MDH Minnesota Department *of* Health

Minnesota Medical Cannabis Program
Petition to Add a Qualifying Medical Condition

Making your petition

- Any person may petition the Minnesota Department of Health ("the department" or "MDH") to add a qualifying medical condition to those listed in subdivision 14 of Minnesota Statutes section 152.22.

Petitions will be accepted only between June 1 and July 31, 2018.
Petitions received outside of these dates will not be reviewed.

Petitions must be sent by certified U.S. mail to:

Minnesota Department of Health
Office of Medical Cannabis
P.O. Box 64882
St. Paul, MN 55164-0882

- You must mail the original copy of the petition with an original signature.
- Complete each section of this petition and attach all supporting documents. Clearly indicate which section of the petition an attachment is for.
- Each petition is limited to one proposed qualifying medical condition. If your petition includes more than one medical condition, it will be dismissed.
- If you are petitioning for the addition of a medical condition that was considered but not approved in a prior year's petition process, you **must include** new scientific evidence or research to support your petition or describe substantially different symptoms. Please refer to our website to see which medical conditions were reviewed in prior years (http://www.health.state.mn.us/topics/cannabis/rulemaking/addconditions.html).
- If the petition is accepted for consideration, MDH will send the petition documents to the Medical Cannabis Review Panel ("Review Panel"). MDH staff will also provide information to the Review Panel about the proposed qualifying condition, its prevalence, and the effectiveness of current treatments.
- You may withdraw your petition any time before the Review Panel's first public meeting of the year by submitting a written statement to the Department stating that you want to withdraw it.

Petition review process

- An appointed citizens Review Panel will meet to review all eligible petitions and supporting documentation.
- MDH will post notice of the public meetings of the Review Panel on its medical cannabis website.
- After the public meeting and by November 1, 2018 the Review Panel will provide the Commissioner of Health a written report of findings.
- The Commissioner will approve or deny the petition by December 3, 2018.

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Section A: Petitioner's Information		
Name (First, Middle, Last): [redacted]		
Home Address (including Apartment or Suite #): [redacted]		
City: [redacted]	State: MN	Zip Code: [redacted]
Telephone Number: [redacted]	E-mail Address: [redacted]	

Section B: Medical Condition You Are Requesting Be Added

Please specify the name and provide a brief description of the proposed qualifying medical condition. Be as precise as possible in identifying the condition. **Optional:** Include diagnostic code(s), citing the associated ICD-9 or ICD-10 code(s), if you know them. *Attach additional pages as needed.*

Hepatitis C ICD-10-CM B18.2
(chronic)

*see attached

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Section C: Symptoms of the Proposed Medical Condition and/or Its Treatment

Describe the extent to which the proposed qualifying medical condition or the treatments cause suffering and impair a person's daily life. *Attach additional pages if needed.*

*see attached

Section D. Availability of conventional medical therapies

Describe conventional medical therapies available and the degree to which they ease the suffering caused by the proposed qualifying medical condition or its treatment. *Attach additional pages if needed.*

* see attached

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Section E: Anticipated benefits from Medical Cannabis

Describe the anticipated benefits from the medical use of cannabis specific to the proposed qualifying medical condition. *Attach additional pages if needed.*

* see attached

Section F (optional): Scientific Evidence of Support for Medical Cannabis Treatment

It will strengthen your petition to include evidence generally accepted by the medical community and other experts supporting the use of medical cannabis to alleviate suffering caused by the proposed medical disease or its treatment. This includes but is not limited to full text, peer-reviewed published journals or other completed medical studies. Please attach complete copies of any article or reference, not abstracts.

☑ ***I have attached relevant articles.*** *(check box if you have attached scientific articles or studies)*

Section G (optional): Letters in Support of Adding the Medical Condition

Attach letters of support for the use of medical cannabis from persons knowledgeable about the proposed qualifying medical condition, such as a licensed health care professional.

☑ ***I have attached letters of support.*** *(check box if you have attached letters of support)*

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Minnesota Medical Cannabis Program
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Section H: Acknowledgement and Signature

Please Note: Any individually identifiable health information relating to any past, present, or future health condition or health care contained in this Petition is classified as a health record under Minnesota Statutes §144.291, and is not subject to public disclosure.

I certify that the information provided in this petition is true and accurate to the best of my knowledge.

S [redacted] 07/29/2018

DATE (mm/dd/yyyy)

To obtain this information in a different format, call:
(651) 201-5598 in the Metro area and (844) 879-3381 in the Non-metro.

Section A: Petitioner's Information

[redacted]

Co-petitioner:

[redacted]

Section B: Medical Condition You Are Requesting Be Added

Clinical Information: **Hepatitis C**

- Condition: **Chronic Hepatitis C**, 2018 ICD-10-CM B18.2
- Inflammation of the liver in humans that is caused by hepatitis c virus lasting six months or more. A small percentage of patients' bodies may clear the virus on their own. Chronic hepatitis c can lead to liver cirrhosis.[i]
- The liver is a large organ that sits just under the rib cage on the right side of the abdomen. The liver is essential for digesting food and ridding the body of toxic substances.[ii]
- Viral hepatitis C (HCV) spreads from one person to another from shared blood. One may contract hepatitis C if one had a blood transfusion before 1990, shared needles, unclean tattoo needles, and (sometimes) unsafe sex. A 12-week treatment of an antiviral medication (Harvoni) is utilized to specifically target the virus to stop the virus from producing enzymes that promote viral replication or production. Serious complications from HCV may require a liver transplant.[iv]

Section C: Symptoms of Proposed Medical Condition and/or Its Treatments

- Many people don't experience symptoms from months to years, but when they do occur, they may be severe. According to Mayo Clinic, symptoms of chronic hepatitis C include bleeding easily, bruising easily, fatigue, poor appetite, jaundice, dark-colored urine, itchy skin, ascites, swelling in the legs, weight loss, hepatic encephalopathy, spider angiomas, nausea, fever, muscle aches. During the acute phase of hepatitis C infection (first one to three months after exposure to the virus), symptoms may include jaundice, fatigue, nausea, fever, and muscle aches.[iii]
- Hepatitis C can cause complications such as, cirrhosis (scarring of the liver) – making it difficult for your liver to function, liver cancer, and/or advanced cirrhosis – which, causes liver failure.[iii]
- Harvoni (sofosbuvir 400mg + 90mg) (antiviral therapy/ 12 weeks) side effects are rarely severe, but some patients do experience them. Common side effects include: fatigue, headache, nausea, diarrhea, insomnia, and weakness. Severe depression or anxiety are possible side effects, as well. Serious side effects may include: interactions with anti-viral

drugs, interactions with medicine used to treat certain heart problems – such as amiodarone – causing bradycardia (slow heart rate); medical assistance must be sought immediately if patients taking both amiodarone and Harvoni experience the following symptoms: fainting or near-fainting, dizziness or lightheadedness, not feeling well, weakness, extreme fatigue, shortness of breath, chest pains, confusion, or memory problems. Harvoni has a 94-97% success rate in curing Hep. C when patients adhere to treatment.[v]

Section D: Availability of Conventional Medical Therapies

Hepatitis C may go unnoticed in some patients. People who may need to be tested or talk to their doctor about screening for hepatitis C infection include:

- A person who has injected or inhaled illicit drugs, such as crystal meth or heroin.
- A person who has abnormal liver function test results with no identified cause.
- Babies born to mothers with hepatitis C.
- Healthcare and emergency workers who have been exposed to blood or accidental needle sticks.
- People with hemophilia who were treated with clotting factors before 1987.
- People who have ever undergone transfusions with hepatitis C infection.
- People living with HIV infection.
- Anyone born from 1945 to 1965.
- A person who has been in prison.[iv]

If an initial blood test shows that one is positive for HCV, additional blood tests will measure the viral load (quantity of the HCV in your blood), and to identify the genotype of the virus.[iv]

Next, doctors will test for liver damage with magnetic resonance elastography (MRE), transient elastography, or a liver biopsy to collect a small sample of liver tissue for laboratory testing.[iv]

Antiviral medications are used to remove the virus from a person's body. A 12-week, one pill a day, of Harvoni is now recommended. A 12-week treatment cost around $95,000, and one must abstain from risky behavior or injection drug use before beginning treatment. Harvoni may cause a few side effects or interact with other medications, described above.[iv]

If a person develops serious complications from chronic HCV, a liver transplantation may be necessary. During surgery, the surgeon removes a person's damaged liver and replaces it with a healthy liver. Most liver transplant donors come from deceased persons, although, a small number come from living donors that donate a healthy portion of their liver. A liver transplant alone doesn't cure HCV; the infection is likely to return – requiring antiviral treatment described above.[iv]

There is no vaccine for HCV, but a doctor will likely recommend that a person with HCV receive vaccines against the hepatitis A and B viruses – as they may cause liver damage, and complicate effective treatment of HCV.[iv]

Lifestyle remedies:

- Stop drinking alcohol. (Alcohol increases the progression of liver disease).
- Avoid drugs/ medications that may cause liver damage.
- Don't share needles. Use sterile needles. Some clinics and charities offer sterile needle exchange programs for people diagnosed with a chemical dependency. But, some jurisdictions don't allow such programs and many people in rural Minnesota don't have access to said programs.
- Practice safe, safer, or safest sex. Inform your partner you have HCV before you engage in intercourse.
- Help prevent other people from coming in contact with your blood during HCV infection. Don't share razors or toothbrushes. Don't donate blood, body organs, or semen.[iv]
- Discovering and living with HCV can be an emotional and traumatizing experience because of stigma associated with infectious diseases; it's important to have a network of support from family, friends, counselors, and other health professionals.

Section E: Anticipated Benefits from Medical Cannabis

Anticipated benefits from medical cannabis include the amelioration of liver damage and reduced progression of liver disease, relief from symptoms of HCV, and relief from symptoms associated with the treatment of HCV. Symptomology which may benefit from medical cannabis treatment include: inflammation, pain in the abdomen and legs, muscle pain, joint pain, itchy skin, chronic fatigue, weight loss, nausea or vomiting, headaches, depression, anxiety, and loss of appetite. Many patients with liver disease cannot take pain medications due to side-effects of stress on liver functioning.

States that allow patients with hepatitis C access to medicinal cannabis treatment include: Alaska (any chronic disease or treatment of such diseases with side effects of cachexia, severe pain, severe nausea, seizures, & muscle spasms), Arizona, Arkansas, California, Colorado (any chronic disease or treatment of such diseases with side effects of cachexia, severe pain, severe nausea, seizures, & muscle spasms), Delaware, District of Columbia, Florida, Hawaii (any chronic disease or treatment of such diseases with side effects of cachexia, severe pain, severe nausea, seizures, & muscle spasms), Illinois, Maine, Massachusetts, Michigan, New Hampshire, New York (any chronic disease or treatment of such diseases with side effects of cachexia, severe pain, severe nausea, seizures, & muscle spasms), North Dakota, Ohio, Oregon (any chronic disease or treatment of such diseases with side effects of cachexia, severe pain, severe nausea, seizures, & muscle spasms), Rhode Island, Vermont (any chronic disease or treatment of such diseases with side effects of cachexia, severe pain, severe nausea, seizures, & muscle spasms), and Washington.[vi]

Section F: Scientific Evidence of Support for Medical Cannabis Treatment

Endocannabinoids and Liver Disease

In a scientific review of studies up to the year 2005 by the Department of Metabolism and Human Nutrition, Hadassah-Hebrew University Medical School, The Liver Unit, Hadassah-Hebrew University Medical Center in Jerusalem, Israel, Gabbay et. al. described the major findings relating to endocannabinoids and liver disease. It was found that alterations to the liver due to hemodynamic changes resulting from cirrhosis (scarring of the liver from chronic inflammation) are moderated by CB1 receptors located on splanchnic (abdominal organs) and hepatic vascular endothelium (membrane lining the interior surface of blood and lymphatic vessel; in this case, blood vessels within the liver). The scientists referenced a study completed in 2001 indicating that when compared with non-cirrhotic controls, in cirrhotic human livers there was a three-fold increase in CB1 receptors on isolated vascular endothelial cells indicating up-regulation of these receptors in chronic liver disease. Cannabis has been shown to modulate the inflammatory process and neurological function due to cirrhosis via endocannabinoid receptors. As previously described in the petition, inflammation of the liver is a precursor to liver disease - resulting in cirrhosis, if not addressed. Complications of cirrhosis include portal hypertension with a possibility of systemic vasodilation further complicating this condition, causing a decrease in effective blood volume, hypotension, fluid and salt retention, worsening ascites, and deterioration of renal function. Ascites (retention of fluid in the peritoneal cavity – causing abdominal swelling) is associated with increased plasma levels of the bacterial endotoxin lipopolysaccharide (LPS). LPS has been shown to increase with the progression of liver disease and can cause hypotension (low blood pressure) and tachycardia (increased heart rate). Hypotension in the liver can lead to complications in blood flow and disease. Gabbay et. al. referenced a study on LPS-treated donor rats where hypotension was shown to be prevented by pretreatment of the recipient rat with the CB1 receptor antagonists SR141716A (Cannabidiol (CBD) acts as an indirect antagonist of cannabinoid agonists (THC) – also, inhibiting hypotension). Δ9-tetrahydrocannabinol (THC) is an agonist at both the CB1 and CB2 receptors. THC, and it's synthetic, was shown to not have a vasodilator effect in rat models – vasodilation can lead to hypotension and ascites. As this specific review is from 2005, the authors stated that some epidemiological data supports the notion of a hepatotoxic effect for marijuana; however, methodological problems preclude conclusion in this context. Further, more current studies will be reviewed and will explain that cannabis does not lead to hepatoxicity in patients with liver disease and co-infections. Conclusions from Gabbay et. al., suggest there is convincing evidence for the role in the hemodynamic compromise, as seen in cirrhosis, that "certain cannabinoids may improve hepatic inflammation and pruritus secondary to liver disease" – due to the possible synergistic or "entourage" effect of cannabinoids.[vii]

Marijuana Use is not Associated with Progression to Advanced Liver Fibrosis in HIV/HCV Coinfected Women

The endocannabinoid system is an important impactful player on a variety of liver related conditions; fibrosis, steatosis, regeneration, and portal hypertension. Endocannabinoid ligands are pervasive and interact with cannabinoid receptors 1 and 2 (CB1 and CB2), which have high affinity for tetrahydrocannabinoid (THC). Under normal physiologic conditions, hepatic

expression of CB1 and CB2 is absent or weak. However, both receptors are upregulated in a variety of liver diseases, including alcoholic and non-alcoholic liver disease, liver fibrosis, chronic hepatitis C, primary biliary cirrhosis and hepatocellular carcinoma.

Use of THC in HIV/HCV coinfected patients is common. Given that cannabis is becoming more widely available and more regularly consumed, it is critical to assess its clinical effects including any negative impact of THC use on liver fibrosis progression.

Chronic liver disease modulates hepatic cannabinoid receptor expression. CB1 is upregulated in chronic liver disease, and CB2 is also upregulated in chronic liver disease and prevents fibrosis progression. It is this balance between CB1 vs CB2 activation which may modulate fibrosis progression in patients with liver disease. If over-expression of both receptors is balanced, there is no change in liver fibrosis.

This 2016 longitudinal study of HIV/HCV co-infected women shows THC was not associated with progression to significant liver fibrosis on univariable or multivariable analyses in light or heavy users. Mean THC use per week during the observation period was not independently associated with a greater risk of progression to significant fibrosis in multivariable analysis when evaluated as a continuous variable. Similarly, no association between fibrosis progression and THC use was detected when mean THC use per week was treated as a categorical variable. There was no association between THC use and fibrosis progression among those women with fibrosis at entry. Of the 489 participants, with at least two years of follow up, 15% reported weekly or greater THC use and 6% daily use for two years or more. Among these women, neither duration nor frequency of THC use was found to be predictive of significant fibrosis for weekly THC use compared to no use. Similarly, no association was detected between the number of intervals with weekly THC use and significant fibrosis when compared to abstainers with a similar length of follow-up. Similar results were seen in the subgroup of women with baseline fibrosis at entry of study.[viii]

A Novel Synthetic Cannabinoid Derivative Inhibits Inflammatory Liver Damage via Negative Cytokine Regulation

This Israeli study, published by The American Society for Pharmacology and Experimental Therapeutics in 2003, studied the mechanism of action of a synthetic cannabinoid (PRS-211,092) on female mice with injections of concanavalin A (con. A) - inducing an immune-mediated liver injury (mimicking liver disease), by expressing pro-inflammatory cytokines. Control mice were injected with saline. Con. A was used as a model for hepatitis mediated by cellular immunity. The authors state that "all procedures used in this study were done according to internal guidelines for usage of animals in medical research and Israeli law". [12] Blood was drawn from the mice prior and post injection of con A. After drug administration, the liver and spleen of the mice were removed, and a quantitative real-time polymerase chain reaction was conducted to increase gene expression of the liver and spleen samples of con. A-injected mice and samples from saline-injected control animals. Liver tissue was observed under a microscope and evaluated for the degree of vascular congestion, dilatation, and telangiectasia (a.k.a. spider veins) in the portal tract, the degree of vascular congestion and dilatation in the centrilobular area, and the degree of inflammatory cell infiltration, liver cell degeneration, and

necrosis in the midzone liver parenchyma. Statistical analysis and average scores 0 (normal) – 4 (highest severity) were performed (histopathology scoring). It was indicated that treatment with PRS-211,092 diminished con. A-induced liver damage demonstrated by decreased plasma levels of alanine aminotransferase (enzyme found in liver; ALT). When compared to animals only treated with con. A, efficacy of PRS-211,092 pretreatment and posttreatment of con. A were both effective in reducing ALT levels. High ALT levels are indicative of liver health issues. It was also shown that PRS-211,092 reduced disruption of liver tissue confirmed by the histopathology scoring for the "degree of vascular congestion and dilatation as well as inflammatory cell infiltration and liver cell degeneration."[12] During severe inflammation, acute phase proteins are secreted by hepatocytes. High levels of cytokines are toxic to the liver. Treatment with PRS-211,092 inhibited the expression of acute phase proteins by half. It was also determined that PRS-211,092 affects cytokine levels in spleen and plasma by increasing interleukin-6 (IL-6) and interleukin-10 (IL-10) gene expressions (anti-inflammatory proteins). The anti-inflammatory actions of IL-6 and IL-10 involves stimulation of suppressors of cytokine signaling (SOCS), SOCS-1 and -3 (proteins). Treatment with PRS-211,092 increased SOCS-1 and -3 expression significantly in the spleen and liver, indicating PRS-211,092 inhibits inflammatory damage via negative cytokine regulation (increased suppressors of cytokine signaling). It is suggested by the researchers that the negative feedback control of cytokine signaling by the SOCS may be a generic feature of cannabinoids. The researchers conclude that PRS-211,092 is "highly effective in diminishing Con. A-induced liver damage" and may provide a basis for developing immunomodulatory treatment for hepatitis and other short- or long-term inflammatory disease, utilizing cannabis.[ix]

Cannabidiol Improves Brain and Liver Function in a Fulminant Hepatic Failure-induced Model of Hepatic Encephalopathy in Mice

A study from Hadassah-Hebrew University Medical School, Jerusalem, Israel of 2010 investigated the effects of cannabidiol (CBD) and its anti-inflammatory properties on 20 mice models with induced hepatic encephalopathy associated with fulminant hepatic failure and 20 control animals-injected with saline. Hepatic encephalopathy is a neuropsychiatric disorder caused by acute or chronic liver failure, usually observed in patients with end-stage liver disease. The CBD utilized was extracted from cannabis resin and mixed with ethanol, emulphor, and saline with a ratio of 1:1:18. It was determined that CBD, derived from *Cannabis sativa* activates the 5-hydroxytryptamine receptor (5-HT). CBD did not activate 5-HT in control animals but was shown to be an agonist of the 5-HT receptor ameliorating brain damage in a chronic model of hepatic encephalopathy induced by bile duct ligation (resulted obstructive jaundice model – symptom of an underlying disease such as liver disease). Female mice were injected with either saline or thioacetamide (induces liver failure with hepatic encephalopathy) and were then treated with either saline or CBD. After the induction of hepatic failure, the brains and livers were removed for histopathological analysis and blood was taken for analysis of plasma liver enzymes. Cognitive function of a separate group of mice were tested. Neurological and motor functions in thioacetamide-treated mice were evaluated, and it was concluded that cognitive functions were restored by CBD while motor activity was partially restored by CBD. Increased plasma levels of ammonia, bilirubin, liver enzymes, and 5-HT levels were normalized following CBD treatment. The researchers concluded that CBD restores liver function and improves brain pathology. It is inferred that the effects of CBD may be due to a combination of its actions in the

liver and brain because of CBDs ability to cross the blood-brain barrier – indicating CBD acting both centrally and peripherally. The researchers note that in previous studies both CB1 receptor antagonist (CBD) and a CB2 receptor agonist (THC) have been shown to diminish brain and liver damage that occurs with liver disease. Their results indicated that CBD has a neuroprotective role in hepatic encephalopathy induce by fulminant hepatic failure. The researchers concluded that "CBD improves the symptoms of fulminant hepatic failure by affecting both brain histopathology and liver function, and thus may serve as therapeutic agent for treating human hepatic encephalopathy."[x]

Cannabis Use and Reduced Risk of Insulin-resistance in HIV-HCV Infected Patients: A Longitudinal Analysis

A French study from 2015 examined whether cannabis use was consistently associated with reduced insulin-resistance (IR) risk in 703 HIV-Hepatitis C Virus infected patients, utilizing annual self-administered questionnaires every 12 months over 60 months of follow-up data for patients with at least one medical visit where IR and cannabis use were assessed. A mixed logistic regression model evaluated the association between IR risk and cannabis use (occasional, regular, daily). IR and an increased risk of diabetes is frequent in HIV-HCV co-infected patients and associated with the progression of liver disease. The researchers state that "although cannabis use can increase appetite, it has been associated with a reduced risk of obesity and therefore IR in the general population" due to the widespread use of cannabis within the population.[14] Data collected from the study included: HIV RNA plasma viral load (detectable or not), CD4 count, and degree of liver fibrosis combined with data on HCV treatment initiation. The researchers also gathered HCV genotype, fibrosis stage, HCV plasma viral load, body mass index, history of HCV and HIV treatment, fasting glycemia (blood glucose level assessment), insulinemia (associated with type-2 diabetes), lipid panel, and comorbidities (diabetes, hypertension, cardiovascular problems, and renal dysfunction). Three sensitivity analyses showed that cannabis use (whether occasional, regular or daily) was dramatically associated with lower risk of IR. The scientists also noted that their research is in line with previous studies on humans and animal models. It's stated that "when administered to obese rats, cannabis was associated with weight reduction and an increase in the weight of the pancreas, implying beta-cell protection."[14] It was determined by the researchers that cannabis use is associated with a lower IR risk in HIV/HCV-coinfected patients.[xi]

HU-444, A Novel, Potent Anti-Inflammatory, Non-Psychotropic Cannabinoid

Inflammation is a significant concern in the progression of liver disease, as well as with the symptoms experienced as a result of liver disease or treatment of liver disease. In a 2015 published study from Israel, it is reported that a cannabidiol (CBD) derivative, HU-444, expressed potent activity in both *in vitro* (experiments outside of living organisms; done with macrophages) and *in vivo* (research within a living organism; in this case: mice models for both autoimmune hepatitis and rheumatoid arthritis) anti-inflammatory assays. The synthetic pathway from CBD to HU-444 is short, but the yield is relatively low. Anti-inflammatory activity was expressed in both *in vitro* and *in vivo* models of experimentation, with *in vivo* leading to the suppression of production of tumor necrosis factor-alpha (TNF-α) (a pro-inflammatory cytokine)

and amelioration of liver damage as well as lowering of mouse collagen-induced arthritis. Con. A was used to induce liver damage in mice, promoting the increase of the liver enzymes interleukin-2 and inflammatory cytokines. Con. A-induced hepatitis is considered to mimic autoimmune hepatitis in humans. Con. A treated mice experienced a reduction in alanine aminotransferase (ALT), aspartate aminotransferase (AST), and TNF-α levels were greatly reduced following the injection of HU-444. In studying the effects of HU-444 on con. A-induced liver damage, histopathological evaluations of the livers were performed. Con. A treatment marked liver damage with necrosis and mononuclear cell infiltration (white blood cells, macrophages and lymphocytes, collection at the site of injury to help clear away the debris - a sign of graft/liver transplant rejection). After the administration of the CBD derivative, HU-444, it was observed that HU-444 significantly diminished liver damage and reduced mononuclear infiltration, leading to an optimally preserved normal liver histology. HU-444 researchers also provided clinical benefits in terms of protecting joints and the prevention of damage caused by disease. The noted amelioration of hepatitis by HU-444, suggests a promising curative therapeutic role for CBD in human autoimmune hepatitis – according to the researchers.[xii]

The Endocannabinoid System as a Key Mediator During Liver Diseases: New Insights and Therapeutic Openings

Chronic liver disease remains a major health concern due to cirrhosis and its complications. The endocannabinoids and their receptors have been identified as key regulators of several pathophysiological aspects associated with chronic liver disease progression. Progression of fibrosis combines enhanced production of extracellular matrix by hepatic myofibroblasts and impaired matrix turnover. Effective antifibrotic treatments are not available to humans, yet. Studies have revealed a major impact of the endocannabinoid system in the regulation of liver fibrogenesis. It was found that the activation of CB1 receptors enhances fibrogenesis, whereas, stimulation of CB2 receptors counteracts progression of fibrosis. CB2-deficiant mice showed enhanced survival of liver fibrogenic cells – resulting in increased fibrosis. Subsequently, rats with established cirrhosis showed the administration of the CB2-selective agonist JWH-133 improves liver fibrosis, decreases the inflammatory infiltrate and reduces the density of hepatic myofibroblasts following increased apoptosis. Administration of rimonabant to wild-type mice or genetic inactivation of CB1 receptors were both associated with a significant reduction in fibrosis progression. Reduced hepatic expression of the profibrogenic cytokine TGF-B1, and a decrease in the number of fibrogenic cells were observed, as well. Results from CB2-deficient mice and mice treated with JWH-133 also demonstrated that CB2 receptors accelerate the regenerative response that follows acute liver injury. The latter study indicates that paracrine mechanisms originating from hepatic myofibroblasts account for beneficial effects of CB2 receptors on hepatocyte survival and regeneration following acute liver damage.[xiii]

Cannabis Use Improves Retention and Virological Outcomes in Patients Treated for Hepatitis C

This study aims to exam data pertaining to cannabis use on treatment outcomes; as many patients turn to cannabis for hepatitis C (HCV) treatment-related side-effects. A prospective observational study of standard interferon and ribavirin treatment in 71 recovering substance

users was conducted to define the impact of cannabis use during HCV treatment. Thirty-one percent (31%) of observed patients were cannabis users and 69% did not use cannabis. Results indicated that cannabis users were more likely to remain on HCV treatment for at least 80% of the projected treatment duration compared to 67% of non-cannabis users treatment retention. The study's results suggest that cannabis may offer symptomatic and virological benefit to patients undergoing HCV treatment by assisting patients in maintaining adherence to HCV treatment.[xiv]

Conclusion:

It is important for the well-being of patients with compromised immune systems to have access to safe, regulated, and tested medicinal cannabis. Cannabis makes people feel better. And if they feel better and more hopeful about their lives, they're more likely to continue treatment.

Approving hepatitis C for medicinal cannabis is an available solution for reducing harm. Based on the evidence presented on the ability of cannabis to heal or reverse liver damage, cannabis' ability to provide relief of symptoms of HCV and treatments of HCV, and cannabis' ability to increase patient adherence to HCV treatment – it is recommended that HCV be approved as a qualifying condition in Minnesota's Medical Cannabis Program.

Section G: Letters in Support of Adding the Medical Condition

***see attached.**

"Dear Health Commissioner,

In January of 2015, I was diagnosed with HIV with co-infections. One of the co-infections was hepatitis C. For the first year, I struggled not only with physical symptoms, such as nausea/ vomiting/ pain/ and fatigue, but with my mental health – as I attempted to process everything that I was going through. Because I was HIV positive, I qualified for Minnesota's medicinal cannabis program. I found cannabis to be the only tool in my available kit that provided me relief from my physical symptoms. I also became a much happier person, and was able to process the stigma associated with infectious diseases. During treatment of a 12-week regimen of Harvoni, I used cannabis daily to ease the side effects of the drug (fatigue, nausea, loss of appetite, headaches).

Cannabis allowed me the ability to return to school during the course of my treatment and maintain an honors status with my GPA. I don't think I could have completed my treatment without medicinal cannabis, or to have been able to go to school full-time. I use medicinal cannabis daily, and I graduated from Century College with Distinction in Horticulture Science A.S.

Currently, I am hepatitis C free and continue to medicate with cannabis. I am a research assistant and student at the University of Minnesota, Twin Cities, College of Food, Agriculture, and Natural Resource Sciences. I truly believe I'm able to live an improved quality of life because of medicinal cannabis. I urge you to approve hepatitis C as a qualifying condition for medicinal cannabis in Minnesota. Many states already have hepatitis C as a qualifying condition

for medicinal cannabis. Minnesotans living with hepatitis C should have the same opportunity to improve their quality of life."

Best Regards,

[redacted]

Citations and research:

[i]ICD-10-CM code for insurance billing purposes.

[ii]Mayo Clinic description of the liver.

[iii]Mayo Clinic description of symptoms and progression of hepatitis C.

[iv]Mayo Clinic treatment and diagnosis of HCV.

[v]Harvoni side effects.

[vi]States that allow patients with HCV access to medicinal cannabis treatment.

[vii]Endocannabinoids and the Liver.

[viii]Marijuana Use is not Associated with Progression to Advanced Liver Fibrosis in HIV/ HCV Coinfected Women.

[ix]A Novel Synthetic Cannabinoid Derivative Inhibits Inflammatory Liver Damage via Negative Cytokine Regulation.

[x]Cannabidiol Improves Brain and Liver Function in a Fulminant Hepatic Failure-induced Model of Hepatic Encephalopathy in Mice.

[xi]Cannabis Use and Reduced Risk of Insulin-resistance in HIV-HCV Infected Patients: A Longitudinal Analysis.

[xii]HU-44, A Novel, Potent Anti-Inflammatory, Non-Psychotropic Cannabinoid

[xiii]The Endocannabinoid System as a Key Mediator During Liver Diseases: New Insights and Therapeutic Openings.

[xiv]Cannabis improves symptomology and retention outcomes in patients undergoing HCV treatment.

[i] ICD-10-CM Codes. (n.d.). Retrieved from https://www.icd10data.com/ICD10CM/Codes/A00-B99/B15-B19/B18-/B18.2

[ii] Mayo Foundation for Medical Education and Research (MFMER), 1998-2017. Mayo staff at Mayo Clinic: "Diseases and conditions: liver disease." Web. http://www.mayoclinic.org/diseases-conditions/liver-disease/basics/definition/CON-20025300?p=1.

[iii] Hepatitis C. (2018, March 06). Retrieved from https://www.mayoclinic.org/diseases-conditions/hepatitis-c/symptoms-causes/syc-20354278

[iv] Hepatitis C. (2018, March 06). Retrieved from https://www.mayoclinic.org/diseases-conditions/hepatitis-c/diagnosis-treatment/drc-20354284

[v] Harvoni Side Effects. (n.d.). Retrieved from https://www.generichepatitiscdrugs.com/harvoni-side-effects/

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Sensible Minnesota

P.O. Box 18741
Minneapolis, Minnesota 55418

Sensible policies, safer communities.

July 25, 2018

Commissioner Jan Malcolm
Minnesota Department of Health
Office of Medical Cannabis
PO Box 64882
St. Paul, MN 55164-0882

Re: Petition to add Hepatitis C as a Qualifying Condition for Medical Cannabis

Dear Commissioner Malcolm:

I submit this letter on behalf of Sensible Minnesota in support of our petition for Hepatitis C as a qualifying condition for medical cannabis in Minnesota. Hepatitis C is a commonly covered condition in medical cannabis programs throughout the country due to cannabis's efficacy in treating the illness and its symptoms.

Patients in Minnesota deserve this option in their treatment, and although this disease is curable, treatment can still be a struggle. Cannabis offers relief from the side effects of treatment, chronic infection symptomology, and has been shown to assist patients in adhering with their treatment plan.

Minnesotans living with Hepatitis C deserve the benefit of safe and legal access to medical cannabis. We urge you to approve its inclusion in Minnesota's Medical Cannabis Program.

Sincerely,

[redacted]

July 29, 2018

Commissioner Jan Malcolm
Minnesota Department of Health
Office of Medical Cannabis
PO Box 64882
St. Paul, MN 55164-0882

Re: Petitions to add Opioid Use Disorder and HCV as Qualifying Conditions for Medical Cannabis

To Whom It May Concern,

My name is [redacted], in 2014 I lost my 29-year-old son to the opioid epidemic. We watched in horror as my beautiful, handsome, son slowly killed himself for 14 1/2 years. He became a heroin addict because of my meds that was prescribed by a doctor, I had taken a traumatic fall off my front step in 2001.

I was diagnosed at Mayo Clinic in 2001, with Pudendal Neuralgia, a rare nerve disorder that involves the pudendal nerve, the main motor and sensory of the pelvis. It innervates the vagina, the rectum, hip, and low back and inner thighs. I was given the option of three CT guided injections at Mayo, and secondary, surgery in Nantes, France, yes, the country France. I chose both, the injections first, to confirm the diagnoses, then I went to France per Mayo Clinic's advice to have the decompression and transposition surgery. This type of pain is comparable to stage 4 cancer. I needed something for this kind of pain, without it I for sure would have killed myself.

While I was dealing with my son's demise, watching him slowly kill himself for 14 1/2 years, I also watched myself gain 140 lbs., I became bed ridden after my surgery in France, they went in two inches, made two five-inch incisions in each buttock, cut through the sacrospinous and sacrospinous ligament in order to release the entrapped nerve, that was done bilaterally. The right side was damaged quite severe Professor Robert told me, he didn't' hold out for much hope.

I was on so many opioids, methadone 80 plus methadone 3 times a day plus muscle relaxers, anti-depressants, trazadone to help me sleep, 600 mg of gabapentin 3 times a day, I was in bed for five years from that surgery, I was lost to my family and [redacted] was lost to us all and himself.

My son suffered greatly with Opioid Use Disorder, at the end of his life, he was having multiply seizures a week, he had been in and out of so many treatment places, I literally lost count, we tried tough love, we tried no love, we tried wiping the slate clean, to being used multiply times over and all the while terrified that I would get the call that I had always dreaded. I got that phone call numerous times, [redacted] overdosed multiply times over the course of those years. Nothing seemed to help.

He was in severe pain, his muscles ached, he looked jaundice a lot of the time, and that's when we found out he had contracted Hepatitis C from his IV drug use. Because of the severe prolonged exposure, which was left untreated for a number of years, he could not hold down a job, he couldn't function. He couldn't remember anything, He would cry in pain some days, he would become very bloated, confused, he would shake violently some days, especially towards the end of his life.

In 2016 when Minnesota opened their medical cannabis program up to those of us who suffer with intractable pain, I enrolled immediately. Since using medical cannabis, I have been able to get off so many medications, deadly, highly addictive medications. I went from 80 mg of methadone a day to only needing 20 mg of methadone total for the day. I was able to cut the majority of my other breakthrough meds, my clonazepam, and also my hydromorphone. That is huge, I never thought I'd be able to do that.

You can't imagine how awful it is to live everyday knowing that it was your fault, it was your ignorance of the dangers of these drugs, not knowing the severity of harm that these drugs can do to someone if fallen into the wrong hands. I live my life every day, trying to end my 16 plus year usage of opioids. I need pain control, and medical cannabis has helped me get off of my meds and also has helped what little meds I do take work better.

I wish there would have been a medical cannabis program when my son was alive. I know he would have benefited greatly from it. Some people can't get off of everything. Some people need some help, and cannabis is that help for so many. I have countless stories of people using harm reduction as a power tool to step away from opioids. It's awful what these drugs to your brain, how I perceive pain, is different than someone who hasn't been on these drugs for as many years as I have.

My son refused to get treatment for his Hepatitis C because at the time of his diagnosis, the treatment caused a lot of discomfort. He was also going through withdrawal so many times I lost count. To watch your child in that state, is torture. It was torture for him and it was torture for those who loved him.

PLEASE, I'm begging you, please add Opioid Use Disorder and hepatitis C to the Minnesota's Medical Cannabis Program. We have yet to see the peak of this epidemic and there is not time to wait. Cannabis has been shown to greatly reduce the symptoms associated with Hep C and Opioid Use Disorder. If I can cut down to 20 mg of methadone a day from 240 mg a day after 16 years of use, someone who's struggling to stay sober the conventional way, could greatly benefit from cannabis.

Harm Reduction works.

Thank you for reading my plea, and I hope you add Opioid Use Disorder and Hepatitis C to the program

Sincerely,

[redacted]

RAAN
RURAL AIDS ACTION NETWORK

July 26, 2018

Commissioner Jan Malcolm
Minnesota Department of Health
Office of Medical Cannabis
PO Box 64882
St. Paul, MN 55164-0882

Re: Support for additional disorders as qualifying conditions for Medical Cannabis

Dear Ms. Malcolm:

I am writing to you in support of Sensible Minnesota's request to add qualifying conditions to the Medical Cannabis Program, specifically for those living with Hepatitis C and those dealing with Opioid Use Disorder (OUD).

The Rural AIDS Action Network (RAAN) has been working with folks diagnosed with Hepatitis C for several years. While treatments have advanced and are less toxic to the individual, we still hear that folks are dealing with side effects, particularly related to decreased appetite and some pain related to their condition. While folks can successfully clear the Hepatitis C virus and go on to lead long productive lives, we know that treatment challenges can be a barrier to initiating medication and feel allowing those patients to access Medical Cannabis can reduce that barrier AND limit seeking other pain relief methods, including opioids.

For the past four years, RAAN has been actively involved in the Opioid Use Disorder (OUD) epidemic. Our work began training community members and distributing Narcan through our five offices in greater Minnesota. Last year that work expanded as part of DHS STR response and funding providing by SAMSHA. Our work now includes working more closely with communities to ensure much needed Narcan is available statewide. As experts in Harm Reduction, we know that minimizing risks is paramount and that is the basis for our request. Many of our clients began using opioids as a result of an accident or some other physical trauma. Some may become dependent while others truly have an ongoing need. Recovery from OUD can be difficult and painful at times so we promote Medical Cannabis, when available, to reduce opioid dependence and/or ongoing use while also minimizing side effects of detox. For many, the physical and emotional feelings experienced through detox are often enough of a deterrent that folks continue to use opioids, especially when other options are not available or supported.

Please consider this request as it will aid in providing those living with HCV and dealing with OUD other options for managing their conditions.

Sincerely,

[redacted]

300 East St. Germain Street, Suite 220 ☨ Saint Cloud, MN 56304
Phone: 320.257.3036 ☨ Toll Free: 800.966.9735 ☨ Fax: 320.257.3036 ☨ Website: www.raan.org

sSdp

Students for Sensible Drug Policy of MN

(651) 760-7727
1536 Hewitt Ave, MS-1808
St. Paul, MN 55104
ssdp.org

July 28, 2018

Commissioner Jan Malcom
Minnesota Department of Health
Office of Medical Cannabis
PO Box 64882
St. Paul, MN 55164-0882

Re: Support for new qualifying conditions

To whom it concerns:

We are writing to you today in support of adding Opioid Use Disorder and Hepatitis C as qualifying conditions for medical cannabis in the State of Minnesota.

As a group of students from two of Minnesota's top universities who have personal, academic, and professional interests in studying and implementing science and evidence-based drug and harm reduction policies, we have reviewed and contributed towards these petitions extensively to ensure there is ample scientific evidence to support program expansion.

Our collective studies of drug policy have begun during the height of the opiate crisis, prompting our interest in and focus on principles of harm reduction. Opiate overdose is a leading cause of death among young people, and it is our classmates, friends, families, and neighbors who are paying the human price of this crisis. Though we recognize that access to medical cannabis is not in and of itself a solution to the opiate epidemic, by studying other states, we can see that cannabis is one of many tools for reducing the harms of opiate addiction that are not yet available in our state.

We are also alarmed by increased rates of new HCV infections in our state and across the country, especially among young adults who inject drugs. While preventative education and ongoing efforts to increase access to sterile injection materials in our state will help reverse the trend, we are most concerned with the health and wellbeing of those who have already been impacted but cannot access pre-existing treatments due to chemical dependency and / or economic constraints.

The approval of medical cannabis as a treatment for these conditions would have a positive impact on our state by allowing our medical professionals and recovery community to have all available tools to combat this issue, thereby improving and saving lives.

Sensibly,

Students for Sensible Drug Policy
Hamline University chapter
ssdp@hamline.edu

Students for Sensible Drug Policy
University of Minnesota – Twin Cities chapter
umnssdp@umn.edu