returning to play and must be symptom free for 24 hours before being allowed to play. However, many worry that the rules are not as strictly enforced as they should be. Dr. Riley Williams, the team physician for the New York Red Bulls, noted, "There's always a differential between what policy says and what the actual application of the policy is on the field." FIFA, the international league that governs the World Cup, leaves decisions up to the team.

http://www.aans.org/Patients/Neurosurgical-Conditions-and-Treatments/Concussion

The goal of concussion treatment is to allow the brain injury to heal. Treatment of concussions differs depending on the level of severity.

http://www.neurosurgery.pitt.edu/centers-excellence/brain-and-spine-injury/concussions

1,085,272 Players: Football Remains No. 1 H.S. Sport in USA for 2016.
Over 800,000 high schoolers played soccer in 2016.

http://www.cnsnews.com/news/article/terence-p-jeffrey/1085272-players-football-remains-no-1-hs-sport-usa

(Data provided by National High School Federation of Associations)

- Scholastic wrestling ranks 7th of all boys' sports in terms of participation at the high school level with 258,208 nation-wide.

http://www.nwcaonline.com/growing-wrestling/facts-resources/

To describe the characteristics of wrestling injuries occurring in male athletes aged 7–17 treated in United States (U.S.) emergency departments (ED) from 2000–2006
During the study period, there were an estimated 167,606 ED visits for wrestling injuries in 7–17 years old U.S. males, with 152,710 (91.1%) occurring in the older (12–17 years old) group.
There were a total of 676 Traumatic Brain Injuries reported for children Ages 7–11 and 9437 Traumatic Brain Injuries for Ages 12-17.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3027436/

Post-concussion symptoms include:

- Headaches
- Dizziness
- Fatigue
- Irritability
- Anxiety
- Insomnia
- Loss of concentration and memory
- Ringing in the ears
- Blurry vision
- Noise and light sensitivity
- Rarely, decreases in taste and smell

Post-concussion headaches can vary and may feel like tension-type headaches or migraines. Most often, they are tension-type headaches. These may be associated with a neck injury that happened at the same time as the head injury.

http://www.mayoclinic.org/diseases-conditions/post-concussion-syndrome/symptoms-causes/dxc-20343348

In January 1997, the White House Office of National Drug Control Policy (ONDCP) asked the Institute of Medicine (IOM) to conduct a review of the scientific evidence to assess the potential health benefits and risks of marijuana and its constituent

> cannabinoids (see the Statement of Task on page 9). That review began in August 1997 and culminates with this report.

https://www.nap.edu/catalog/6376/marijuana-and-medicine-assessing-the-science-base

The 1999 Institute of Medicine report states:

> Neurological disorders affect the brain, spinal cord, or peripheral nerves and muscles in the body. *Marijuana has been proposed most often as a source of relief for* three general types of neurological disorders: muscle spasticity, particularly in multiple sclerosis patients and *spinal cord injury victims*; movement disorders, such as Parkinson's disease, Huntington's disease, and Tourette's syndrome; and epilepsy. Marijuana is not proposed as a cure for such disorders, but it might relieve some associated symptoms.
>
> *There are numerous anecdotal reports that marijuana can relieve the spasticity associated with* multiple sclerosis or *spinal cord injury*, and animal studies have shown that cannabinoids affect motor areas in the brain--areas that might influence spasticity.

While the MMMA covers “severe and persistent muscle spasms”, someone who suffers from a spinal cord injury or other CNS injury may have only mild or moderate, not “severe” muscle spasms in order to be recognized as a qualifying patient.

Further, the report goes on:

> Spinal Cord Injury
>
> In 1990, there were about 15 million patients worldwide with spinal cord injury, and an estimated 10,000 new cases are reported each year in the United States alone.134,138 About 60% of spinal cord injuries occur in people younger than 35 years old. Most will need long-term care and some lifelong care.
>
> Many spinal cord injury patients report that marijuana reduces their muscle spasms. Twenty-two of 43 respondents to a 1982 survey of people with spinal cord injuries reported that marijuana reduced their spasticity. One double-blind study of a paraplegic patient with painful spasms in both legs suggested that oral THC was superior to codeine in reducing muscle spasms. *Victims of spinal cord injury reporting at IOM workshops noted that smoking marijuana reduces their muscle spasms, their nausea, and the frequency of their sleepless nights.* The caveats described for surveys of spasticity relief in MS patients also apply here.

More related studies on marijuana and spinal cord injury can be found here:

Science and Research

1974 The perceived effects of marijuana on spinal cord injured males.

1980 Marihuana as a therapeutic agent for muscle spasm or spasticity.

1982 Cannabis effect on spasticity in spinal cord injury.

1986 The effect of delta-9-THC on human spasticity.

1990 Delta-9-tetrahydrocannabinol shows antispastic and analgesic effects in a single case double-blind trial.

1995 Treatment of spasticity in spinal cord injury with dronabinol, a tetrahydrocannabinol derivative.

1996 The effect of orally and rectally administered delta-9-tetrahydrocannabinol on spasticity: a pilot study with 2 patients.

1997 Involvement of Dynorphin B in the Antinociceptive Effects of the Cannabinoid CP55,940 in the Spinal Cord.

1999 Cannabis and cannabinoids: pharmacology and rationale for clinical use.

2001 Selective cannabinoid CB1 receptor activation inhibits spinal nociceptive transmission in vivo.

2001 Clinical investigation of delta-9-tetrahydrocannabinol (THC) as an alternative therapy for overactive bladders in spinal cord injury (SCI) patients.

2003 The treatment of spasticity with D9-tetrahydrocannabinol (D9-THC) in patients with spinal cord injury.

2003 Therapeutic potential of cannabinoids in CNS disease.

2004 Are oral cannabinoids safe and effective in refractory neuropathic pain?

2006 Treatments for Chronic Pain in Persons With Spinal Cord Injury: A Survey Study.

2006 Antinociceptive effect of cannabinoid agonist WIN 55,212–2 in rats with a spinal cord injury.

2006 Effects of a Cannabinoid Agonist on Spinal Nociceptive Neurons in a Rodent Model of Neuropathic Pain.

2006 Cannabinoids In Medicine: A Review Of Their Therapeutic Potential.

2006 The treatment of spasticity with Delta(9)-tetrahydrocannabinol in persons with spinal cord injury.

2008 Effects of palmitoylethanolamide on signaling pathways implicated in the development of spinal cord injury.

2009 Sustained antinociceptive effect of cannabinoid receptor agonist WIN 55,212-2 over time in rat model of neuropathic spinal cord injury pain.

2009 The nonpsychotropic cannabinoid cannabidiol modulates and directly activates alpha-1 and alpha-1-Beta glycine receptor function.

2010 Cannabinoid receptor-mediated antinociception with acetaminophen drug combinations in rats with neuropathic spinal cord injury pain.

2010 Effect of dronabinol on central neuropathic pain after spinal cord injury: a pilot study.

2010 Cannabinoid subtype-2 receptors modulate the antihyperalgesic effect of WIN 55,212-2 in rats with neuropathic spinal cord injury pain.

2010 The endocannabinoid 2-arachidonoylglycerol reduces lesion expansion and white matter damage after spinal cord injury.

2010 A randomized, double-blinded, crossover pilot study assessing the effect of nabilone on spasticity in persons with spinal cord injury.

2011 Cannabinoid Agonists Inhibit Neuropathic Pain Induced by Brachial Plexus Avulsion in Mice by Affecting Glial Cells and MAP Kinases.

2011 Effects of palmitoylethanolamide on release of mast cell peptidases and neurotrophic factors after spinal cord injury.

2011 Targetting CB1 Cannabinoid Receptor for Neuroprotetion in Spinal Cord Injury.

2011 Spinal Cord Injuries Induce Changes of CB1 Cannabinoid Receptor and C-C Chemokine Expression in Brain Areas Underlying Circuitry of Chronic Pain Conditions.

2011 Modulation of inflammatory responses by a cannabinoid-2-selective agonist after spinal cord injury.

2011 Activation of spinal and supraspinal cannabinoid-1 receptors leads to antinociception in a rat model of neuropathic spinal cord injury pain.

2011 Cannabidiol-treated Rats Exhibited Higher Motor Score After Cryogenic Spinal Cord Injury.

2011 Spinal cannabinoid CB2 receptors as a target for neuropathic pain: an investigation using chronic constriction injury.

2012 A Role for the Cannabinoid 1 Receptor in Neuronal Differentiation of Adult Spinal Cord Progenitors in vitro is Revealed through Pharmacological Inhibition and Genetic Deletion.

2012 The interaction between intrathecal administration of low doses of palmitoylethanolamide and AM251 in formalin-induced pain related behavior and spinal cord IL1-β expression in rats.

2012 Early Endogenous Activation of CB1 and CB2 Receptors after Spinal Cord Injury Is a Protective Response Involved in Spontaneous Recovery

2012 A cell population that strongly expresses the CB1 cannabinoid receptor in the ependyma of the rat spinal cord

2012 The interaction between intrathecal administration of low doses of palmitoylethanolamide and AM251 in formalin-induced pain related behavior and spinal cord IL1-β expression in rats.

2012 Specific inhibition of the JNK pathway promotes locomotor recovery and neuroprotection after mouse spinal cord injury

2013 Neuroprotective effects of Cannabis sativa leaves extracts on α-Motoneurons density after sciatic nerve injury in rats

2013 A new co-ultramicronized composite including palmitoylethanolamide and luteolin to prevent neuroinflammation in spinal cord injury

2013 Palmitoylethanolamide in Homeostatic and Traumatic Central Nervous System Injuries

2013 Glia and Mast Cells as Targets for Palmitoylethanolamide, an Anti-inflammatory and Neuroprotective Lipid Mediator

2013 Neuroprotection and reduction of glial reaction by cannabidiol treatment after sciatic nerve transection in neonatal rats.

2013 Metabolomics uncovers dietary omega-3 fatty acid-derived metabolites implicated in anti-nociceptive responses after experimental spinal cord injury.

A safety profile of Medical Marijuana can be found in the first year report of the Minnesota medical marijuana program. The Minnesota Department of Health surveyed 1500+ patients enrolled in the program.

> Adverse Side Effects: At this point, the safety profile of the medical cannabis products available through the Minnesota program seems quite favorable. Approximately 20-25% of enrolled patients report negative physical or mental side effects of some kind, with the majority – around 60% - reporting only one and 90% reporting three or fewer. The vast majority of adverse side effects, around 90%, are mild to moderate in severity. An assessment of the 30 patients reporting severe side effects, meaning “interrupts usual daily activities,” found no apparent pattern of patient age, medical condition, or type of medical cannabis used. The most common adverse side effects are dry mouth, drowsiness, and fatigue. Fortunately, up to the present no serious adverse events (life threatening or requiring hospitalization) have been reported.

http://www.health.state.mn.us/topics/cannabis/about/firstyearreport.html

Medical Marijuana's mild to moderate side effects of dry mouth, drowsiness and fatigue are easily tolerated by the vast majority of patients.

The Mayo Clinic website has assembled dosage information on Medical Marijuana.
http://www.mayoclinic.org/drugs-supplements/marijuana/dosing/hrb-20059701

As evidenced by the included medical marijuana patient surveys in other states and countries, adults are using medical marijuana to treat these diseases. Patients will continue to use medical marijuana to treat symptoms whether or not you approve these conditions. Approving these conditions to add them to the list of Qualifying Conditions in the MMMA has the only effect of protecting sick people from arrest or penalty, who are currently breaking the law by using a safe and non-toxic plant that they can grow themselves versus prescriptions that cost thousands of dollars per month.

LARA and the Medical Marihuana Review Panel are not the FDA.
LARA and the Medical Marihuana Review Panel are not tasked with “calling for more research”.
LARA and the Medical Marihuana Review Panel are not deciding “if marihuana is a medicine”, the people of Michigan already decided and declared that in 2008.

The director of LARA, in previous denials of petitions, stated that there are a “lack of studies” on using medical marijuana with the conditions presented. A fact that is true. That is the whole point of medical marijuana laws. The people of 29 states and the District of Columbia know there is a lack of research on medical marijuana, but they created laws to protect patients who are using medical marijuana anyway. BECAUSE MEDICAL MARIJUANA WORKS. Research on medical marijuana has been stymied by the US federal government (DEA and FDA Denials on rescheduling marijuana for research purposes), blocked by NIDA and the NIH (requiring researchers to have extreme hoops to jump through, these hoops are not required to study any other drug).

Health professionals, Medical Marihuana Review Panel members and the Director of LARA have all called for more research. I fully agree more research is required and useful and beneficial for all.

How long must sick patients wait for research? Must they wait for more research until they die? All because the FDA wants a mono chemical therapy instead of a whole botanical plant medicine?

As an example for how long people have been waiting for “more research”, look at this study:

“The perceived effects of marijuana on spinal cord injured males.” 1974 included with the petition.
https://www.ncbi.nlm.nih.gov/pubmed/4453421
Spinal cord injury patients have been waiting 43 years for marijuana research.
43 YEARS of waiting for a safe non-toxic plant chemical that reduces or eliminates spasms in spinal injury.
Do you have any idea how many spinal cord patients have died in those 43 years?
THOUSANDS of patients whose condition was uncontrolled by prescription medications have died in those 43 years.

That is 43 years from that single study. Historically, medical marijuana has been used for spasms and pain for over 5000 years. Because it works.

If you deny this petition for “lack of research”, please detail how many years patients should continue to wait. Please detail exactly how many people you are accepting to die waiting just because you think there is some risk of medical marijuana use that will manifest itself. Even though people have been using medical marijuana for 5000+ years. As well as 21 years since California started its medical marijuana law in 1996. Plus the US Federal Government IND program, started in 1978, which still currently sends 8 ounces of medical marijuana (300 cigarettes in a metal tin) to two people in the USA each month. That is 6+ pounds of medical marijuana each year for 35 years that Irv Rosenfeld has smoked, every day, to treat his bone tumor condition.

https://en.wikipedia.org/wiki/Compassionate_Investigational_New_Drug_program
There is a study on the IND patients and medical marijuana safety here:
http://www.cannabis-med.org/jcant/russo_chronic_use.pdf

Further, if you deny this petition, please provide articles published in peer-reviewed scientific journals reporting the results of research on the effects of marihuana on the medical condition supporting why the condition should not be added to the list of debilitating medical conditions under the Michigan Medical Marihuana Act.

NIDA finds it difficult to put the words together, but finally admits there is no gateway theory of marijuana use.

> These findings are consistent with the idea of marijuana as a "gateway drug." However, the majority of people who use marijuana do not go on to use other, "harder" substances.

https://www.drugabuse.gov/publications/research-reports/marijuana/marijuana-gateway-drug

NIDA finds it very difficult to backtrack on the faulty studies they fund as well. When other researchers tried to duplicate the results of the first study on marijuana and IQ points, they were

unable to find any IQ loss due to marijuana use. I hope that any knowledge you have on marijuana is up to date, and that you are paying attention when NIDA's biased research grants backfire on them, over and over again.

> In a recent study sponsored by NIDA and the National Institute of Mental Health, teens who used marijuana lost IQ points relative to their nonusing peers. However, the drug appeared not to be the culprit. The new findings contribute to an ongoing scientific exploration of the drug's impact on users' cognition.

https://www.drugabuse.gov/news-events/nida-notes/2016/08/study-questions-role-marijuana-in-teen-users-iq-decline

3. Provide a summary of the evidence that the use of medical marihuana will provide palliative or therapeutic benefit for this medical condition or is a treatment for this condition.

1. Effect of Marijuana Use on Outcomes in Traumatic Brain Injury BRIAN M. NGUYEN, M.D., DENNIS KIM, M.D., SCOTT BRICKER, M.D., FRED BONGARD, M.D., ANGELA NEVILLE, M.D., BRANT PUTNAM, M.D., JENNIFER SMITH, M.D., DAVID PLURAD, M.D.

Despite these limitations inherent to any retrospective study, our data suggest an important link between the presence of a positive THC screen and improved survival after TBI. With continued research, more information will be uncovered regarding the therapeutic potential of THC, and further therapeutic interventions may be established.

2. https://www.ncbi.nlm.nih.gov/pubmed/24961520/
Cannabinoids: Well-Suited Candidates for the Treatment of Perinatal Brain Injury
Altogether, these studies using both rodent and non-rodent animal models of NHIE strongly suggest that CBD may be a safe and effective drug to be used during the acute and sub-acute phases after NHIE, and is currently the best suited cannabinoid to be implemented for clinical use in babies affected by neonatal encephalopathy.
These studies covered different modes of neonatal brain injury including NHIE, perinatal asphyxia and neonatal stroke, and revealed the high potential of the endocannabinoid system as a novel therapeutic target for the prevention of permanent brain damage in newborns. The characterization of CBD, a non-psycoactive cannabinoid, as a safe and effective protective drug in non-rodent models of NHIE further encouraged the use of CBD as an adjuvant therapy for the acute treatment of the affected newborns.

3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4604192/
The studies reviewed here are all concordant with the view that cannabinoid-based medicines may serve as a novel therapy able to delay/arrest neurodegeneration in acute and chronic neurodegenerative conditions, owing to their capability of normalizing glutamate homeostasis, reducing oxidative injury, and/or attenuating local inflammatory events, and possibly also by

their capability of activating cellular responses (e.g., induction of autophagy) in controlling the toxicity of protein aggregates, although this has not been addressed here.

4. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5314139/
However, clinical and pre-clinical findings provide evidence suggesting that the primary psychoactive constituent of *Cannabis sativa*, THC, is neuroprotective when administered prior to a traumatic insult.
Even though 80–90% of THC is excreted from individuals within 5 days of administration, the remaining slow release of lipophilic THC from lipid-storage compartments result in its long terminal half-life in plasma (Huestis, 2007). As such, individuals may experience very low plasma THC concentrations for prolonged periods after each application. Although the clinical study of TBI-induced mortality reported no data to quantify levels of THC in the THC positive individuals, the low dose THC in CNS injured mice may mimic the pharmacokinetics of THC in humans. This presumed prolonged exposure of THC due to its pharmacokinetics, as well as other potentially neuroprotective cannabinoids, such as CBD (Perez et al., 2013), may be responsible for the survival effects found in cannabis-exposed TBI patients.

5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3202504/
Reduction in the inflammatory response in the brain and spinal cord was also noted in animals treated with dexanabinol (HU-211 a nonpsychoactive synthetic cannabinoid).101 In another trial in rats, all animals treated with placebo developed severe clinical EAE and more than 98 % died, while THC-treated animals had either no clinical signs or mild signs, with delayed onset with survival greater than 95 %.102 WIN-55,212-2, another synthetic cannabinoid, also was found to ameliorate the clinical signs of EAE and to diminish cell infiltration of the spinal cord, partially through CB2.103 Using a chronic model of MS in mice, it was shown that clinical signs and axonal damage in the spinal cord were reduced by the synthetic cannabinoid HU210.

6. https://www.ncbi.nlm.nih.gov/pubmed/12617697
This review highlights recent advances in understanding of the endocannabinoid system and indicates CNS disorders that may benefit from the therapeutic effects of cannabinoid treatment. Where applicable, reference is made to ongoing clinical trials of cannabinoids to alleviate symptoms of these disorders.

7. https://www.ncbi.nlm.nih.gov/pubmed/12952500
Another phase III trial of THC:CBD (narrow ratio) in patients with spinal cord injury is also being conducted.

8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3057300/
Cannabidiol restores liver function, normalizes 5-HT levels and improves brain pathology in accordance with normalization of brain function. Therefore, the effects of cannabidiol may result from a combination of its actions in the liver and brain.

9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5165161/

Cannabinoids have been shown to have neuroprotective effect due to their antioxidative, anti-inflammatory actions and their ability to suppress exitotoxicity. Plant-derived cannabinoids such as THC and CBD can provide neuroprotection against the in vivo and in vitro toxicity of 6-hydroxydopamine and this was thought to be due to their antioxidative property or modulation of glial cell function or a combination of both.

10. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3728280/
A recent review of the clinical trials conducted with Sativex® and other cannabis extracts in various types of pain observed a benefit in a range of conditions, including MS, cancer, irritative urinary symptoms, neuropathy, peripheral nerve injury and *spinal cord injury*. The only condition where benefit was not noted was post-herpetic neuralgia . THC has analgesic and other beneficial effects in fibromyalgia and rheumatoid arthritis as well

11. 10.1111/j.1742-1241.2004.00271.x
Over the period 1998–2002, 3663 questionnaires were distributed, and 2969 were returned (81% response rate).
Patients reported using medical marijuana for CNS injuries over multiple years :
Spinal pain 62 patients
Spinal cord injury 39 patients
Spinal disorder 22 patients
Spinal surgery 22 patients
Spinal disc disorder 16 patients
Spinal paralysis 16 patients
Overall Effectiveness. Of 948 reported users, 648 (68%) reported that cannabis made their symptoms overall much better, 256 (27%) said a little better, 36 (4%) said no difference and eight subjects said a little worse (four subjects) or much worse (four subjects).
Effectiveness Compared to Other Medications. When asked how cannabis compared to other medications overall, 412 of 916 subjects (45%) said it worked much better than prescribed medications, 261 (28%) said it was somewhat better and 45 (5%) said it was about the same; only 27 subjects said that prescription medicines worked better than cannabis (18 somewhat better and nine much better). One hundred and seventy-one (19%) subjects said it was impossible to tell.
Side Effects Compared to other Medications. When asked to compare the undesirable effects of cannabis to those of prescribed medicines, 872 subjects responded, of whom six found that cannabis produced much worse side effects, 23 found somewhat worse side effects and 54 said the side effects were about the same. Two hundred and sixty-four (30%)

subjects stated that side effects of prescribed medicines were somewhat worse and 294 (34%) said they were much worse. Two hundred and thirty-one (26%) stated that it was impossible to tell.
Effects on Other Medication Use. Of the 909 subjects responding to this question, 374 stated that their use of cannabis had changed their use of other medications, while 521 said it had not. Fourteen were not coded.
Return of Symptoms on Stopping. Of the 876 subjects responding, 673 said their symptoms returned or got worse when they stopped using cannabis, and 203 denied any worsening on stopping cannabis.

12. 10.1016/j.jpain.2016.05.010
Using an 11-point numerical pain intensity rating scale as the primary outcome, a mixed effects linear regression model showed a significant analgesic response for vaporized cannabis. When subjective and psychoactive side effects (eg, good drug effect, feeling high, etc) were added as covariates to the model, the reduction in pain intensity remained significant above and beyond any effect of these measures (all $P < .0004$). Psychoactive and subjective effects were dose-dependent. Measurement of neuropsychological performance proved challenging because of various disabilities in the population studied. Because the 2 active doses did not significantly differ from each other in terms of analgesic potency, the lower dose appears to offer the best risk-benefit ratio in patients with neuropathic pain associated with injury or disease of the spinal cord.

13. 10.1080/02791072.2013.805976
The survey was completed by 953 participants, of whom 614 (64%) were male and 339 (36%) were female. The mean age was 40.7 years old (range 14–76).
The majority of subjects in our study were current users who had a health professional involved in the management of their illness, and were using CBMs for at least several years
22 patients reported using medical marijuana for Spinal cord injury.
4 patients reported using medical marijuana for Head or brain injury.

14. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4707667/
Activity in models of neuronal injury, neurodegeneration, and psychiatric disease suggest that CBD may also be effective for a wide range of central nervous system disorders that may complicate the lives of individuals with epilepsy; a treatment for both seizures and comorbid conditions is highly desirable.

15. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3673028/
A review of 72 randomized, double-blind, placebo-controlled studies from 1975 to 2004 evaluating the therapeutic effects of cannabinoids concludes that “Cannabinoids present an interesting therapeutic potential as antiemetics, appetite stimulants in debilitating diseases

(cancer and AIDS), analgesics, and in the treatment of multiple sclerosis, *spinal cord injuries*, Tourette's syndrome, epilepsy and glaucoma" (Ben Amar, 2006).

16. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1864800/
Seventy-three percent of the respondents had tried at least 1 of 7 alternative pain treatments, and the most frequently tried were massage, *marijuana*, and acupuncture. The most relief was provided by massage (mean, 6.05 ± 2.47] on the 0–10 relief scale) *and marijuana (mean, 6.62 ± 2.54 on the 0–10 relief scale).*

17. Survey of Australians using cannabis for medical purposes
13% of patients surveyed reported using cannabis to treat symptoms of Spinal Cord Injury.

18. https://www.ncbi.nlm.nih.gov/pubmed/4453421
The perceived decrease in pain and spasticity shown by this survey, even though replies may be biased, indicates that better controlled studies would be worth while.

19. https://www.ncbi.nlm.nih.gov/pubmed/4453421
Questionnaire to spinal cord injury patients. 9/24 users reported no spasticity while using cannabis, 11/24 reported some benefit.

20. 10.1007/978-1-59259-092-6
Marijuana or its synthetic derivatives may reduce spasticity in patients with spasticity of spinal-cord origin. Most of the literature consists of anecdotal reports or reports including a very small number of patients. A survey taken by spinal-cord injured males at the Miami VA Hospital reported 10 patients who had used marijuana. Five patients reported a decrease in spasticity, whereas there was no effect in three (36). In a double-blind pilot study, nine patients were given either 10 mg, 5 mg, or no synthetic ? 9 -tetrahydrocannabinol (THC) (37). Deep tendon reflexes, muscular resistance to stretch in the legs, spasticity score, and EMG-interference pattern were evaluated. The differences between the groups in regards to change in spasticity score was significant (p ? 0.01) (37). Side effects were minimal at these dosages. The long-term tolerance and addictive effects of these agents may limit their use and beneficial effects need to be proven in large clinical trials.

4. Provide articles published in peer-reviewed scientific journals reporting the results of research on the effects of marihuana on the medical condition or treatment of the medical condition and supporting why the medical condition should be added to the list of debilitating medical conditions under the Medical Marihuana Act. Attach a copy of all articles that are discussed in this section. Please do not attach articles that are not discussed in this section.

See enclosed.