

Section A: Petitioner's Information



Section B: Medical Condition You Are Requesting Be Added

ICD-10:R11.0 Nausea

ICD-10:R11.2 Nausea with vomiting, unspecified

ICD-10:R11 Nausea and vomiting

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

Nausea is a condition characterized primarily by a strong queasy sensation and the urge to vomit. It involves an unpleasant feeling in one's stomach, and the sense that one is about to vomit. Nausea itself is not a disease but a symptom of many different conditions and medical treatments, such as chemotherapy. Patients suffering from nausea are often unable to consume food, and frequent vomiting can lead to dehydration.

Section D: Availability of Conventional Medical Therapies

Nausea is often treated with antiemetics, such as over-the-counter antihistamines and anticholinergics. These can cause side effects such as blurred vision, dizziness, and insomnia. Dopamine antagonists and serotonin antagonists are also often recommended for the treatment of nausea; these may have side effects such as sedation, dizziness, and muscle cramps.

Dronabinol, a pill containing synthetic delta-9-THC, is approved for chemotherapy-related nausea and may be prescribed off-label for other types of nausea.¹ However, it can take up to an hour to take effect. Also, unlike inhaled cannabis, the dose cannot be precisely titrated, which can lead to increased side effects such as paranoia. It also does not include any other beneficial cannabinoids.

¹ See *Tagney v. Burwell*, 186 F.Supp.3d 45 (2016). Available at: <https://docs.justia.com/cases/federal/district-courts/massachusetts/madce/1:2014cv14149/165455/23>.

Section E: Anticipated Benefits from Medical Cannabis

Medical research clearly demonstrates that cannabis is associated with the prevention, regulation, and elimination of nausea and nausea symptoms. In its 1999 report “Marijuana and Medicine: Assessing the Science Base,” the Institute of Medicine concluded, “Nausea, appetite loss, pain and anxiety are all afflictions of wasting, and all can be mitigated by marijuana.” Marijuana and its active components (cannabinoids) can both stimulate appetite and reduce the nausea, vomiting, and weight loss experienced by patients in many circumstances, including the side effects of drug therapies given for cancer, HIV infection, and hepatitis C. Observational studies suggest this may improve treatment adherence among patients experiencing gastrointestinal toxicity from drug therapy.²

1) Nausea and the Endocannabinoid System

The endocannabinoid system is a series of receptors located in the brain and throughout the central and peripheral nervous systems. These receptors help regulate numerous bodily functions. In a 2014 paper published in the *European Journal of Pharmacology*, Drs. Keith Sharkey, Nissar Darmani, and Linda Parker discuss the relationship between the endocannabinoid system of the body and nausea.³ As the authors note in the paper’s introduction, cannabis is one of the oldest known remedies for nausea. The paper details a comprehensive review of the literature available on the subject. The study concludes that cannabinoids are effective in treating both acute and delayed emesis (vomiting). They specifically write “the endocannabinoid system has the potential to be used for the treatment of nausea and likely as an adjunct therapy for the treatment of emesis, particularly delayed emesis, where current therapies are limited in their degree of efficacy.”⁴

2) Regulation of Symptoms by THC and THCA

Cannabis contains numerous chemical compounds; two of the most well known are the psychoactive ingredients THC and THCA. A rat study concluded that both THC and THCA reduced conditioned gaping — a sign of nausea — in the rats, and found that while both were effective, THCA was determined to be “potently effective” at treating nausea and vomiting.⁵

² Institute of Medicine, *Marijuana and Medicine: Assessing the Science Base*, National Academies Press (1999). <https://www.nap.edu/download/6376>.

³ Sharkey, K.A., Darmani, N.A., and Parker, L.A., Regulation of Nausea and Vomiting by Cannabinoids and the Endocannabinoid System, *European Journal of Pharmacology* (2014). <https://www.ncbi.nlm.nih.gov/pubmed/24184696>.

⁴ *Id.*

⁵ Parker, L.A., Mechoulam, R., Schlievert, C. et al., Effects of Cannabinoids on Lithium-Induced Conditioned Rejection Reactions in a Rat Model of Nausea, *Psychopharmacology* (2003). <https://link.springer.com/article/10.1007%2Fs00213-002-1329-2?LI=true>.

3) Regulation of Symptoms by CBD

CBD is the primary non-psychoactive element in cannabis, and several studies have found it effective in the regulation of nausea. For example, a study on rats and shrews in 2011 concluded that “CBD effectively prevented conditioned retching and conditioned gaping.”⁶ And a 2004 study found CBD reduced retching induced by a chemotherapy drug in musk shrews.⁷ A 2015 study of vomiting and retching musk shrews found combined doses of CBD and THC greatly reduced the symptoms in the animals.⁸ A 2012 study of the effects of CBD on rats also found nausea suppression, concluding CBD activates receptors in the dorsal raphe nucleus, a part of the brainstem, which achieves these remarkable results.⁹

4) Reduced Nausea in Human Trials

Human studies have also been conducted that show similarly effective results. A 2001 study of 13 healthy volunteers all experienced reduced emesis and feelings of nausea from smoked marijuana.¹⁰ And a 2012 study strongly concluded antiemetic effects are among the many therapeutic uses of cannabis.¹¹ In another study in 2001, the authors specifically extolled the effectiveness of treating acute nausea with cannabis.¹²

A 2007 review of literature regarding cannabis and chemotherapy-induced nausea found cannabinoids help control long-term nausea in addition to temporary emesis.¹³ This review concludes that cross-sectional research shows cannabinoids are more effective in reducing

⁶ Parker, L.A., Rock, E.M., and Limebeer, C.L., Regulation of Nausea and Vomiting by Cannabinoids. *British Journal of Pharmacology* (2011). <http://doi.org/10.1111/j.1476-5381.2010.01176.x>.

⁷ Kwiatkowska, M., Parker, L.A., Burton, P. *et al.*, A Comparative Analysis of the Potential of Cannabinoids and Ondansetron to Suppress Cisplatin-Induced Emesis in the *Suncus murinus* (House Musk Shrew), *Psychopharmacology* (2004). <https://www.ncbi.nlm.nih.gov/pubmed/14740147>.

⁸ Rock, E., and Parker, L., Behavioral Neuroscience: Synergy Between Cannabidiol, Cannabidiolic Acid, and [Delta] -Tetrahydrocannabinol in the Regulation of Emesis in the *Suncus murinus* (House Musk Shrew), *Behavioral Neuroscience* (2015). <http://doi.apa.org/doiLanding?doi=10.1037%2Fbne0000057>.

⁹ Rock, E., Bolognini, D., Limebeer, C., Cascio, M., Anavi-Goffer, S., Fletcher, P., Mechoulam, R., Pertwee, R., and Parker, L. (2012), Cannabidiol, a Non-Psychotropic Component of Cannabis, Attenuates Vomiting and Nausea-like Behaviour via Indirect Agonism of 5-HT Somatodendritic Autoreceptors in the Dorsal Raphe Nucleus, *British Journal of Pharmacology* (2012). <https://www.ncbi.nlm.nih.gov/pubmed/21827451>.

¹⁰ Söderpalm, A. H. V., and Söderpalm, A., Pharmacology, biochemistry and behavior: Antiemetic efficacy of smoked marijuana subjective and behavioral effects on nausea induced by syrup of ipecac Elsevier, *Pharmacology, Biochemistry, and Behavior* (2001). <https://www.ncbi.nlm.nih.gov/pubmed/11509190>.

¹¹ Grotenhermen, F., and Müller-Vahl, K., The Therapeutic Potential of Cannabis and Cannabinoids, *Deutsches Ärzteblatt International* (2012). <https://www.aerzteblatt.de/int/archive/article?id=127603>.

¹² Kumar, R.N., Chambers, W.A. and Pertwee, R.G., Pharmacological Actions and Therapeutic Uses of Cannabis and Cannabinoids, *Anaesthesia* (2001). <http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2044.2001.02269.x/full>.

¹³ Slatkin, N.E., Cannabinoids in the Treatment of Chemotherapy-Induced Nausea and Vomiting: Beyond Prevention of Acute Emesis, *The Journal of Supportive Oncology* (2007). <https://www.ncbi.nlm.nih.gov/pubmed/17566383>.

chemotherapy-induced nausea than dopamine agents, though a combination of the two therapies is the best recommended course of treatment.¹⁴

A 1988 clinical trial sponsored by the state of New York found, "Fifty-six patients who had no improvement with standard antiemetic agents were treated and 78% demonstrated a positive response to marijuana ... inhalation marijuana is an effective therapy for the treatment of nausea and vomiting due to cancer chemotherapy."¹⁵

The researchers who conducted this double blind, placebo-controlled clinical trial concluded that compared to the placebo, the whole plant cannabis (marijuana) medicine "added to standard antiemetic therapy was well tolerated and provided better protection against delayed CINV [chemotherapy-induced nausea and vomiting]."¹⁶

Section F: Scientific Evidence in Support of Medical Cannabis Treatment

Below is a table of contents listing all of the scientific studies referenced in this petition and included in this packet.

- 1) Institute of Medicine, *Marijuana and Medicine: Assessing the Science Base*, National Academies Press (1999).
- 2) Sharkey, K.A., Darmani, N.A., & Parker, L.A., Regulation of Nausea and Vomiting by Cannabinoids and the Endocannabinoid System, *European Journal of Pharmacology* (2014).
- 3) Parker, L.A., Mechoulam, R., Schlievert, C. et al., Effects of Cannabinoids on Lithium-Induced Conditioned Rejection Reactions in a Rat Model of Nausea, *Psychopharmacology* (2003).
- 4) Parker, L.A., Rock, E.M., & Limebeer, C.L., Regulation of Nausea and Vomiting by Cannabinoids, *British Journal of Pharmacology* (2011).
- 5) Kwiatkowska, M., Parker, L.A., Burton, P. et al., A Comparative Analysis of the Potential of Cannabinoids and Ondansetron to Suppress Cisplatin-Induced Emesis in the *Suncus murinus* (house musk shrew), *Psychopharmacology* (2004).
- 6) Rock, E., and Parker, L., Behavioral Neuroscience: Synergy Between Cannabidiol, Cannabidiolic Acid, and [Delta] -Tetrahydrocannabinol in the Regulation of Emesis in the *Suncus murinus* (House Musk Shrew), *Behavioral Neuroscience* (2015).
- 7) Rock, E., Bolognini, D., Limebeer, C., Cascio, M., Anavi-Goffer, S., Fletcher, P., Mechoulam, R., Pertwee, R., and Parker, L. (2012), Cannabidiol, a Non-Psychotropic Component of Cannabis, Attenuates Vomiting and Nausea-like Behaviour via Indirect Agonism of 5-HT Somatodendritic Autoreceptors in the Dorsal Raphe Nucleus, *British Journal of Pharmacology* (2012).

¹⁴ *Id.*

¹⁵ Vincent Vinciguerra, et al., Inhalation Marijuana as an Antiemetic for Cancer Chemotherapy, *New York State Journal of Medicine* (1988). <https://web.acsalaska.net/~warmgun/es016.html>.

¹⁶ Marta Duran, et al., "Preliminary efficacy and safety of an oromucosal standardized cannabis extract in chemotherapy-induced nausea and vomiting," *Journal of Clinical Pharmacology* (2010). <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2997305/>.

- 8) Söderpalm, A.H.V., and Söderpalm, A., Pharmacology, biochemistry and behavior: Antiemetic efficacy of smoked marijuana subjective and behavioral effects on nausea induced by syrup of ipecac Elsevier, *Pharmacology, Biochemistry, and Behavior* (2001).
- 9) Grotenhermen, F., and Müller-Vahl, K., The Therapeutic Potential of Cannabis and Cannabinoids, *Deutsches Ärzteblatt International* (2012).
- 10) Slatkin, N.E., Cannabinoids in the Treatment of Chemotherapy-Induced Nausea and Vomiting: Beyond Prevention of Acute Emesis, *The Journal of Supportive Oncology* (2007).
- 11) Vincent Vinciguerra, et al., Inhalation Marijuana as an Antiemetic for Cancer Chemotherapy, *New York State Journal of Medicine* (1988).
- 12) Marta Duran, et al., "Preliminary efficacy and safety of an oromucosal standardized cannabis extract in chemotherapy-induced nausea and vomiting," *Journal of Clinical Pharmacology* (2010).

Section G: Letters in Support of Adding the Medical Condition

We have included two letters of support. They are from Dr. Jacob Mirman and Bethe Cross, a Minnesota resident and medical patient.

Section H: Acknowledgement and Signature

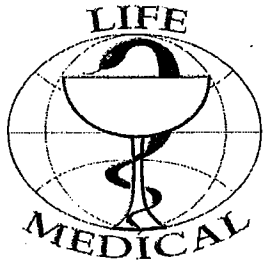
I certify that the information provided in this petition is true and accurate to the best of my knowledge.



7/31/17

Section F studies
(everything else in
packet)

- 1) Institute of Medicine, Marijuana and Medicine: Assessing the Science Base, *National Academies Press* (1999).
- 2) Sharkey, K. A., Darmani, N. A., & Parker, L. A., Regulation of Nausea and Vomiting by Cannabinoids and the Endocannabinoid System, *European Journal of Pharmacology* (2014).
- 3) Parker, L.A., Mechoulam, R., Schlievert, C. et al., Effects of Cannabinoids on Lithium-Induced Conditioned Rejection Reactions in a Rat Model of Nausea, *Psychopharmacology* (2003).
- 4) Parker, L. A., Rock, E. M., & Limebeer, C. L., Regulation of Nausea and Vomiting by Cannabinoids, *British Journal of Pharmacology* (2011).
- 5) Kwiatkowska, M., Parker, L.A., Burton, P. et al., A Comparative Analysis of the Potential of Cannabinoids and Ondansetron to Suppress Cisplatin-Induced Emesis in the *Suncus murinus* (house musk shrew), *Psychopharmacology* (2004).
- 6) Rock, E., and Parker, L., Behavioral Neuroscience: Synergy Between Cannabidiol, Cannabidiolic Acid, and [Delta] -Tetrahydrocannabinol in the Regulation of Emesis in the *Suncus murinus* (House Musk Shrew), *Behavioral Neuroscience* (2015).
- 7) Rock, E., Bolognini, D., Limebeer, C., Cascio, M., Anavi-Goffer, S., Fletcher, P., Mechoulam, R., Pertwee, R., and Parker, L. (2012), Cannabidiol, a Non-Psychotropic Component of Cannabis, Attenuates Vomiting and Nausea-like Behaviour via Indirect Agonism of 5-HT Somatodendritic Autoreceptors in the Dorsal Raphe Nucleus, *British Journal of Pharmacology* (2012).
- 8) Söderpalm, A. H. V., and Söderpalm, A., Pharmacology, biochemistry and behavior: Antiemetic efficacy of smoked marijuana subjective and behavioral effects on nausea induced by syrup of ipecac Elsevier, *Pharmacology, Biochemistry, and Behavior* (2001).
- 9) Grotenhermen, F., and Müller-Vahl, K., The Therapeutic Potential of Cannabis and Cannabinoids, *Deutsches Ärzteblatt International* (2012).
- 10) Slatkin, N. E., Cannabinoids in the Treatment of Chemotherapy-Induced Nausea and Vomiting: Beyond Prevention of Acute Emesis, *The Journal of Supportive Oncology* (2007).
- 11) Vincent Vinciguerra, et al., Inhalation Marijuana as an Antiemetic for Cancer Chemotherapy, *New York State Journal of Medicine* (1988).
- 12) Marta Duran, et al., "Preliminary efficacy and safety of an oromucosal standardized cannabis extract in chemotherapy-induced nausea and vomiting," *Journal of Clinical Pharmacology* (2010).



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Section G

07-20-2017

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

To the Minnesota Department of Health,

My name is Dr. Jacob Mirman, I graduated from the University of Minnesota Medical School and completed my residency in primary care internal medicine at Illinois Masonic Medical Center in Chicago. I specialize in integrative medicine and I am the Medical Director of Life Medical, an integrative medicine clinic in St. Louis Park.

I write to you today in support of the petitions to add nausea, autism, dementia, Alzheimer's disease, liver disease, and chronic pain to Minnesota medical cannabis program. As a physician treating patients for all these conditions, I believe my patients who suffer from these conditions would benefit from being added to the state's program.

I am a primary care internist. I am not a politician, a law enforcement officer or a cannabis policy expert. Yet, as an internist with 25 years of experience working with patients, I hope you will consider my views on whether to expand Minnesota's medical cannabis program.

I have been certifying patients for medical cannabis for over a year now, and have seen a tremendous benefit to patients when they return to me for follow-ups. Notably, in addition to the medical condition that qualifies them for the program, many patients who I have certified suffer from some other ailment — including several listed above — and have seen their conditions improved with medical cannabis use.

Patients come to me because they need help. I agree to see them and do my best to help them. The buck stops with me. If I send a patient to a specialist and he or she is unable to help, the patient comes back to me and their medical care is again my responsibility.. When standard approaches do not help the patient, my responsibility as their physician does not end.

For the last few months, around 20% of my practice has involved treating patients benefiting from medical cannabis. I certify on average two-three new patients per day. Notably, many patients are finding relief for not just the condition they have been certified for, but also secondary conditions. Further, my patients are happier, suffer from less anxiety (many have

Leon B. Frid, DC

Jacob I. Mirman, MD

ceased use of anti-anxiety medication), and are significantly reducing their pain. Quite a few have gotten off of narcotics and other pain killers altogether.

Practicing integrative medicine allows me to find the best treatment for my patients, and their success stories are what make my work so much fun. The beauty of integrative medicine is that it brings together different treatment methods to get the best effect for each individual patient. We use whatever modality we consider best for each patient's case. Our patients get the benefit of customized treatment plans that include conventional and complementary therapies. We combine all possible treatment options; whatever may help the patient in the most effective and safest way. And we are seeing great results using integrative approach.

Nausea is a common symptom of many conditions, or their treatments, including cancer and pain. Migraines are often accompanied by nausea, adding nausea to the program could significantly help my patients. Nausea is also often associated with PTSD, muscle spasms, and pain, all of which are currently covered by the program. Adding nausea to the program just makes sense.

Marinol — which is pure, synthetic THC — has been approved as a prescription drug since 1985 for nausea and vomiting associated with cancer chemotherapy in patients. Like other medications, Marinol can also be prescribed for off-label uses. However, Marinol is an inadequate substitute for many nauseated patients because, as a pill it is slow-acting. Also, unlike vaporized cannabis, a patient cannot precisely titrate their dosage and many end up overly intoxicated.

Autism, dementia, and Alzheimer's disease, are all marked by anxiety. Cannabis causes people to calm down. I have seen this many times with children in particular. For example, I had a young patient with seizures who, upon being placed on cannabis, changed her behavior drastically, she became better in school, improved in gymnastics, and had a higher quality of life. Offering cannabis to patients suffering from autism, dementia, and Alzheimer's disease, will result in a reduction in their anxiety and likely benefit these patients as to other symptoms they suffer from as well.

In addition, cannabis has been helpful at reducing self-injurious and aggressive behavior in autistic individuals who have not responded to other treatments. In Texas and Georgia, parents have talked to the media about their decision to break state law to help their autistic children, who were engaging in self-harm.

Liver disease often results in decreased appetite and nausea. Granting access for patients who suffer from this condition to medical cannabis, will likely help them battle these afflictions tremendously. Cannabis's alleviation of a decreased appetite is well-documented, and it is in the interest of my liver disease patients to have access to this important treatment option.

In my opinion, medical cannabis is the best pain medication of any pain medication available today either prescription or over the counter. It is much safer than opioids, and even safer than over-the-counter drugs like ibuprofen and Tylenol. Not only is cannabis incredibly effective, but there are few if any side effects and no risk of fatal overdose. Indeed in all my years of practicing

medicine, I have never seen a drug that has such a remarkable effect on patients with almost zero side effects.

Please add nausea, autism, dementia, Alzheimer's disease, liver disease, and chronic pain, to Minnesota medical cannabis program.

Sincerely,

A handwritten signature in black ink, consisting of several overlapping loops and a long horizontal stroke extending to the right.

Jacob I. Mirman, MD

Section 6

[REDACTED]

July 19, 2017

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

Re: Petition to add nausea to Minnesota's medical cannabis program

To the Minnesota Department of Health,

My name is [REDACTED] and I am a resident of Minnesota. Since I was a child, I have suffered from migraine headaches. I have tried many treatment options to alleviate the pain these migraines cause me and have found medical cannabis to be the most effective.

My migraines cause me to become incredibly nauseated and vomit. Once I begin to vomit, I cannot stop. The only other course of treatment I have found relief from is to visit the hospital to receive an injection, which dulls the pain and knocks me out. In order to recover from this injection, I am forced to spend hours or even days in bed. It is very common for me to again suffer anew from a migraine once the effects of the shot have worn off, and I am put into a cycle I cannot escape. The shots often will leave me with a rash as a side effect. I am often unable to go to work for days at a time or get sent home because I cannot function while in the midst of a migraine.

Medical marijuana stops my nausea — which then stops the vomiting. It is very effective, and does not cause me to break out into a rash. Use of medical cannabis drastically improves my quality of life, allowing me to spend less time in the hospital and more time with my family doing the things I love like traveling and gardening.

My physician would recommend medical cannabis for me if nausea were added to our state's program. And I urge the Department of Health to have compassion on me, and others, who are suffering from this terrible affliction.

Sincerely,

[REDACTED]