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, 2017.
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.
☐ 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, the Review Panel will provide the Commissioner of Health its written report of findings.
☐ The Commissioner will approve or deny the petition by December 1.

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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.*
See attached B. response.

A. Petitioner's Contact information.

B. 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.

I propose that obstructive sleep apnea (OSA) a sleep disorder be recognized as a qualifying condition to receive medical cannabis under subdivision 14 of the Minnesota Statutes section 152.22.

Sleep disorder can be classified into major groups that include insomnia (ICD-10-CM G47.XXs), sleep-related breathing disorders, parasomnias, sleep-related movement disorders, and circadian rhythm sleep–wake disorders (Sateia, 2014).

Fifty million to 70 million adults in the United States report having some type of sleep disorder (ASA, 2016). In 2010, insomnia generated 5.5 million office visits in the United States (Ford et al., 2014). Insomnia as a subset category of sleep disorder is defined by the Mayo Clinic as a persistent disorder that can make it hard to fall asleep, hard to stay asleep or both, despite the opportunity for adequate sleep. Insomnia per say failed to achieve MDH approval as a qualifying condition for medical cannabis in 2016. Subsequently, on review of the prior application, I would agree with the MDH that a research gap exists as pertains to sleep outcomes in individuals with primary chronic insomnia. Moreover, the current list of 10 medical conditions already approved that suffices for obtaining medical cannabis in Minnesota covers many diagnoses where sleep disorder is appropriately a secondary concern. However, my choice of **Obstructive Sleep Apnea** is different (ICD-9-CM 780.51 converts approximately to 2017 ICD-10-CM G47.30 Sleep apnea, unspecified.) ***OSA as a sleep-related breathing disorder, is actually supported with greater evidence-basis for the use of medical cannabis in its treatment than insomnia alone***, and newer research may have been overlooked or unavailable (not cited previously) in 2016 petition, that I would like to bring to the attention of the medical cannabis decision-makers at MDH in determining new adds to the medical condition list.

OSA represents a significant public health concern. Afferent vagal activation is implicated in increased apnea susceptibility by reducing upper airway muscle tone via activation of serotonin receptors in the nodose ganglia. Previous investigations demonstrated that systemically administered cannabinoids can be used therapeutically to decrease the apnea/hypopnea index in rats and in humans but the exact mechanism of the effect is unknown. Recently, scientists (Calik et al., 2014,2016) showed in rats that an intranodose ganglion injection of dronabinol (an FDA-approved pill containing THC) will attenuate 5-HT-induced reflex apnea and increase upper airway muscle tone by increasing phasic but not tonic, activation of the genioglossus. This data support the view that dronabinol stabilizes

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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 E response.

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)*

grogginess and mental lethargy. Fall risk and addiction to sleep aides can be serious side effects especially for the elderly.

E. Describe the anticipated benefits from the medical use of cannabis specific to the proposed qualifying medical condition.

Medical Cannabis would give OSA patients a less-addictive plant-based option that works to help them sleep and has been shown to be efficacious. In the attached articles, it is demonstrated that medical cannabis helps people fall asleep faster, stay asleep, and sleep meaningfully (REM stage). Thus when OSA patients are awake they can apply themselves appropriately to tasks of daily living and occupation, that become more manageable with their night time rest assured.

Are Cannabis or Cannabinoids an Effective Treatment for Improving Sleep Outcomes?

Systematic Reviews

The review by Whiting et al. (2015) was the most recent good-quality review. Two RCTs (54 participants) evaluated cannabinoids (nabilone, dronabinol) for the treatment of sleep problems. A trial deemed to have a high risk of bias conducted in **22 patients with obstructive sleep apnea** showed a greater benefit of dronabinol (maximum dose of 10 mg daily) than with a placebo on sleep apnea/hypopnea index (mean difference from baseline −19.64, p = 0.02) at 3 weeks follow-up. A crossover trial deemed to have a low risk of bias in 32 patients with fibromyalgia found improvements for nabilone 0.5 mg daily compared with 10 mg amitriptyline in insomnia (mean difference from baseline, −3.25, 95% CI = −5.26 to −1.24) and greater sleep restfulness (mean difference from baseline, 0.48, 95% CI = 0.01–0.95) at 2 weeks follow-up. Although the antidepressant amitriptyline is an established treatment for fibromyalgia, it is not FDA approved for insomnia, and its use is limited by adverse effects. Nineteen trials (3,231 participants) enrolled patients with other conditions (chronic pain or multiple sclerosis) and reported on sleep outcomes. Nabiximols (13 studies), THC/CBD capsules (2 studies), smoked THC (2 studies), and dronabinol or nabilone were compared to a placebo. Sleep outcomes were assessed at 2–15 weeks after randomization. Eleven of the 19 trials were judged to have a high risk of bias, 6 had an uncertain risk of bias, and the other 2 were judged to have a low risk of bias. The meta-analysis found greater improvements with cannabinoids in sleep quality among 8 trials (weighted mean difference [WMD], −0.58, 95% CI = −0.87 to −0.29) and sleep disturbance among 3 trials (WMD, −0.26, 95% CI = −0.52 to 0.00). These improvements in sleep quality and sleep disturbance were rated on a 10-point scale and would be considered small improvements. The summary estimate showing benefit was based primarily on studies of nabiximols.

Primary Literature

I was unable to find any good-quality primary literature that reported on medical cannabis as an effective treatment to improve sleep outcomes and that were published subsequent to the data collection period of the most recently published good- or fair-quality systematic review (Whiting et. al, 2015) addressing the research question above.

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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 C response.

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 D response.

respiratory pattern and augments upper airway muscles by acting at the nodose ganglia located in the ***peripheral nervous system, and not the central nervous system.*** Such findings underscore a therapeutic potential of dronabinol for the treatment of OSA. As THC increases the muscle tone in the upper airway during sleep, it thereby prevents the loss of muscle tone which is likely the cause of these apneas. Thus, there is evidence to suggest that the endocannabinoid system has a role in sleep. Also THC is associated in a dose-dependent manner with changes in slow-wave sleep, which is critical for learning and memory consolidation. Cannabis may also have effects on sleep latency, decreasing time to sleep onset at low doses and increasing time to sleep onset at higher doses (Garcia and Salloum, 2015). Thus, cannabinoids could have a role in treating sleep disorders.

C. Describe the extent to which the proposed qualifying medical condition or the treatment cause suffering and impair a person's daily life.

Obstructive sleep apnea is a medical condition where a person's breathing is interrupted during sleep due to a lack of oxygen to the brain. Apneas (moments of interrupted breathing) are incredibly disruptive- they can even cause hypertension, stroke or heart failure in those that suffer without treatment. It can affect anyone at any age, but is most common in overweight men after age 40. There are 2 types of sleep apnea: OSA and central sleep apnea. OSA is when the soft tissues in the back of the throat collapses while sleeping and central sleep apnea is when the brain fails to signal the lungs to breathe.

Daytime somnolence resulting from OSA makes affected people feel irritable secondary to sleep deficits that accumulate. When people have not rested adequately, they may develop cognitive impairments, or suffer from underemployment due to lack of focus or in attention to details important to their occupation or professional careers. The occupational hazards of sleep deprivation are well described. Over time this causes much stress to the individual and can lead to other health problems that lead to comorbidity evaluations in the nation's emergency rooms and sizeable numbers of hospital admissions. The most common treatment is CPAP which is cumbersome and not well adhered to by OSA patients and/or sleep medication which may be highly addictive and in the elderly sedative hypnotic medications are often associated with increased fall risk that may make limit the ADLs of the patient making the treatment worse than the ailment.

D. Describe conventional medical therapies available and the degree to which they ease the suffering caused by the proposed qualifying medical condition or its treatment.

Conventional therapies range from naturalistic approaches with herbal remedies such as melatonin and velarion root, to chiropractic care, to cognitive/behavioral approaches including possible discomfiture from various sleep posture modifications, to cumbersome and expensive machinery for CPAP worn at night, to FDA approved medications, acupuncture, and invasive surgical therapies such as implantable pacers or stimulators, and more permanent uvulectomy. As the tolerability of each of these therapy options is different and often individualized, some or all of these remedies may not work and have the potential to add the risks of comorbidities. Medication can be habit forming and often only prescribed for short periods of time, because of side effects of headaches, dizziness, morning after use

According to the National Academies of Sciences, Engineering, and Medicine report on research on medical cannabis recently published (2017) that summarizes the valuable human findings in 10,000 research papers for 1999 to Sept 2016 concluded that:

There is moderate evidence that cannabis or cannabinoids are effective for:

• Improving short-term sleep outcomes in individuals with sleep disturbance associated with obstructive **sleep apnea syndrome**, fibromyalgia, chronic pain, and multiple sclerosis (cannabinoids, primarily nabiximols)

F. 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.

Citations (bold citations are attached)

ASA (American Sleep Association). 2016. Sleep and sleep disorder statistics. https://www.sleepassociation.org/sleep/sleep-statistics (accessed October 25, 2016).

Bradford, A. C., and W. D. Bradford. 2016. Medical marijuana laws reduce prescription medication use in Medicare part D. Health Affairs 35(7):1230–1236.

Calik MW, Radulovacki M, Carley DW. 2014. Intranodose ganglion injections of dronabinol attenuate serotonin-induced apnea in Sprague-Dawley rat. Respiratory Physiology &Neurobiology 190(1):20-24.

Calik MW, D.W. Carley. 2016 Intracerebroventricular injections of dronabinol, a cannabinoid receptor agonist does not attenuate serotonin-induced apnea in Sprague-Dawley rats. Journal of Negative Results in Biomedicine 15(8):126-8.

Garcia, A. N., and I. M. Salloum. 2015. Polysomnograhic sleep disturbances in nicotine, caffeine, alcohol, cocaine, opioid, and cannabis use: A focused review. American Journal of Addiction 24(7):590–598.

Ford, E. S., A. G. Wheaton, T. J. Cunningham, W. H. Giles, D. P. Chapman, and J. B. Croft. 2014. Trends in outpatient visits for insomnia, sleep apnea, and prescriptions for sleep medications among US adults: Findings from the National Ambulatory Medical Care survey 1999–2010. Sleep 37(8):1283–1293.

IOM (Institute of Medicine). 1999. Marijuana and medicine: Assessing the science base. Washington, DC: National Academy Press.

Jetly, R., A. Heber, G. Fraser, and D. Boisvert. 2015. The efficacy of nabilone, a synthetic cannabinoid, in the treatment of PTSD-associated nightmares: A preliminary randomized, double-blind, placebo-controlled cross-over design study. Psychoneuroendocrinology 51:585–588.

National Academies of Sciences, Engineering, and Medicine. 2017. ***The health effects of cannabis and cannabinoids: The current state of evidence and recommendations for research.*** Washington, DC: The National Academies Press. doi: 10.17226/24625. Pages: 120-130. [Reports document the evidence-based consensus of an authoring committee of experts. Reports typically include findings, conclusions, and recommendations based on information gathered by the committee and committee deliberations. Reports are peer reviewed and are approved by the National Academies of Sciences, Engineering, and Medicine.] Accessible free PDF is available @ DOI: https://doi.org/10.17226/24625

Prud'homme, M., R. Cata, and D. Jutras-Aswad. 2015. Cannabidiol as an intervention for addictive behaviors: A systematic review of the evidence. Substance Abuse: Research and Treatment 9:33–38.

Russo, E. B., G. W. Guy, and P. J. Robson. 2007. Cannabis, pain, and sleep: Lessons from therapeutic clinical trials of Sativex, a cannabis-based medicine. Chemistry & Biodiversity 4(8):1729–1743.

Sateia, M. J. 2014. International classification of sleep disorders, third edition: Highlights and modifications. Chest 146(5):1387–1394.

van den Elsen, G. A. H., A. I. A. Ahmed, M. Lammers, C. Kramers, R. J. Verkes, M. A. van der Marck, and M. G. M. Olde Rikkert. 2014. Efficacy and safety of medical cannabinoids in older subjects: A systematic review. Ageing Research Reviews 14(1):56–64.

Walther, S., R. Mahlberg, U. Eichmann, and D. Kunz. 2006. Delta-9-tetrahydrocannabinol for nighttime agitation in severe dementia. Psychopharmacology 185(4):524–528.

Whiting, P. F., R. F. Wolff, S. Deshpande, M. Di Nisio, S. Duffy, A. V. Hernandez, J. C. Keurentjes, S. Lang, K. Misso, S. Ryder, S. Schmidlkofer, M. Westwood, and J. Kleijnen. 2015. Cannabinoids for medical use: A systematic review and meta-analysis. Journal of the American Medical Association 313(24):2456–2473.

Wilsey, B. L., R. Deutsch, E. Samara, T. D. Marcotte, A. J. Barnes, M. A. Huestis, and D. Le. 2016. A preliminary evaluation of the relationship of cannabinoid blood concentrations with the analgesic response to vaporized cannabis. Journal of Pain Research 9:587–598.

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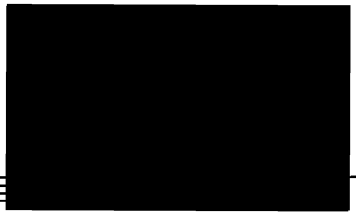
Section H: Acknowledgement and Signature

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.



SIGNATURE

July 30, 2017

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.

July 28, 2017

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

Dear MDH Medical Cannabis Petition Review Committee,

I am writing a letter in support of [redacted] application to include Obstructive Sleep Apnea to the list of accepted medical conditions for use of medical cannabis. As you may know, the National Academies Press this year published the most comprehensive medical evidence review of cannabis and found that there is moderate evidence linking cannabis use to improved short term sleep outcomes in individuals with obstructive sleep apnea.

As an emergency medicine physician with many state licenses including Minnesota, I know that obstructive sleep apnea is a medical problem that leads to increased morbidity and mortality. While there has been some success in treating this condition by no means has modern medical science come up with a good solution for this important health problem.

If the evidence shows that medical cannabis may be a solution I would encourage your board to consider offering this option to citizens of Minnesota.

Sincerely,

Kevin Takakuwa, MD
Co-founder and CEO
American Medical Center for Cannabis Research
P.O. Box 27574
San Francisco, CA 94127

Due to Copyright issues, Section F has been redacted. They will be considered by the panel members during the review process.