1. Medical condition proposed:

Tourette's Syndrome

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

Tourette's Syndrome is an approved medical marijuana qualifying condition in Arkansas, Illinois, Minnesota and Ohio. https://medicalmarijuana.procon.org/view.resource.php?resourceID=000881

In a study on 367 medical marijuana patients in Arizona, researchers found:

4 patients used medical marijuana to treat symptoms of Tourette's Syndrome. General relief of symptoms when using medical marijuana was 100%. Relief of symptoms with medical marijuana compared to other medications was 100%.

http://dx.doi.org/10.1080/02791072.2015.1074766

A review of 72 randomized, double-blind, placebo-controlled studies from 1975 to 2004 evaluating the therapeutic effects of cannabinoids concludes that "Cannabinoids present an interesting therapeutic potential as antiemetics, appetite stimulants in debilitating diseases (cancer and AIDS), analgesics, and in the treatment of multiple sclerosis, spinal cord injuries, <u>Tourette's syndrome</u>, epilepsy and glaucoma" (Ben Amar, 2006) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3673028/

In response to public pressure to allow the medical use of marijuana, the Office of National Drug Control Policy, Washington, DC, funded a study by the Institute of Medicine evaluating the scientific evidence for benefits and risks of using marijuana as a medicine. The report used scientific reviews, public hearings, and reports from other agencies, and was evaluated by knowledgeable advisors and reviewers.

The 1999 Institute of Medicine report states that marijuana can be used to treat Tourettes Syndrome.

Neurological disorders affect the brain, spinal cord, or peripheral nerves and muscles in the body. Marijuana has been proposed most often as a source of relief for three general types of neurological disorders: muscle spasticity, particularly in multiple sclerosis patients and spinal cord injury victims; movement disorders, such as Parkinson's disease, Huntington's disease, and <u>Tourette's syndrome</u>; and epilepsy. <u>Marijuana is not proposed as a cure for such disorders, but it might relieve some associated symptoms.</u>

Clinical reports consist of four case histories indicating that marijuana use can reduce tics in Tourette's patients. In three of the four cases the investigators suggest that beneficial effects of marijuana might have been due to anxiety-reducing properties of marijuana rather than to a specific anti tic effect.

https://medicalmarijuana.procon.org/sourcefiles/IOM_Report.pdf

The Michigan LARA department can add any medical condition or treatment to the qualifying conditions in the MMMA. The condition does not have to be severe, chronic, debilitating, serious or persistent.

MCL 333.26423 (3) <u>Any other medical condition or its treatment</u> approved by the department, as provided for in section 6(k).

MCL 333.26426 (k) Not later than 6 months after the effective date of the amendatory act that added this subsection, the department shall appoint a panel to review petitions to approve medical conditions or treatments for addition to the list of debilitating medical conditions under the administrative rules. The panel shall meet at least twice each year and shall review and make a recommendation to the department concerning any petitions that have been submitted that are completed and include any documentation required by administrative rule.

MCL 333.26425 Sec. 5. (a) Not later than 120 days after the effective date of this act, the department shall promulgate rules pursuant to the administrative procedures act of 1969, 1969 PA 306, MCL 24.201 to 24.328, that govern the manner in which the department shall consider the addition of medical conditions or treatments to the list of debilitating medical conditions set forth in section 3(a) of this act. In promulgating rules, the department shall allow for petition by the public to include additional medical conditions and treatments. In considering such petitions, the department shall include public notice of, and an opportunity to comment in a public hearing upon, such petitions. The department shall, after hearing, approve or deny such petition shall be considered a final department action, subject to judicial review pursuant to the administrative procedures act of 1969, 1969 PA 306, MCL 24.201 to 24.328. Jurisdiction and venue for judicial review are vested in the circuit court for the county of Ingham. http://legislature.mi.gov/doc.aspx?mcl-Initiated-Law-1-of-2008

There is no requirement or restriction that a medical condition added to the act must be chronic, severe, debilitating, serious or persistent.

Courts all over Michigan have questioned patients' qualifying condition and have ruled on if a condition was chronic and severe enough to qualify, thus the courts have overridden a doctor's medical opinion in many cases.

The Michigan Supreme Court has said patients are only protected if they suffer from a serious or "debilitating medical conditions" or symptoms from its ruling in case 142850:

The MMMA does not create a general right for individuals to use and possess marijuana in Michigan. Possession, manufacture, and delivery of marijuana remain punishable offenses under Michigan law. <u>Rather, the MMMA's protections are limited to individuals suffering from serious or debilitating medical conditions or symptoms</u>, to the extent that the individuals' marijuana use "is carried out in accordance with the provisions of [the MMMA]."

http://courts.mi.gov/Courts/MichiganSupremeCourt/Clerks/Recent%20Opinions/11-12-Term-Opinions/142850-Opinion.pdf

The words "chronic" "debilitating" "severe" "persistent" and "serious" are not defined within the MMMA law.

This means that prosecutors and courts rule <u>in a case by case basis</u> what these words mean, and if a patient's condition meets these definitions or not. Which means felonies and possible prison if the patient's condition is not severe enough to qualify.

The MMMA states that a "Debilitating medical condition" means 1 or more of the following:

(2) A chronic or debilitating disease or medical condition or its treatment that produces 1 or more of the following: cachexia or wasting syndrome; severe and chronic pain; severe nausea; seizures, including but not limited to those characteristic of epilepsy; or severe and persistent muscle spasms, including but not limited to those characteristic of multiple sclerosis.

Some patients with Tourette's may not have tics which qualify under "A chronic or debilitating disease or medical condition or its treatment that produces <u>severe</u> and persistent muscle spasms".

It is important to specifically add the Tourettes condition so that these patients are protected by the law, not falsely shielded from the law until a court rules otherwise.

It makes no sense that a patient with severe Tourettes muscle tics can qualify under the MMMP while the patient with mild to moderate Tourettes muscle tics cannot qualify under the act.

Tourette Syndrome (TS) causes people to have "tics". Tics are sudden twitches, movements, or sounds that people do repeatedly. People who have tics cannot stop their body from doing these things.

https://www.cdc.gov/ncbddd/tourette/index.html

The early symptoms of TS are typically noticed first in childhood, with the average onset between the ages of 3 and 9 years. TS occurs in people from all ethnic groups; males

are affected about three to four times more often than females. It is estimated that 200,000 Americans have the most severe form of TS, and as many as one in 100 exhibit milder and less complex symptoms such as chronic motor or vocal tics. Although TS can be a chronic condition with symptoms lasting a lifetime, most people with the condition experience their worst tic symptoms in their early teens, with improvement occurring in the late teens and continuing into adulthood.

https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Tourette-Syndro me-Fact-Sheet

Tourette syndrome involves both motor tics, which are uncontrolled body movements, and vocal or phonic tics, which are outbursts of sound. Some motor tics are simple and involve only one muscle group. Simple motor tics, such as rapid eye blinking, shoulder shrugging, or nose twitching, are usually the first signs of Tourette syndrome. Motor tics also can be complex (involving multiple muscle groups), such as jumping, kicking, hopping, or spinning.

Vocal tics, which generally appear later than motor tics, also can be simple or complex. Simple vocal tics include grunting, sniffing, and throat-clearing. More complex vocalizations include repeating the words of others (echolalia) or repeating one's own words (palilalia). The involuntary use of inappropriate or obscene language (coprolalia) is possible, but uncommon, among people with Tourette syndrome.

In addition to frequent tics, people with Tourette syndrome are at risk for associated problems including attention deficit hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), anxiety, depression, and problems with sleep.

https://ghr.nlm.nih.gov/condition/tourette-syndrome

For many years, medication was the only real treatment option for children and adults with TS. Medication can help control tics, but it doesn't always work. It can also cause side effects that make people feel bad and can lead to other health problems. Researchers working with the Tourette Syndrome Association began developing and testing a promising treatment option1, 2 that does not use medication, called Comprehensive Behavioral Intervention for Tics, or CBIT (pronounced see-bit).

https://www.cdc.gov/features/tourettesyndromeawareness/index.html

Because of the tics, children with TS are sometimes seen as disruptive or rude. A small number of children with TS also have the urge to use swear words or say inappropriate things, even if they don't want to. These tics can be upsetting to the children with TS and everyone around them.

Children who have tics are more likely to be bullied than children without tics, and those with more severe tics are at greater risk for being bullied. Among children with tics, bullying has been associated with loneliness and anxiety.

https://www.stopbullying.gov/blog/2015/06/03/everyone-can-help-stop-bullying-children-tourettesyndrome

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

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

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

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

The Mayo Clinic website has assembled dosage information on Medical Marijuana.

http://www.mayoclinic.org/drugs-supplements/marijuana/dosing/hrb-20059701

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

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

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

NIDA also finds it very difficult to backtrack on the propaganda research they grant. When other researchers tried to duplicate the results of the first study on marijuana and IQ points, they were unable to find any IQ loss due to marijuana use. I hope that any knowledge you have on

marijuana is up to date, and that you are paying attention when NIDA's biased research grants backfire on them, over and over again.

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

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

As evidenced by the included medical marijuana patient surveys in other states and countries, adults are using medical marijuana to treat this disease. Patients will continue to use medical marijuana to treat symptoms whether or not you approve this condition. Approving this condition to the list of Qualifying Conditions in the MMMA has the only effect of protecting sick people from arrest or penalty. These patients are currently breaking the law by using a safe and non-toxic plant that they can grow themselves. The alternative are prescriptions that cost thousands of dollars per month, that the FDA approves even if it is toxic and poisons and kills many Americans each year.

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

1 10.1038/sj.npp.1300047

Previous studies provide evidence that marijuana (Cannabis sativa) and delta-9-tetrahydrocannabinol (Delta(9)-THC), the major psychoactive ingredient of marijuana, respectively, are effective in the treatment of tics and behavioral problems in Tourette syndrome (TS).

In this randomized double-blind placebo-controlled study, we investigated the effect of a treatment with up to 10 mg Delta(9)-THC over a 6-week period on neuropsychological performance in 24 patients suffering from TS. During medication and immediately as well as 5-6 weeks after withdrawal of Delta(9)-THC treatment, no detrimental effect was seen on learning curve, interference, recall and recognition of word lists, immediate visual memory span, and divided attention.

Measuring immediate verbal memory span, we even found a trend towards a significant improvement during and after treatment. Results from this study corroborate previous data suggesting that in patients suffering from TS, treatment with Delta(9)-THC causes neither acute nor long-term cognitive deficits. Larger and longer-duration controlled studies are recommended to provide more information on the adverse effect profile of THC in patients suffering from TS.

2 10.1007/s13311-015-0376-4

Tourette Syndrome Tics

As in any condition influenced by anxiety, a nonspecific beneficial effect of cannabis might be expected, but given the presence of endocannibinoid receptors in the striatum, it is possible that a direct effect of cannabis is reducing the number of tics.

Success in treating symptoms of Tourette syndrome, including involuntary movements (tics) and compulsive behaviors, was first mentioned in an observation of 3 patients who, in 1988, noted improvement in tics and urges while smoking marijuana cigarettes [25], followed by another case of a patient remaining symptom free for a year while smoking marijuana daily [26]. In 1998 a survey of a larger population confirmed a reduction in tic or complete remission in 82 % of patients [27]. The same authors used ?9-THC capsules of varying strengths in a single dose in 12 patients (class II study) and reported improvement in scores of the Tourette Syndrome Symptom List and obsessive compulsive behavior scores, with a decreased number of complex motor tics observed by the examiner [28]. The following year, in a study of 24 patients using the maximum-strength ?9-THC capsule from the pilot study (10 mg) for 6 weeks, a significant response in self-rated Tourette score and observer-rated scores, including the Tourette Syndrome Clinical Global Impression Scale, the Shapiro Tourette Syndrome Severity Scale, and the Yal Global Tic Severity Scale, as well as the review of video, was noted [29]. These were then summarized in a Cochrane review [30]. Little additional work was summarized in a more recent review [31]. Of note, improvements occurred without exacerbating performance on neuropsychologic testing [32].

Side effects were minimized by a simple technique of providing dronabinol after breakfast in order to slow its absorption and provide a steady level acting in the brain [29].

3 10.1517/14656566.4.10.1717

Anecdotal reports suggested that the use of cannabis might improve not only tics, but also behavioural problems in patients with TS. A single-dose, cross-over study in 12 patients, as well as a 6-week, randomised trial in 24 patients, demonstrated that Delta9-tetrahydrocannabinol (THC), the most psychoactive ingredient of cannabis, reduces tics in TS patients. No serious adverse effects occurred and no impairment on neuropsychological performance was observed. If well-established drugs either fail to improve tics or cause significant adverse effects, in adult patients, therapy with Delta9-THC should be tried.

4 https://www.ncbi.nlm.nih.gov/books/NBK224385/

Two widely used medications for Tourette's syndrome, pimozide (Orap) and haloperidol (Haldol) inhibit the effects of the neurotransmitter dopamine. Cannabinoids, by contrast, increase dopamine release, so one might predict that cannabinoids would actually exacerbate the symptoms of Tourette's syndrome. Yet four clinical case histories indicate that marijuana use can reduce tics in Tourette's patients. In three of the four cases, however, the investigators suggest that marijuana's anxiety-reducing properties—rather than any specific effect on the neural pathway that produces tics—caused the patients' symptoms to improve.6

5 10.1177/026988119300700411

A single case report is described where marijuana appears to have been an effective treatment modality for symptoms of Tourette's syndrome. Other possible treatment modalities are excluded. It is concluded that there is a need for further work examining the interactions between marijuana, nicotine and the symptomatology of Tourette's syndrome.

6 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4357541/

Tics and Tourette Syndrome

Case reports of smoked cannabis.80 oral THC.81-84 and case series of smoked cannabis (N = 3)85 suggest that cannabinoids may be beneficial for tics in patients with Tourette syndrome (TS). Similarly, a survey of 64 TS patients found that 17 (27%) had tried marijuana and 14 of them (82%) found it helpful for tics and behavioral disturbances.86 Although only 2 controlled trials have assessed the efficacy of cannabinoids for tics, the results support these uncontrolled clinical reports. A small (N=12) randomized double-blind placebo-controlled single-dose crossover trial assessed a single dose of 5–10 mg oral THC (dose based on body weight and prior marijuana use) for tics in TS using the Tourette Syndrome Symptom List (TSSL).87 Tics and obsessive compulsive behavior significantly improved on the TSSL with statistically significant improvements or trends towards improvement in other secondary outcomes including the Yale Global Tic Severity Scale. Mild side effects noted by 5 patients included headache, dizziness, nausea and cognitive changes. Another small (N=17) 6-week randomized placebo-controlled parallel group trial of 6-weeks 10 mg daily orally-administered THC assessed tic reduction in TS patients using the Tourette Syndrome Clinical Global Impression scale (TS-CGI).88 This study also found significant improvements in the primary and most secondary outcomes. A related study from the same cohort reported no significant change in neuropsychological performance with THC treatment.89 Limitations of these studies include small sample size, short treatment period, multiple comparisons, fixed or single dose approach, potential blinding issues and possible selection bias. Given these limitations, AAN evidence-based systematic review, as well as a recent Cochran review on the efficacy of cannabinoids in TS, state that there is presently "insufficient evidence to support or refute the clinical use of THC, nabilone, or cannabis for tics".8, 90 However, in treatment resistant adult patients, THC may have the rapeutic effects and is recommended by some experts.91 Positive results of preliminary studies warrant validation of the efficacy and safety of THC for tics in larger randomized clinical trials.

7 10.1055/s-2002-25028

Anecdotal reports in Tourette's syndrome (TS) have suggested that marijuana (cannabis sativa) and delta-9-tetrahydrocannabinol (Delta(9)-THC), the major psychoactive ingredient of marijuana, reduce tics and associated behavioral disorders. We performed a randomized double-blind placebo-controlled crossover single-dose trial of Delta(9)-THC (5.0, 7.5 or 10.0 mg) in 12 adult TS patients.

Using the TSSL, there was a significant improvement of tics (p=0.015) and obsessive-compulsive behavior (OCB) (p = 0.041) after treatment with Delta(9)-THC compared to placebo. Examiner ratings demonstrated a significant difference for the subscore "complex"

motor tics" (p = 0.015) and a trend towards a significant improvement for the subscores "motor tics" (p = 0.065), "simple motor tics" (p = 0.093), and "vocal tics" (p = 0.093). No serious adverse reactions occurred. Five patients experienced mild, transient side effects. There was a significant correlation between tic improvement and maximum 11-OH-THC plasma concentration. Results obtained from this pilot study suggest that a single-dose treatment with Delta(9)-THC is effective and safe in treating tics and OCB in TS.

8 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3036957/

Cannabinoids

Muller-Vahl and colleagues have conducted a number of studies investigating the therapeutic benefit of cannabinoids in treating tics. One of these studies [Muller-Vahl et al. 1998] found that when interviewed, 17 of 64 patients with tics admitted using cannabis, and 14 of these said that it reduced tics, premonitory urges and OCSs. Muller-Vahl and colleagues also reported a case report of a 25-year-old man with tics, ADHD, OCD and self-injurious behaviour, who found that the use of tetrahydrocannabinoid (THC) helped with many of these symptoms [Muller-Vahl et al. 1999]. A single dose of THC was shown to reduce his tic score on the YGTSS from 41 to 7, 2 hours after treatment. The patient also reported reduced premonitory urges and OCSs and neuropsychological testing indicated improvements in signal detection and sustained attention. Another study has also reported that THC is no threat to cognitive performance [Hemming and Yellowlees, 1993].

A later randomized, double-blind, crossover trial [Muller-Vahl et al. 2002] indicated that both motor tic severity and OCSs were significantly improved by THC. Similar findings were found in a 6-week study [Muller-Vahl et al. 2003] in which the dose of THC was gradually titrated up to 10mg. Small improvements in tic frequency and severity were evident according to assessment using different measures of tic severity. The side effects associated with the use of THC were reported to be mild and transient. However, there are limitations associated with these two studies. As noted by Curtis and colleagues, these include the possibility that effect sizes could be artificially inflated, as those participants who drop out may do so due to lack of treatment response [Curtis et al. 2009].

9 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3442177/

In principle, physicians of any discipline without additional qualifications can prescribe dronabinol (prepacked or individually mixed), nabilone, and the cannabis extract, even beyond the licensed indications (off-label), to any individual patient. The most frequent off-label uses of cannabis-based medications are as follows:

In palliative medicine, to increase appetite and alleviate nausea

To treat chronic pain (often together with opiates)

To treat spasticity of causes other than MS (e.g., in paraplegic patients)

To treat tics in patients with Tourette syndrome.

Off-label treatment with cannabinoid medications is difficult in everyday clinical practice, however, because statutory health insurers usually refuse to assume the costs. To avoid

possible subsequent recourse claims, the question of assumption of costs should therefore be clarified with the relevant insurer before writing a prescription. A private prescription, where the patient will bear the costs, can be issued at any time.

10. 10.3233/BEN-120276

Using both self and examiner rating scales, in both studies a significant tic reduction could be observed after treatment with THC compared to placebo, without causing significant adverse effects. Available data about the effect of THC on obsessive-compulsive symptoms are inconsistent. According to a recent Cochrane review on the efficacy of cannabinoids in TS, definite conclusions cannot be drawn, because longer trials including a larger number of patients are missing. Notwithstanding this appraisal, by many experts THC is recommended for the treatment of TS in adult patients, when first line treatments failed to improve the tics. In treatment resistant adult patients, therefore, treatment with THC should be taken into consideration.

11. 10.1055/s-2001-15191

Previous studies have suggested that marijuana (cannabis sativa) and delta-9-tetrahydrocannabinol (delta9-THC), the major psychoactive ingredient of marijuana, are effective in the therapy of tics and associated behavioral disorders in Tourette Syndrome (TS). Because there is also evidence that cannabis sativa may cause cognitive impairment in healthy users, we performed a randomized double-blind placebo-controlled crossover trial for delta9-THC in 12 adult TS patients to investigate whether treatment of TS with a single dose of delta9-THC at 5.0 to 10.0 mg causes significant side effects on neuropsychological performance. Using a variety of neuropsychological tests, we found no significant differences after treatment with delta9-THC compared to placebo treatment in verbal and visual memory, reaction time, intelligence, sustained attention, divided attention, vigilance, or mood.

12. 10.1007/978-3-540-88955-7_17.

Tourette's syndrome (TS) is a chronic disorder characterized by motor and vocal tics and a variety of associated behaviour disorders. Because current therapy is often unsatisfactory, there is expanding interest in new therapeutic strategies that are more effective, cause less side effects and ameliorate not only tics but also behavioural problems. From anecdotal reports and preliminary controlled studies it is suggested that - at least in a subgroup of patients - cannabinoids are effective in the treatment of TS. While most patients report beneficial effects when smoking marijuana (Cannabis sativa L.), available clinical trials have been performed using oral d9-tetrahydrocannabinol (THC).

13. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2701289/

Anecdotal reports from TS patients that marijuana use ameliorates their tics may have scientific relevance given evidence that basal ganglia cannabinoid receptors modulate dopamine, glutamate, and GABA activity governing motoric output.87 Delta-9-tetrahydrocannabinol has shown promise for efficacy88 in a small placebo-controlled crossover study. Further studies using drugs acting on cannabinoid receptors, such as dronabinol or nabilone, may be rational.

14 10.1176/appi.neuropsych.16110310

The authors retrospectively evaluated effectiveness and tolerability of cannabis in 19 adults with Tourette syndrome. Tics scores decreased by 60%, and 18 of the 19 participants were at least "much improved." Cannabis was generally well tolerated, although most participants reported side effects.

15. http://dx.doi.org/10.1080/02791072.2015.1074766

4 patients used medical marijuana to treat symptoms of Tourette's Syndrome. General relief of symptoms when using medical marijuana was 100%. Relief of symptoms with medical marijuana compared to other medications was 100%.

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