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 addendum, Section B.

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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 addendum, Section C.

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 addendum, Section D.

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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 addendum, Section E.

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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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.

[redacted] 1/17/17

SIGNATURE 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 B: Medical Condition You Are Requesting Be Added

Autism Spectrum Disorder (ASD) is a general term for a group of complex disorders of brain development. These disorders are often characterized by difficulties in social interaction, verbal and nonverbal communication and repetitive behaviors. ASD can also be associated with intellectual disability, difficulties with motor coordination and attention and physical health issues such as sleep and gastrointestinal disturbances[1]. These challenges may range from mild to severe, and patients on the more severe end of the spectrum may also exhibit aggressive and/or self-injurious behaviors[2].

With the publication of the Diagnostic and Statistical Manual of Mental Disorders (DSM–5) in May 2013, all autism disorders were merged under one umbrella diagnosis of ASD[3]. This diagnosis now includes the previously distinct subtypes of autistic disorder, childhood integrative disorder, pervasive developmental disorder-not other specified and Asperger Syndrome. The diagnostic code for ASD is ICD-10-CM, F84.0.

According to statistics from the U.S. Centers for Disease Control and Prevention (CDC), approximately 1 in 68 American children now has ASD – for comparison, in the 1970 the number was 1 in 10,000. An estimated 1 in every 42 boys and 1 in every 189 girls are diagnosed with ASD in the United States[4].

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[1] https://www.autismspeaks.org/sites/default/files/sctk_about_autism.pdf
[2] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4922773/
[3] https://www.autismspeaks.org/dsm-5/faq
[4] https://www.cdc.gov/ncbddd/autism/data.html

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

In order to have a full understanding of the impact that ASD may have not only on a patient's life but on the life of the patient's family and caregivers, it is important to not only look at the symptoms of the disorder itself but also on the effects - and general lack of effectiveness - of the very small number of currently available treatments.

Autism spectrum disorders are typically characterized by challenges in three core areas: social-interaction difficulties, communication challenges and a tendency to engage in repetitive behaviors[5]. This standard characterization, however, only describes a small portion of the impairments that may occur to a person with ASD over time due to a lack of effective treatments and possible progression of the disorder - other common impairments include but are not limited to:

- Gastrointestinal (GI) Disturbances. These are common among persons with ASD, and up to 85% of children with ASD are impacted from this. These conditions range in severity from a tendency for chronic constipation or diarrhea to inflammatory bowel disease. Pain caused by GI issues can prompt behavioral changes such as increased self soothing (such as rocking and head banging) or outbursts of aggression and/or self-injury.
- Seizure Disorder. Seizure disorders, including epilepsy, occur in as many as 39% of those with ASD. Seizures associated with ASD tend to start in either early childhood or adolescence but may occur at any time.
- Sleep Dysfunction. This is common among children and adolescents with autism and may likewise affect many adults.

It is becoming increasingly common for ASD patients to exhibit aggression towards caregivers and even self-injurious behaviors over time, despite being administered a sometimes dizzying array of largely ineffective treatments and medications[6]. It is important to note that an expanding body of research indicates that the underpinnings of ASD are medically based - as with any medical condition the longer it goes untreated, incorrectly treated or unmanaged the more it will likely deteriorate over time. The impact of these challenges to both the patients and their families is enormous and extraordinarily difficult to manage[7]. In order to halt the progression of the disorder and address these underlying medical issues, we must ensure that effective treatments are available.

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[5] https://www.autismspeaks.org/what-autism/symptoms

[6] https://www.scientificamerican.com/article/autisms-drug-problem/

[7] https://www.disabilityscoop.com/2013/01/23/families-autism-aggression/17157/

Currently, there are only two medications that are FDA-approved for the treatment of ASD: Risperidone (Risperdal®) and Aripiprazole (Abilify™). Both of these medications are antipsychotics intended to treat the behavioral symptoms of ASD including aggression, self-injurious behavior and severe tantrums. There are two significant issues with these medications as described below:

1. A growing body of medical literature and research points to medical underpinnings for ASD which cannot be effectively treated with antipsychotic medications.
2. These medications often come with severe side effects that are similar or identical to the issues we are trying to solve for. For example, side effects of Risperidone include but are not limited to aggressive behavior, agitation, anxiety, difficulty concentrating, tic-like or twitching movements and trouble sleeping[8]. Side effects of Abilify include but are not limited to seizures, severe agitation, distress, twitching or uncontrollable movements, thoughts of suicide or self-injury[9].

We have in front of us a unique opportunity to learn from all we have observed from the perspectives of both medical practitioners and caregivers, learn from what has worked and what has not, and to take an important step forward toward helping these patients achieve and maintain an improved quality of life and - in some cases - achieve actual healing. There is a better way.

[8] https://www.drugs.com/sfx/risperidone-side-effects.html
[9] https://www.drugs.com/sfx/abilify-side-effects.html

Section D. Availability of conventional medical therapies

As noted in Section C above, Risperdal and Abilify are the only two FDA-approved medications prescribed for the treatment of "irritability in autism". Both of these medications are antipsychotics intended to address the behavioral symptoms of ASD including aggression, self-injurious behavior and severe tantrums. Additionally, as noted in various literature from ASD awareness organizations along with major medical organizations, off-label medical treatments including additional antipsychotics, antidepressants, stimulants and mood stabilizers are also often prescribed to address these symptoms[10].

While professional and scientific debate continues regarding the specific causes of autism, research has shown that irrespective of the causes ASD patients often suffer from painful chronic inflammation, particularly in the brain and in the digestive tract. Additionally, researchers studying brains affected by ASD found a common pattern: widespread activation of brain immune cells that produce inflammation[11]. Chronic inflammation in the brain has been shown to lead to encephalitis - an acute inflammation (swelling) of the brain usually resulting from either a viral infection or due to the body's own immune system mistakenly attacking brain tissue[12]. Additionally, chronic inflammation in the digestive tract is a known factor behind many of the challenging GI disorders ASD patients may experience[13].

It is important to note that antipsychotic and other off-label medications used to treat ASD typically do not address inflammation in the human body. Antipsychotics such as Risperdal and Abilify are from the class of medications known as Selective Serotonin Reuptake Inhibitors (SSRIs). SSRIs are designed to ease depression by increasing levels of serotonin in the brain. Serotonin is one of the chemical messengers (i.e. neurotransmitters) that carry signals between brain cells. SSRIs block the reabsorption (or reuptake) of serotonin in the brain, making more serotonin available which is believed to contribute to a feeling of well-being and happiness[14]. These medications may cause chemical reactions to occur in the human body that actually mask the underlying medical conditions which ultimately must be treated to improve the quality of these patients' lives.

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[10] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4450669/

[11] https://www.nature.com/articles/ncomms6748

[12] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4717322/

[13] http://journals.lww.com/ibdjournal/Abstract/2015/10000/Prevalence_of_Inflammatory_Bowel_Disease_Among.6.aspx

[14] http://www.mayoclinic.org/diseases-conditions/depression/in-depth/ssris/art-20044825

According to a report published by the National Institute of Health in 2013[15], there is no evidence to support the use of SSRIs to treat ASD in children. There is also limited evidence to suggest effectiveness of SSRIs in adults with ASD. In addition to a general lack of long-term effectiveness in treating the symptoms of ASD, treatment with SSRIs may cause side effects as noted above in Section C that not only do not improve patient outcomes but may actually cause them to further deteriorate over time.

[15] https://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0012940/

Section E: Anticipated benefits from Medical Cannabis

Clinical research regarding the therapeutic benefits of cannabis has been almost non-existent in the United States since cannabis was given Schedule I status in the Controlled Substances Act of 1970. Despite this challenging research environment, some research has been or is being conducted demonstrating the positive effects of cannabis on ASD patients or on non-ASD patients who share common symptoms with ASD patients. We will provide our findings organized into two primary categories: research-supported symptom improvements and anecdotal symptom improvements.

Research-Supported Symptom Improvements

In 2013, a study[16] published in the journal Neuron revealed that autism-related mutations in mice resulted in "deficits in endocannabinoid signaling." The study concluded that "alterations in endocannabinoid signaling may contribute to autism pathophysiology." Also in 2013, researchers at Stanford University found that the symptoms of autism are caused by a mutation in the neurologin-3 gene that both blocks the body's natural production of endocannabinoids and also interferes with the way cannabinoids communicate with the brain. Cannabinoids in cannabis interact with the body's endocannabinoid system and act not only to regulate emotion and focus but also serve as a neuroprotectant preventing further degradation of brain cells[17]. Researchers at the University of Irvine in California believe they have also discovered a link between endocannabinoids and ASD, concluding that "increasing natural marijuana-like chemicals in the brain can help correct behavioral issues related to Fragile X syndrome, the most common known genetic cause of autism"[18].

Yet another study[19] from 2013 that was published in the Journal of Autism and Developmental Disorders revealed a link between the endocannabinoid system and immune cells in children with autism. Because immune dysfunction is a factor that contributes to autism, the condition is believed to be linked to higher levels of CB2 receptors in cells (CB1 receptors, on the contrary, were not overexpressed). CB2 receptors play a significant role in regulation of the immune system. Because problems with the immune system are so closely related to autism, the authors of the study concluded that the use of cannabinoids and therapies that target CB2 receptors might be helpful for those who suffer from ASD.

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[16] http://www.cell.com/neuron/abstract/S0896-6273(13)00225-0

[17] https://www.ncbi.nlm.nih.gov/pubmed/18220777

[18] https://news.uci.edu/press-releases/boosting-natural-marijuana-like-brain-chemicals-treats-fragile-x-syndrome-symptoms/

[19] https://www.ncbi.nlm.nih.gov/pubmed/23585028

In 2014, the Hawaii Journal of Medicine & Public Health published the results of a patient survey[20] where 97% of respondents used cannabis primarily for chronic pain. Average pain improvement on a 0–10 pain scale was 5.0, which translates to a 64% relative decrease in average pain. Half of all respondents also noted relief from stress/anxiety, and nearly half (45%) reported relief from insomnia. Most patients (71%) reported no adverse effects. No serious adverse effects were reported.

In 2015, the Kluger study[21] observed that the endocannabinoid system modulates neurotransmission involved in motor function, particularly within the basal ganglia. The basal ganglia are associated with a variety of functions including control of voluntary motor movements, procedural learning, routine behaviors or "habits" such as teeth grinding, eye movements, cognition and emotion. Preclinical research in animal models of several movement disorders have shown variable evidence for symptomatic benefits but more consistently suggest potential neuroprotective effects. Clinical observations and clinical trials of cannabinoid-based therapies suggest a possible benefit of cannabinoids for tics as well.

In 2016, the independent peer-reviewed journal Gastroenterology & Hepatology also published its findings in the paper "Therapeutic Use of Cannabis in Inflammatory Bowel Disease"[22]. This paper first establishes that inflammatory bowel disease (IBD) is a chronic inflammatory condition comprised of ulcerative colitis
and Crohn's disease and characterized by relapsing and remitting episodes of inflammation primarily involving the gastrointestinal tract. While the pathophysiology of IBD has yet to be fully established, it appears to involve an inappropriate inflammatory response with a dysregulated immune system. Conventional therapies aimed at induction and remission of IBD mainly work through immune suppression and consist of aminosalicylates, antibiotics, corticosteroids, immunomodulators, and biologic therapies. Given the limited therapy options and known adverse side effects with chronic use of the existing therapy options, patients may be prompted to undergo a surgical resection of the diseased bowel. Anecdotal reports have suggested a therapeutic role for cannabis in the treatment of IBD for hundreds of years.

The authors of this study conducted a retrospective, observational study of 30 Crohn's disease patients in Israel who were legally using cannabis due to a lack of

[20] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3998228/
[21] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4357541/pdf/nihms649683.pdf
[22] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5193087/pdf/GH-12-668.pdf

response to conventional treatments and chronic intractable pain. Disease activity before and after cannabis use was estimated using the Harvey-Bradshaw index for Crohn's disease, and patients assessed their general medical well-being before and after use. Patients' hospital records were obtained to monitor disease activity, rate of hospital admission, use of additional drugs, and need for surgical intervention. All 30 patients rated their general medical well-being as improved after cannabis use via a visual analog scale. Twenty-one patients had a notable improvement after treatment with cannabis use. Only 2 patients required surgery during a period of 3 years of cannabis use, a rate that Naftali and colleagues claimed is a significant improvement for the normal operative rate in patients with Crohn's disease. Whereas 26 patients required corticosteroid therapy prior to cannabis use, only 4 patients were still maintained on corticosteroids after cannabis use, suggesting a possible corticosteroid-sparing effect of cannabis. There was also a substantial drop in use of aminosalicylates, thiopurines, methotrexate, and tumor necrosis factor antagonists. The authors cited these data as objective benefits of cannabis use and advocated for more placebo-controlled studies for further evaluation of therapeutic effects of cannabis use.

In 2017, the National Academies of Sciences, Engineering and Medicine published its findings on the health benefits of medical cannabis entitled "The Health Effects of Cannabis and Cannabinoids"[23]. While not specifically focused on ASD patients, a notable finding from this research is that in adults with chronic pain, patients who were treated with cannabis or cannabinoids are more likely to experience a clinically significant reduction in pain symptoms.

Anecdotal Symptom Improvements

Anecdotal reports of symptom improvements due to medical cannabis are primarily sourced from ASD patients and caregivers. Medical cannabis can help to relieve many symptoms commonly associated with ASD, including but not limited to anxiety, aggression, panic disorder, generalized rage, tantrums, property destruction and self-injurious behavior[24]. Here we will highlight a portion of the parent testimony of Victoria Grancarich, whose son Julian qualified for medical cannabis based on his history of seizure disorder:

> *Julian had always been a kind and affectionate boy in his younger years. When Julian turned 13, the onset of puberty brought new challenges. In February of 2016 Julian became extremely violent toward both family and school staff. In August 2016, Julian began to turn the violence on to himself.*

[23] https://www.ncbi.nlm.nih.gov/books/NBK423845/pdf/Bookshelf_NBK423845.pdf
[24] https://www.massroots.com/learn/cannabis-treatment-autism

He began punching himself in the head [and] would use his knee to injure his teeth. He would bang his head into walls. Between October 2016 and January 2017, Julian was hospitalized 3 times. He suffered self-inflicted skull fractures and massive tissue damage.

We enrolled him in the Minnesota Cannabis program in January 2017. Within a week of beginning cannabis therapy Julian was able to go about an hour without harming himself. As the weeks went on and we reached a therapeutic dose Julian's behaviors began to slowly melt away. By early March he was smiling again. Within 6 weeks of beginning cannabis Julian was no longer injuring himself or others. He began to take an interest in his life again. He returned to school full time. We were able to remove his helmets and protective gear. By mid March we were getting smiles and hugs. Julian began to go outdoors again by mid-April. By May, Julian began to show interest in using augmentative communication for the first time in his life.

It is now late June. We have not seen 1 episode of self-injury since early March.

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

Hampson et al. (2003). United States Patent 6,630,507: Cannabinoids as Antioxidants and Neuroprotectants. https://patents.google.com/patent/US6630507B1/en

Bogner et al. The Endocannabinoid System as it Relates to Autism. https://www.scribd.com/document/218971076/The-Endocannabinoid-System-as-it-Relates-to-Autism

Iseger et al. (2015). A systematic review of the antipsychotic properties of cannabidiol in humans. Schizophr Res. 2015 Mar;162(1-3):153-61. doi: 10.1016/j.schres.2015.01.033. Epub 2015 Feb 7.

Schubart et al. (2013). Cannabidiol as a potential treatment for psychosis. Eur Neuropsychopharmacol. 2014 Jan;24(1):51-64. doi: 10.1016/j.euroneuro.2013.11.002. Epub 2013 Nov 15.

Cascio et al. (2014). The phytocannabinoid, Δ9-tetrahydrocannabivarin, can act through 5-HT1A receptors to produce antipsychotic effects. Br J Pharmacol. 2015 Mar; 172(5): 1305–1318. Published online 2015 Feb 13. doi: 10.1111/bph.13000

Rohleder et al. (2016). Cannabidiol as a Potential New Type of an Antipsychotic. A Critical Review of the Evidence. Front Pharmacol. 2016; 7: 422. Published online 2016 Nov 8. doi: 10.3389/fphar.2016.00422

Leweke et al. (2012). Cannabidiol enhances anandamide signaling and alleviates psychotic symptoms of schizophrenia. Transl Psychiatry (2012) 2, e94, doi:10.1038/tp.2012.15

Brzozowska et al. (2016). ABC transporters P-gp and Bcrp do not limit the brain uptake of the novel antipsychotic and anticonvulsant drug cannabidiol in mice.

Servadio et al. (2016). Targeting anandamide metabolism rescues core and associated autistic-like symptoms in rats prenatally exposed to valproic acid. Transl Psychiatry (2016) 6, e902; doi:10.1038/tp.2016.182

Schultz et al. (2016). Acetaminophen Use for Fever in Children Associated with Autism Spectrum Disorder. Autism Open Access. 2016 April ; 6(2): . doi:10.4172/2165-7890.1000170.

Lorenz (2004). On the application of cannabis in paediatrics and epileptology. Neuro Endocrinol Lett. 2004 Feb-Apr;25(1-2):40-4

Karhson et al. (2016). Endocannabinoid signaling in social functioning: an RDoC perspective. Transl Psychiatry (2016) 6, e905; doi:10.1038/tp.2016.169

Denney (2009). Cannabis Treatment in Childhood Autism. http://www.os-extra.cannabisclinicians.org/wp-content/uploads/2016/02/2009-page-6.pdf

Bauman (2010). Medical Comorbidities in Autism: Challenges to Diagnosis and Treatment. Neurotherapeutics. 2010 Jul;7(3):320-7. doi: 10.1016/j.nurt.2010.06.001.

Chakrabarti et al. (2011). Variation in the human cannabinoid receptor CNR1 gene modulates gaze duration for happy faces. Molecular Autism, 2, 10. http://doi.org/10.1186/2040-2392-2-10

Prager et al. (2015). The basolateral amygdala - aminobutyric acidergic system in health and disease. Journal of Neuroscience Research November 2015 DOI: 10.1002/jnr.23690

Xia et al. (2016). p21-activated kinase 1 restricts tonic endocannabinoid signaling in the hippocampus. eLife 2016;5:e14653 DOI: 10.7554/eLife.14653

Haj-Dahmane et al. (2011). Modulation of the serotonin system by endocannabinoid signaling. Neuropharmacology. 2011 Sep;61(3):414-20. doi: 10.1016/j.neuropharm.2011.02.016. Epub 2011 Feb 24.

Caterina et al. (2000). Impaired Nociception and Pain Sensation in Mice Lacking the Capsaicin Receptor. Science. 2000 Apr 14;288(5464):306-13.

Di Marzo et al. (2011). Gut feelings about the endocannabinoid system. Neurogastroenterol Motil. 2011 May;23(5):391-8. doi: 10.1111/j.1365-2982.2011.01689.x.

Krueger et al. (2013). Evidence for a Common Endocannabinoid-Related Pathomechanism in Autism Spectrum Disorders. Neuron. 2013 May 8;78(3):408-10. doi: 10.1016/j.neuron.2013.04.030.

Wei et al. (2016). Enhancement of Anandamide-Mediated Endocannabinoid Signaling Corrects Autism-Related Social Impairment. Cannabis and Cannabinoid Research. March 2016, 1(1): 81-89. https://doi.org/10.1089/can.2015.0008

Qin et al. (2015). Endocannabinoid-mediated improvement on a test of aversive memory in a mouse model of fragile X syndrome. Behav Brain Res. 2015 Sep 15;291:164-71. doi: 10.1016/j.bbr.2015.05.003. Epub 2015 May 12.

Castillo et al. (2012). Endocannabinoid Signaling and Synaptic Function. Neuron Volume 76, Issue 1, 4 October 2012, Pages 70-81 https://doi.org/10.1016/j.neuron.2012.09.020

Chakrabarti et al. (2015). Endocannabinoid Signaling in Autism. Neurotherapeutics. 2015 Oct;12(4):837-47. doi: 10.1007/s13311-015-0371-9.

Olmo et al. (2016). Dissecting the signaling pathways involved in the crosstalk between mGlu5 and CB1 receptors. Mol Pharmacol. 2016 Nov;90(5):609-619. Epub 2016 Jun 23.

Doenni et al. (2016). Deficient adolescent social behavior following early-life inflammation is ameliorated by augmentation of anandamide signaling. Brain Behav Immun. 2016 Nov;58:237-247. doi: 10.1016/j.bbi.2016.07.152. Epub 2016 Jul 21.

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Benito et al. (2008). Cannabinoid CB2 receptors in human brain Inflammation. Br J Pharmacol. 2008 Jan; 153(2): 277–285. Published online 2007 Oct 15. doi: 10.1038/sj.bjp.0707505

Schultz (2010). Can autism be triggered by acetaminophen activation of the endocannabinoid system? Acta Neurobiol Exp (Wars). 2010;70(2):227-31.

Foldy et al. (2013). Autism-Associated Neuroligin-3 Mutations Commonly Disrupt Tonic Endocannabinoid Signaling. Neuron. 2013 May 8; 78(3): 498–509. doi:10.1016/j.neuron.2013.02.036.

Andari et al. (2010). Promoting social behavior with oxytocin in high-functioning autism spectrum disorders. Proc Natl Acad Sci U S A. 2010 Mar 2;107(9):4389-94. doi: 10.1073/pnas.0910249107. Epub 2010 Feb 16.

Meyer-Lindenberg et al. (2011). Oxytocin and vasopressin in the human brain: social neuropeptides for translational medicine. Nature Reviews Neuroscience 12, 524-538 (September 2011) doi:10.1038/nrn3044

Wei et al. (2015). Endocannabinoid signaling mediates oxytocin-driven social reward. Proc Natl Acad Sci U S A. 2015 Nov 10;112(45):14084-9. doi: 10.1073/pnas.1509795112. Epub 2015 Oct 26.

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

Letter in Support – [redacted]

Letter in Support – [redacted]

Letter in Support – [redacted]

Letter in Support – [redacted]

Letter in Support – [redacted]

Letter in Support – [redacted]

Letter in Support – [redacted]

Letter in Support – [redacted]

Letter in Support – [redacted]

Letter in Support – [redacted]

June 6, 2017

[redacted]
Advanced Microglial and Cannabinoid Signaling in Autism
Plant-Based Nutrition Certified,
Cornell University
[redacted]

Re: **Minnesota lawmakers - Expert support for autism as qualifying condition**

Autism & Cannabis – Physician Support

This brief summary provides "additional supportive evidence" for Minnesota lawmakers to justify autism as qualifying condition for their medical marijuana program. Please refer to the first document entitled "The Endocannabinoid System as it Relates to Autism" to appreciate further scientific evidence.

Recommendation

Dear Colleagues, I am the father of a 12 year old son who has autism. I have found great interest in pursuing possible etiologies in the development of the condition and explore safe alternatives to conventional pharmaceutical intervention. I am a speaker at multiple national conferences, specifically focused on autism and cannabis. As you know, several states have autism as qualifying diagnosis and more and more are to follow in the coming years. I have provided testimony in several other states about this same issue at hand including Texas, Maryland, Pennsylvania, Georgia and South Carolina.

Since I am sure you are aware, cannabis is non-lethal to humans. There are no reported deaths in recorded history that are attributed to cannabis as the cause of death.

The only question that really should be asked is if chronic cannabis exposure to the developing brain can be harmful. I share the same passion to protect our children. I am a father of four and am caught in the health-nut movement, where everything I offer them is safe to consume, free of refined sugars, genetically modified foods and more of such nature. Recommending cannabis to this subpopulation comes with a great deal of research.

I am giving my full support for giving parents the choice to choose cannabis as treatment modality in autism spectrum disorders. The reasons are as follows:

- I have seen countless parents' success stories with cannabis treatment, especially self-injurious, severe autism
- I have seen parents with their treated children for several years without adverse effects,
- I have researched this thoroughly. Cannabis is not only safe, but therapeutic (evidence below),
- This is not meant to change novel treatment recommendations for autism in any way. This is meant simply to be a legal choice for those parents that desire to choose cannabis for their child. It offers them legal protection from prosecution,
- Many "do it" without having "cannabis-cards" anyways. This causes additional stress for already struggling families.

I have personally consulted with Professor Grinspoon, who is a renowned Harvard Psychiatrist for 40 years and was reassured that cannabis is the not toxic in the developing brain. I have also consulted Professor Mechoulam, who discovered the THC molecule. In fact, he is still active as professor in Israel and is involved in the first human trial with cannabis and autism [out of all diseases].

If you see the powerful transformation yourself, when you listen to powerful parent testimony, it is our duty to protect these parents from state or federal interference. We must protect these very brave, yet vulnerable parents.

Thank you for your time to hear these parents and physicians and thank you for your time researching this subject as thoroughly as I have.

Scientific evidence

Highlights

- "**These alterations in endocannabinoid signaling may contribute to autism pathophysiology** (Földy 2013, Krueger 2013, Onaivi 2011, Siniscalco 2013)."
- "**Endocannabinoids regulate stress responses, in part via the modulation of the 5-HT system** (Haj-Dahmane 2011)."
- " **Neurogenesis** (Galve-Roperh 2007, Jiang 2005, Avraham 2014, Campos 2013)"
- " **Neuroprotection** (Hampson 2003, Lara-Celador 2013, Sanchez 2012)"
- " **Antioxidants** (Borges 2013, Pertwee 2010, Hampson 1998, Hampson 2003)"
- " **Neuromodulation** (Davis 2007, Lara-Celador 2013, Pertwee 2010, Youssef 2012)"
- " **Anti-inflammatory** (Pertwee 2010, Izzo 2009, Nagarkatti 2009, Klein 2005)"

Direct Links

- NL3 mutations inhibit tonic secretions of endocannabinoids
- ECS is suggested target for fragile X treatment
- CB2 upregulated and is suggested target for ASD treatment
- PPAR alpha/gamma and GPR55 downregulated
- CB1 is key element of perception of basic emotions (like happy faces)

Correlations

- Modulation of GABA efflux via CB1 and CB2
- ECS and 5-HT system closely interrelated
    - eCBs via CB1 modulate 5-HT release
    - 5-HT regulates the release of eCBs via 5-HT2a
    - AEA reduces 5-HT binding
    - THC, THCA, CBD, CBDA are all 5-HT1a agonists
    - THC increases 5-HT1a receptor expression and function
    - Cannabinoid agonists inhibit 5-HT3
    - CBD tryptophan degradation suppressor
- Cannabinoid signaling suppresses cytokine proliferation/release via CB1/CB2 dependent and independent mechanisms
- CB1 regulates synaptic plasticity at synapse onto Purkinje cells
- ECS target for modulating neuronal and glial cell function in epileptogenic developmental pathologies
- Tonic eCBs regulate GI functions (including metabolism)

Phytocannabinoids are compounds that are useful as tissue protectants, such as neuroprotectants. The compounds and compositions may be used, for example, in the treatment of neurological insults due to inflammation, such as autism spectrum disorders.

Cannabinoid receptor type 1 (CB1) receptors are thought to be one of the most widely expressed G protein-coupled receptors in the brain, making cannabinoids an integral part in brain homeostasis. CB2

receptors are mainly expressed on T cells of the immune system, on macrophages and B cells, and in hematopoietic cells, making cannabinoids an integral part in human immune function.

Cannabinoids as antioxidants and neuroprotectants – US Patent 6630507 B1

United States Patent 6630507 by the Department of Health and Human Services, 'Cannabinoids as antioxidants and neuroprotectants'. Cannabinoids have been found to have antioxidant properties, unrelated to NMDA receptor antagonism. This new found property makes cannabinoids useful in the treatment and prophylaxis of wide variety of oxidation associated diseases, such as ischemic, age-related, inflammatory and autoimmune diseases. The cannabinoids are found to have particular application as neuroprotectants.

"It has surprisingly been found that cannabidiol and other cannabinoids can function as neuroprotectants..." "No signs of toxicity or serious side effects have been observed following chronic administration of cannabinoids to volunteers..." "It is an object of this invention to provide a new class of antioxidant drugs..."

The Shafer Commission Report Evidence

The Controlled Substances Act created the Presidential Commission on Marijuana and Drug abuse specifically to advice on the proper scheduling on cannabis. Thus was born a council that would become one of the most legendary fact-finding bodies ever conceived: the Shafer Commission.

In the early 1970s, President Nixon appointed Gov. Raymond P. Shafer of Pennsylvania, a former prosecutor with a "law-and-order" reputation, to run a commission that would demonstrate enough evidence to re-affirm Marijuana to the "most dangerous" list, Schedule I.

The Shafer Commission "recorded thousands of pages of transcripts of formal and informal hearings, solicited all points of view, including those of public officials, community leaders, professional experts and students. They conducted separate surveys of opinion among district attorneys, judges, probation officers, clinicians, university health officials and 'free clinic' personnel. They commissioned more than 50 projects, ranging from a study of the effects of marijuana on man to a field survey of enforcement of the marijuana laws in six metropolitan jurisdictions."

Shafer brought his report to the White House March 21, 1972. It was **1,184 pages** long.

A short summary of the Shafer Commission for pertinent points relating to the Public hearing on Autism as qualified diagnosis for the Michigan Marihuana Program in Lansing, MI on 5/28/2015:

"No significant physical, biochemical, or mental abnormalities could be attributed solely to their marihuana smoking... No valid stereotype of a marihuana user or non-user can be drawn... Young people who choose to experiment with marihuana are fundamentally the same people, socially and psychologically, as those who use alcohol and tobacco... No verification is found of a causal relationship between marihuana use and subsequent heroin use.... Most users, young and old, demonstrate an average or above-average degree of social functioning, academic achievement, and job performance...

"The weight of the evidence is that marihuana does not cause violent or aggressive behavior; if anything marihuana serves to inhibit the expression of such behavior... Marihuana is not generally viewed by participants in the criminal justice community as a major contributing influence in the commission of delinquent or criminal acts... Neither the marihuana user nor the drug itself can be said to constitute a danger to public safety... Research has not yet proven that marihuana use significantly impairs driving ability or performance...

-**Shafer Commission report** 3/21/1972

Cytokine levels higher in autism

Cytokines are small secreted proteins released by cells that have a specific effect on the interactions and communications between cells. Pro-inflammatory cytokines are involved in the up-regulation of inflammatory reactions. **[1]** Elevated pro-inflammatory cytokine levels are associated with autism spectrum disorders (ASD) **[1].** In ASD, as well as a number of conditions, the expression level of CB2 receptors increases in response to the inflammatory nature of the condition. **[2][3]** Given that CB2 is up-regulated, and that it's believed to play a neuroprotective role, CB2 is being investigated as a potential target for treatment of ASD. **[3]** CB1 variations modulate the striatal function that underlies the perception of signals of social reward, such as happy faces. This suggests that CB1 is a key element in the molecular architecture of perception of certain basic emotions. This may have implications for understanding neurodevelopmental conditions marked by atypical eye contact and facial emotion processing, such as ASC. **[4]** Endocannabinoids are key modulators of synaptic function. **[5]** Endocannabinoids regulate stress responses, in part via the modulation of the 5-HT system. **[6][7]** Additional targets of endocannabinoids (and exogenous cannabinoids), PPARα, PPARγ, and GPR55 expression levels have shown reductions in a valproic acid model of autism in rats.**[8]**

Toxicity

No signs of toxicity or serious side effects have been observed following chronic administration of cannabidiol to healthy volunteers (Cunja et al., Pharmacology 21:175-185,1980), even in large acute doses of 700mg/day (Consroe et al., Pharmacol. Biochem. Behav. 40:701-708,1991) but cannabidiol is inactive at the NMDA receptor **[9],** indicating that THC is warranted. According to **US patent 6630507**, safety is demonstrated by stating that in the presence of glutamate alone, and in the presence of glutamate and cannabidiol (CBD) or THC, it was demonstrated that CBD and THC were similarly protective.

Government patents on cannabinoid safety

United States patents specifically demonstrating evidence of safety:

NMDA receptor antagonism can be achieved with a subset of cannabinoids.
U.S. Pat. No. 5,538,993 (3S,4S-delta-6-tetrahydrocannabinol-7-oic acids),
U.S. Pat. No. 5,521,215 (stereospecific (+) THC enantiomers), and
U.S. Pat. No. 5,284,867 (dimethylheptyl benzopyrans)
have reported that these cannabinoids are effective NMDA receptor blockers.

Terpenes

Phytocannabinoids aid in neuroprotection against oxidative stress in patients affected with neurological diseases. In addition to the cannabinoids, terpens have been found to be helpful in providing CB2 activation. Caryophyllene is the only terpene known to interact with the endocannabinoid system (CB2). β–caryophyllene selectively binds to the CB2 receptor and that it is a functional CB2 agonist. Further, β–caryophyllene was identified as a functional non-psychoactive CB2 receptor ligand in foodstuff and as a macrocyclic anti-inflammatory cannabinoid in cannabis. **[16]**

Many of the other cannabinoids, terpenoids and flavonoids found in medical marijuana play a role in boosting the therapeutic effect of cannabis**. The FDA and other agencies have generally recognized terpenes as "safe."**

For example, humulene and caryophyllene displayed comparable anti-inflammatory responses to steroid alternatives. **[17]** Humulene was simultaneously effective in reducing inflammation and offering pain relief. **[18]** The oral effects of humulene were analyzed and the results suggested that again, this terpene was highly effective at reducing inflammation, proving its usefulness as a topical or oral supplement. **[19]**

Conclusion

There is evidence that aggressive autism behaviors can be explained by chemical imbalances in the body leading to a multitude of health concerns, including neuro-inflammation. Cannabinoids such as CBD and THC were found to be neuroprotective according to United States Patent #6630507 by the Department of Health and Human Services and many studies as presented above. Rather than causing harm to the developing brain, phytocannabinoids appear to aid in brain neuropsychiatric homeostasis. A strong support towards approval in this case will create relief on many levels.

Please call me directly for questions or concerns or further opportunities to clarify uncertainties,

Sincerely,

[redacted], MD

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My name is [redacted] and I would like to share the story of my 21 year old son as a testimonial to the powers of medical cannabis, which I have found to be nothing short of miraculous. [redacted] has severe autism and a history of severe self-injury and aggression towards others. We are originally from Wisconsin, where we lived until 2012 when we moved to Missouri. During the 2.5 years we were in that state, my son's behaviors became extremely violent. He was kicked out of school and out of an adult day program for individuals with developmental disabilities. He literally ripped half of his own bottom lip completely off and to this day has numerous scars on his hands and legs from other self-injury. He was abusive and dangerous to our entire family. We attempted to have him hospitalized in an inpatient psychiatric facility numerous times; around 30 attempts to get help for him over those 2.5 years but they only took him 4 times, for 4-5 days each stay. During those hospitalizations, they just kept adding more and more psychotropic medications until he was at a point where he slept up to 18 hours/day and when he wasn't sleeping, he was violent and self-injurious - increasingly so. He was taking up to 18 pills/day towards the end of our residency in that state.

My husband was given the opportunity to move again, and we chose California. I had just heard of cannabis potentially helping people on the autism spectrum. This was our very last hope to keep him home and keep him and everyone else within our home safe. I had no idea if it would work. I had always believed cannabis was nothing more than a bad street drug. I believed it made people lazy and that there was absolutely no value to it at all. After seeing a video of a young child taking medicinal cannabis which almost immediately ended his violent behaviors, I began to reconsider all I knew about it. By this point, we had nothing left to lose. We were already expecting to have to institutionalize my son in California if the cannabis didn't work and this was our absolutely final thing to try in order to keep him home, since none of the other medications we tried in the past had helped him.

We started the cannabis within a couple of months of arriving in our new state. The results were almost immediate. I could see a change in his demeanor. He looked so calm, made eye contact, and just seemed to be more "present" in our world. Three days after beginning cannabis, we went to a National Park and he smiled and posed for the camera on his own. Before this, it was very rare to get him to smile for a photo. Now he does it all the time. Everything preconceived notion I had about cannabis in the past was incredibly wrong. It has helped and began to heal my son more than anything else, ever.

We slowly began weaning him from those 18 pills he was taking. It took 7 months to remove them all, but it happened! It has now been 19 months since he stopped taking pharmaceuticals. He no longer sleeps 18 hours/day. Instead of being violent every single day, he might have a minor episode once every 3-4 months and it can generally be stopped in under 5 minutes. Before cannabis, it might have lasted all day long or we had to give him extra doses to make him sleepy so we wouldn't get beaten by him. It has changed his life and our entire family's lives drastically. He is happily living at home with us and we have no plans to find another home for him anymore. He also spends part of his days at a new day program with his peers and he seems to enjoy it. We no longer fear him or his future.

I am asking the State of Minnesota to add autism as a qualifying condition in your state's medical cannabis program. No child or adult should suffer needlessly. No parent should be prevented from trying everything they absolutely can to help their child. Zip codes and legalities should not be a reason a parent is unable to at least try every available option, especially one that is far less harmful than many of the pharmaceuticals they are oftentimes overprescribed. Please help this vulnerable population.

My son [redacted] was diagnosed with Autism at age 3..He didn't speak or respond to his name and was constantly flapping his arms. He would shriek uncontrollably and bang his head forcefully on the floor, walls, and doors. He was unconsolable. He was constantly moving and showed no interest in what others were doing or saying. He had unusual obsessions (the washer, the microwave, the ceiling, holes.) He has cycled through countless repetitive behaviors. Stomping, spitting, clearing his throat, jumping,pushing his younger brothers, pinching, spinning, and most recently echoing the same word or phrase. His aggression and destructive behaviors only got more intense with age. Punching himself in the face, biting his legs and arms, throwing his whole body on the floor, scratching until he bleeds, punching holes in walls, throwing objects. He has multiple scars and has given me 3 black eyes

He had no interest in his brothers and was unable to make eye contact, use gestures, or communicate in any way. He has been nonverbal for most of his life. Lack of communication led to much of the aggressive behaviors, but at times it was random and seemed like he was in pain..

He had Speech Therapy, but was unable to focus or follow simple directions. He did Occupation Therapy but was discharged due to "unknown underlying medical conditions." Kindergarten was a nightmare. He was left out of special events and spent most of his day in a room with only two other students. He was not allowed to join the mainstream classroom or participate in Kindergarten graduation because they did not want to upset him by changing his routine He started ABA (Applied Behavior Analysis) Therapy in August of 2015. The behaviors continued and we felt there was no choice but to try medication, in retrospect this was a mistake. Within a year my 7 year old son was on Buspirone,Tenex, Prozac, Klonopin, Hydroxyzine and Abilify. These medications had zero effect. put him to sleep, or put him into a violent rage. The risks outweighed the benefits.Risperdal was prescribed as a last resort, but thankfully he was re-evaluated and given a diagnosis of Tourette's Syndrome.

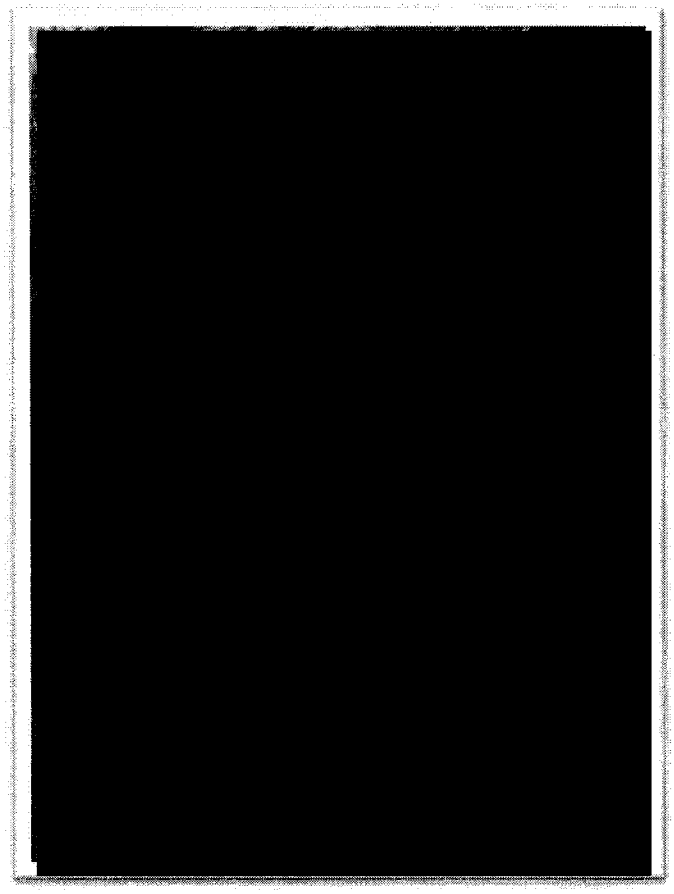
[redacted] was certified through the Medical Cannabis Program last November. While it has only been a short period of time, his quality of life has dramatically improved.He is able to communicate by speaking simple words and using his AAC (augmentative and alternative communication) device. He is generally in a very good mood and smiling. Eye contact has improved and he plays with his brothers.He can wave at us, label objects, and says mom and dad. He is of all other medications and is much easier to redirect and calm down. Of course we still have off times, but they are rare. I don't have to worry he will have an allergic reaction or hurt himself or others. Medical cannabis has given my family hope.

[redacted]

To whom it concerns,

My name is [redacted] I am the very proud mom of [redacted]

[redacted] is 11 yo and has severe autism, as well as Lowe Syndrome (brain/eye and kidney disease) and Tourettes. He has been certified to use Medical Marijuana in the State of MN for his Tourettes condition since September of 2016, nearly one year.



In his one year since beginning Medical Marijuana- [redacted] has potty trained daytime hours, he has learned to dress himself with 1:1 step direction, he is able to transition 80% better, his anxiety levels have been decreased significantly, he has returned to fulltime school and is doing well, he is learning new tasks all the time, he is playing appropriately with toys, he is interested in other children and joining in on their play, he is willing to eat new foods and eats them regularly (cucumbers, raw apples, carrots, almonds, walnuts) he is able to receive a haircut with electric clippers without any behavior. His kidney function has increased, he was functioning at 66%, last check he was functioning at 80%- recheck due in August.

[redacted] has been weaned off Abilify- please see side effects of this med. He has also weaned ½ off Risperidone, we had to stop weaning as the withdrawal was horrific- he remains at 0.5mg day, we are working up the courage to try again...the withdrawal was heartbreaking for all.

We are very fortunate to have a Tourettes diagnosis as it gives us legal access to Medical Marijuana, I come forward to petition with others again this year as I believe in this medicine, I believe in it- I'm living the difference and feel every person with Autism should have the same freedoms my son does.

Medical Marijuana has been life changing for my son and our entire family.

I wish to remain anonymous. My 17 year old son has been diagnosed with ASD, ADHD and Depression with Severe Anxiety. Over the years, his aggression (rage attacks) and anxiety have gotten worse. During a rage attack, he punches holes in the wall, smashes windows, bangs his head and breaks items by kicking or throwing stuff. Walking in our house resembles a battle zone. His siblings often lock their bedroom doors, barricaded inside, to avoid him and his behaviors. His anxiety has gotten so bad that he is unable to order food for himself at Mcdonalds or any sit down restaurant. He doesn't leave my side when we're in public as he's afraid of being abducted. He's tried Abilify and Risperdal for ASD, Adderall, Ritalin and Concerta for ADHD, Seraquil, Zoloft, Paxil and Hydroxizine for Anxiety. None seems to help. His current prescriptions are Adderal, Abilfy, and trazadone to help with sleep. My son hates taking these meds and often refuses as they make him feel "out of it", sick to his stomach with no appetite, and his body aches all the time, not to mention what these meds do to his sleep cycle. During his rage attacks he also bites himself, punches us (his parents), and cuts himself. He usually ends up restrained and the police are called to calm him down.

Recently, my son has been self-medicating with marijuana. We as parents disapproved strongly at first. However, since he started using, we've noticed a huge difference in his demeanor. He is calm, rational, happy and we no longer see any rage attacks. He's nice to his siblings and to us, his parents! I don't see him constantly worrying, he has an appetite and he is able to sleep without medications. Please consider adding ASD to the list of approved conditions for medical marijuana use. My son's happiness\life depends on it.

My son [redacted] - now 10 years old - was diagnosed with Autism at age 3. He also has ADHD, and Intellectual Disability. I knew he had this disease at 15 months old as he stopped meeting his milestones. He started screaming sometimes continuously on and off for days intermittently as if in pain, and beating on the right side of his head under the ear. Although [redacted] is verbal, his cognition is delayed to the level of a 3-4 year old. [redacted] can obey one step commands but no more.

Self-injurious behavior and aggression are the biggest concerns although there are many. [redacted] has adverse reactions to medications, limiting him to certain ones. One medication required me to have him transported by ambulance to the hospital for a very long admission. [redacted] has signs and symptoms of sub-clinical seizures, although numerous EMG's have detected nothing. I have recorded these episodes and others have admitted these episodes are possibly absent seizures.

[redacted] has had very thorough ABA therapy and treatment along with placement at a behavior facility in Wisconsin for one year. These approaches have not been effective. Redirection has only been successful 22% of the time. ABA has never been successful and has resulted in discharge of the ABA facility. [redacted] has head pain in the right back side the head in which he beats under the ear at full force – his hair has ceased to regrow in the area due to consistency of striking and digging in that area.

[redacted] is afraid of children thinking they will hurt him which makes [redacted] aggressive. We cannot go to waiting areas of clinics. We must be immediately directed to a quiet room or he will attack others due to noises. [redacted] needs to be reduced in his medications. Risperdone causes obesity and trying other medications causes adverse reactions. Depakote was used and continues to be used for aggression although recently [redacted] had a high toxicity and was admitted to the hospital. His head pain continues and there is no medication to calm and treat. Nothing works and Benzodiazepines cause adverse reactions.

I discharged [redacted] recently due to neglect at a Crisis home as another child abused him. I believe this could have been avoided if put on the program and [redacted]s cognition and verbalisation would have cleared a lot more up. I believe I have a right to this natural medication after multiple have failed and we have nowhere to turn.

My son also vocally ticks in the morning and randomly throughout the day. He has resorted to biting his forearms as his way of crying out in pain. Do I think he is in pain? Your doggone right I do. When a child tells you that, you don't consider them a liar.

These strong medications need to be reduced and I believe Medical Cannabis administration is the key to keep [redacted] healthy. Please make Autism a qualifying condition to help my child - I feel I have tried everything and I don't want to lose my child. I believe after reading about the endocannabinoid system and the benefits of getting [redacted] certified by the Minnesota Medical Cannabis Program that we could save [redacted]'s life and save lots of time and money spent. The expense of multiple admits, inpatient facilities, safety of others and safety of a suffering child, far out way the benefits of the medication itself.

Thank you for understanding my concern.

[redacted]

Please see photos on following page.

My name is [redacted]. I'm the mother of a 14 year-old boy named [redacted]. [redacted] has severe Autism and a seizure disorder. [redacted] began having seizures in June of 2011. We have tried many medications over the last 6 years, however seizures and motor tics continued to be an issue.

[redacted] had always been a kind and affectionate boy in his younger years. When [redacted] turned 13, the onset of puberty brought new challenges. In February of 2016 [redacted] became extremely violent toward both family and school staff. He began raging daily and would physically attack us. It got to the point where we as his family needed to wear protective clothing to avoid being bitten, having our hair pulled, and being kicked and punched. His younger sister could not be in the same room and she had to spend all of her time at home locked in her room for her own protection.

In August 2016, [redacted] began to turn the violence on to himself. He began punching himself in the head full force thousands of times per day. He would use his knee to injure his teeth. He would bang his head into walls. We were powerless to stop him. We were trying to protect him using helmets, arm immobilizers and at times we had to physically restrain him for hours at a time to keep him from harming himself. We believed our son was in terrible pain and was suffering from debilitating headaches. We saw this once vibrant boy lose his will to live. He seemed determined to end his life and came close several times. Between October 2016 and January 2017, [redacted] was hospitalized 3 times. He suffered self-inflicted skull fractures and massive tissue damage. He had black eyes and giant hematomas on his skull regularly. The hospital staff offered psychiatric medications as well as gabapentin but nothing could stop the daily rages that lasted every moment that he was awake. I felt certain that if we could not get [redacted] cannabis that he would find a way to end his life.

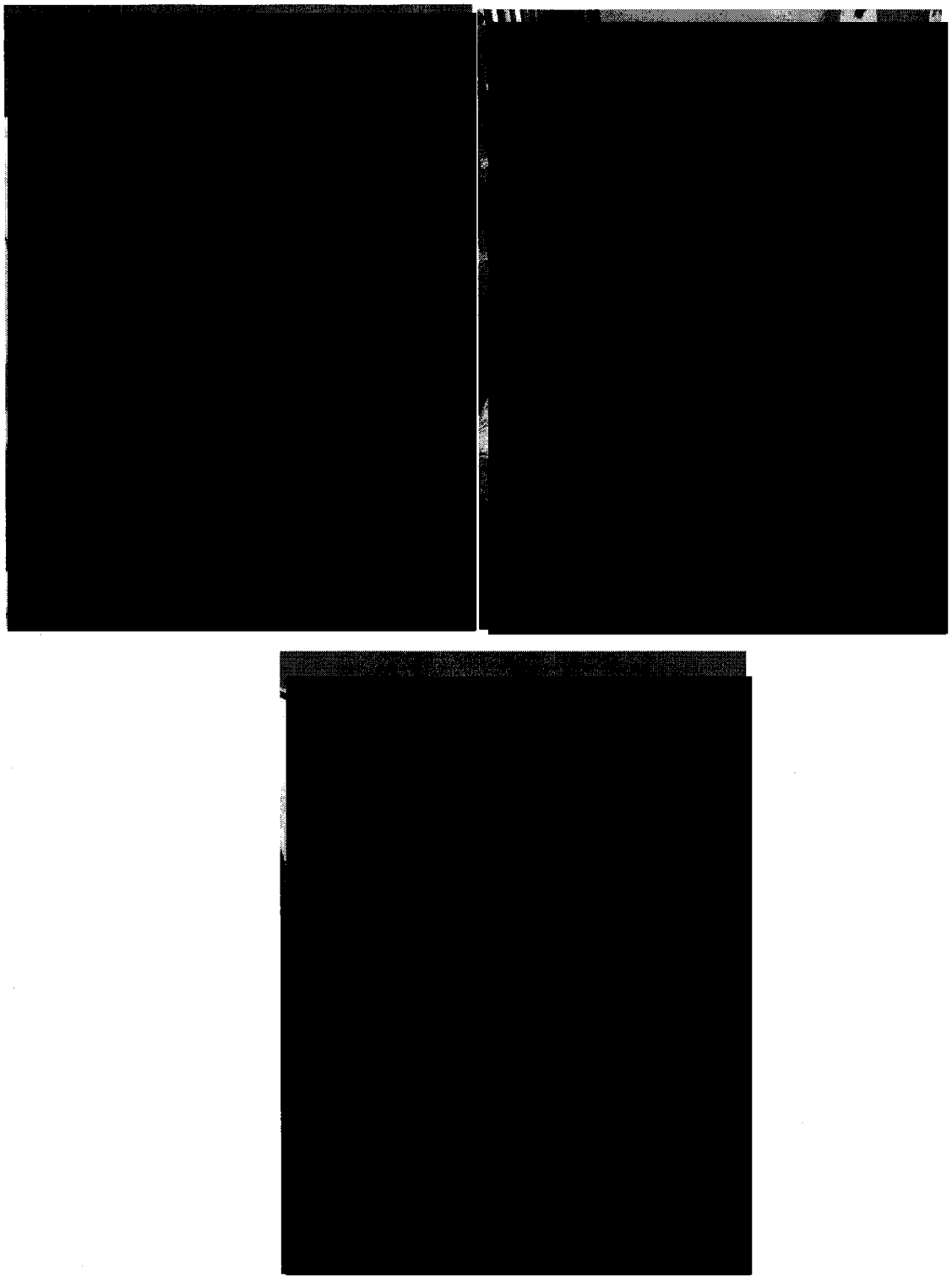
[redacted] qualified for cannabis through the state program because of his seizure disorder. After being sent home from Children's Hospital in Minneapolis after another life-threatening episode of self-injury with no plan in place to heal our son we felt cannabis was our only hope. The excruciating pain our son was in was getting worse and we knew no pharmaceutical medication could help him. We had tried everything the doctors offered and had absolutely no success.

We enrolled him in the Minnesota Cannabis program in January 2017. Within a week of beginning cannabis therapy [redacted] was able to go about an hour without harming himself. As the weeks went on and we reached a therapeutic dose, [redacted]'s behaviors began to slowly melt away. By early March he was smiling again. Within 6 weeks of beginning cannabis [redacted] was no longer injuring himself or others. He began to take an interest in his life again. He returned to school full time. We were able to remove his helmets and protective gear. By mid-March we were getting smiles and hugs. [redacted] began to go outdoors again by mid-April. By May [redacted] began to show interest in using augmentative communication for the first time in his life.

It is now late June. We have not seen 1 episode of self-injury since early March. [redacted] has not struck me since February. [redacted] is enrolled in a day camp for children with special needs where he spends 8 hours a day. He is exploring outside and making friends. He is happy and smiling. [redacted] and his sister have a relationship once again. [redacted] spends hours in our backyard enjoying bouncing on his trampoline, moving his body and taking in fresh air. He lives safely and happily in our home. He is free from pain. His seizures and motor tics are well managed to the point they are not interfering in his daily life.

Cannabis gave us our beautiful son back. [redacted] is alive and well today because of this miracle medication.

On the following page are photos of my son before cannabis therapy and after.



[redacted], MD
[redacted]

Woodbury, New York 11797

July 15, 2017

Re: [redacted]

To whom it may concern:

[redacted] has been a patient of mine for 10 years. He was diagnosed with autism spectrum disorder; PDD-NOS, speech and language delay. After many years of biomedical investigation, it was determined that [redacted] also had inflammatory bowel disease (IBD), mitochondrial disorder, occult bacterial infections in the gastrointestinal tract, heavy metal poisoning, seizures and metabolic problems. He has intermittently failed to thrive. He suffers from extreme anxiety and obsessive compulsive behaviors that often present as aggressive self-injurious behavior and aggression to others. This is typical of adrenal insufficiency and dysregulation of the hypothalamic-pituitary- adrenal axis (H-P-A axis)

Recent reports based on past and present medical literature support the use of essential oils from the cannabis plants or medical marijuana. Cannabis therapy is now legal in New York State . Cannabis has been shown to be anti-inflammatory and antimicrobial in its function via activation of the endocannabinoid system. It also has a regulatory effect on the H-P-A axis. Clinical effects that have been observed are optimization of bowel function, reduction of inflammation when IBD has been confirmed. It has served as an antiepileptic often with better results in autistic patients than the usual pharmaceutical anti-seizure drugs. Cannabis has been used in children since the 1930's and continued to be part of the pharmacopeia in the US until the 1960's. It has an excellent safety profile, is not addictive and has no known overdose issues.

I have recommended that [redacted] be considered for legal use of cannabinoids to aid in the treatment of his IBD, OCD, anxiety, pain and seizures. I thank you for your consideration in the care of this special needs boy. If you have any questions feel free to contact me at this office.

Sincerely yours,

[redacted] MD

July 16, 2017

Dear Legislator,

I am writing to you today to ask for your support in making medical cannabis available for pediatric use in patients with autism.

I am a board certified registered nurse and mother to a fourteen-year-old son recovered from autism. I have been a practicing nurse for twenty-three years and have worked in all facets of patient care with most of my experience in large, university setting, acute care hospitals. I also practice as an independent legal nurse consultant, working on litigation for vaccine injury claims filed with the United States Federal Claims Court under the National Vaccine Injury Compensation Program.

I am the co-founder/co-director of AIM, Autism Is Medical, a 501(c)(3) that supports efforts focused on educating parents, practitioners, and school personnel on the underlying medical issues that affect children and adults diagnosed with autism spectrum disorder. It is our strong belief and mission that all patients with autism should have the same access to an appropriate diagnostic investigation of their health problems as all other patient populations. Patient centered focused care is the standard of practice in all settings and we will continue to promote the inclusion of this large group of medically complex individuals. This non-profit was created by myself and two other mothers, who both have children with complex health issues and a diagnosis of autism.

Providing comprehensive medical care is driven by national goals and patient centered care is that model. Providing the patient what they need to regain health and treating them based on their individual health care needs is the standard of practice. In care of our pediatric patient population, the medical home model is that standard and provides the most comprehensive, multidisciplinary medical management of children who have chronic illness, are medically fragile and those that live with illnesses affecting them globally. These children require cutting edge diagnostic and therapeutic treatments provided by highly skilled practitioners. Children affected by autism, are at the pinnacle of this need for the most comprehensive, most cutting edge, and most effective treatments. Autism is a neurobiological disorder and can affect all systems of the body.

Children with autism have a high prevalence of other medical illnesses including gastrointestinal disorders, seizures and epilepsy, anxiety, allergies, recurrent infections and metabolic disorders including mitochondrial disease (Frye, 2015). There are many children with a diagnosis of autism that are considered medically fragile. These children may have severe refractory seizure disorder that does not respond to traditional pharmaceutical management. Some children suffer from upwards of forty to sixty seizures daily. Children with autism suffer from altered pain response and atypical expression of pain including self-injurious behaviors. These can be severe and can cause trauma sometimes requiring emergency medical attention (Courtemanche, Black & Reese 2016). Our medical systems are not well equipped, or adequately trained to serve this ever growing patient population. Our emergency rooms are not able to accommodate the expanding numbers of adult-sized pediatric patients with severe autism that are brought for treatment of escalating behaviors or the resulting injuries. These children need to have available to them, all the possible treatment modalities that may help treat their symptoms and alleviate the devastating effects of these serious medical problems.

The American Academy of Pediatrics policy states, "medical care of infants, children and adolescents ideally should be accessible, continuous, comprehensive, family centered, coordinate, compassionate and culturally effective," and goes on to say that, "physicians should seek to improve the effectiveness and efficiency of health care for all children and strive to attain a medical home for every child in their community" (AAP,2002).

This clearly outlines that pediatric care must be continually improving to provide the most effective treatments to those who are in need. This comprehensive plan of care must include medical cannabis for pediatric use. By not supporting making medical cannabis available to pediatric patients in your state, you will be denying them the opportunity to have access to all of the treatment modalities that are available to remediate some of the devastating effects of autism, seizure disorder and other debilitating illnesses.

My journey began with my now fourteen-year-old son being diagnosed on the autism spectrum before the age of three. He was low verbal at having under ten words, had severe auditory processing disorder preventing him from being able to communicate or express himself. His brain was unable to process speech and he did not recognize language. More difficult to obtain treatment for, where his underlying severe medical issues. Those included small bowel disease, abnormal EEG, failure to thrive, lymphopenia and multiple allergies. My son had severe bowel disease which prevented him from absorbing any nutrients. At age seven, he weighed thirty-nine pounds and was very sick. After extensive treatment of his underlying medical diagnoses, along with intensive therapies, he has recovered from autism and his bowel disease is in remission. He has been formally evaluated and his diagnosis of autism spectrum disorder removed. He is a happy, healthy and independent teenager who requires no assistance in school, and will go on to attend college and be a successful adult. This was only possible with him receiving patient centered care. His specific needs were met when he received targeted medical diagnostic testing and treatment. This should be available to all children.

Nurses as their primary role, are patient advocates. It is within this framework I ask you to support medical cannabis for the use in the pediatric population. Autism is a neurobiological

disorder with devastating associated serious health issues. Patients and families have a right to choose their treatment based on individual need. Medical cannabis can be used to decrease many of the symptoms and there have been many parent reports that it has substantially decreased seizure activity. Cannabinoids offer neuroprotective and antioxidant effects and can improve behaviors, decrease anxiety, and assist with sleep disturbances. Pharmaceutical options available today are often not metabolized well in children with autism, who have altered mitochondrial and metabolic function. Dangerous side effects and long term consequences of antipsychotic use in children, often the first line of treatment, have been well documented. It is imperative that legislators and health care providers work to ensure that children have every available resource and treatment option to improve the quality of their health and life.

Thank you in advance for your critical attention to this important need to serve the children of your community. Please do not hesitate to contact me for any reason. I look forward to hearing about this important legislative initiative moving forward with your support.

Respectfully,

[redacted] RN-BC, PCCN, LNC

References

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American Academy of Pediatrics (2002). The medical home: medical home initiatives for children with special needs project advisory committee. *Pediatrics,* 122(2), 184-186. doi:10.1542/peds.110.1.184, retrieved from http://pediatrics.aappublications.org/content/110/1/184

I am a mother of a 10-year-old boy. We did not learn about his Autism Spectrum Disorder until he was 7 1/2 years old. Looking back now, we can see the signs were there in a subtle way starting from infancy. It was at age 6, when he was ready to move to a mainstream school, that his challenges became more apparent. The dominos kept being pushed, and my boy kept having a harder and harder time. He went from being a happy and clever and confident child, to frustrated, sad, anxious and self-doubting in a fairly short amount of time. When we were told that he has High Functioning Autism Spectrum Disorder, we, as parents, grieved. In our grief, we pushed and plugged forward. School was there for us and there has been constant support and communication as changes are happening frequently.

Our son's ASD manifests as high anxiety, and quick triggers. He becomes frustrated with anything that he perceives as a block to a goal or need. He has the emotional maturity of a 3-4-year-old. He has an emotional response and is overwhelmed to what I would compare to a person experiencing a PTSD reaction. He experiences sensory input more than a typical developing person does, and the overwhelming sensory overload leads him to deep frustration and a fear response. He yells and cries and gets in a looping thought pattern that keeps himself stuck in that trauma reaction. These episodes have become a serious block for social interaction and development since other children cannot understand what is happening for him or why he is yelling at them. His ability to understand his own emotions and express his needs and wants as well as lack of problem solving ability keeps other children from wanting to interact. It even triggers other children into pushing buttons to elicit an outburst because it seems "funny" to them. Now we have bullying happening with that. He also has ongoing stories happening in his mind, and he retreats into a world within his imagination. It has become increasingly difficult to get him out of the stories and the retreat world within his head. From all of this, we now have a highly anxious and depressed child. He is a highly intelligent child. With his smarts (high IQ), he actually is aware that he is different from others. He sees that he reacts and experiences things differently, and he knows that it is hard on others. With that, he also knows that he is not able to stop it. With this, he experienced not only sadness, but a deep loneliness. Talk of suicide began at age 9. As he came into the school from recess, a staff-member noticed that he was walking slowly and looking down rather than his typical demeanor. The staff-member asked him what was on his mind and he said that he wished that he had a rope so that he could hang himself. Further discussion of these feelings revealed that his first thoughts like this actually began internally at age 7.

He has been on Adderall XR (amphetamine salts), a stimulant for treating his inability to focus and attention. This has been helpful with focus, but he has had an increase of anxious behavior and panic attack/ PTSD-type trauma reactions. Although I brought this up and asked what we could do differently over numerous visits to his prescribing Nurse Practitioner, she never had any answer except for adding more pharmaceuticals. I am in the Health care industry, and I am not against medications when used appropriately. We added Intuniv (guanfacine extended release) for his impulse control, and that helped, but the anxiety and panic and

frustration tantrums kept getting worse. The clinician suggested a few times that an anti depressant and then after that, a mood stabilizer could be tried. This is where I drew a line. Anti depressants in youth can actually increase the risk of suicidal thoughts, and with an already suicidal boy, that is not an option for our individual child. The mood stabilizers also come with side effects that we refuse to risk. Other medications suggested have frightening side effects and if ever we wanted to take him off of them, risks with withdrawal symptoms are unacceptable.

I am a very scientific thinker, so I read and researched various articles, both academic and anecdotal. The idea of Medical Cannabis crossed my path. From my detailed searches, I found that children are medicated using medical cannabis and they are NOT getting high. I learned about Cannabidiol (CBD), which does not have the psychotropic effect on people. I did not like the idea of Tetrahydrocannabinol (THC), because I did not want to risk my kiddo getting "high" and also because, it is against the law. I found products that we could legally obtain with whole plant extractions of CBD, and purchased CW Advanced. I connected with a non-profit group in Colorado, and they directed me to the "start low and go slow" method. We gave our son his first very small dose of CBD oil on April 19th in the evening. We used the guidance of the non-profit group, and found a dose based on his weight. Within a just over two weeks of adding CBD to his treatment plan, we received an email that said,

> *" Hello All-*
> *I hope [child's name removed] is feeling better.*
> *I wanted to let you know that [he] had a really good week. He was focused, on task, flexible, and able to recover quicker from bumps in the road. It was a drastic improvement from the past couple of weeks, regarding his flexibility and focus."*

His father and I both were seeing improvements at home with his communication and seemingly easier time recovering from frustration. With a lot of research, I found a way to obtain cannabis strains that have THC and are found to be helpful for other parents that have a child similar to mine. As a parent desperate to treat my child, I crossed a legal line. I traveled to a "legal" state and purchased a few strains with guidance from other parents who are further along in their journey. As his parents, we agreed that we would try this in secret.

What we saw since adding a tiny amount of THC is beyond even what we had hoped for. Within a week of adding THC as medication, we watched our child face a challenge that lasted over two hours, and instead of having a full out breakdown, he worked through it. He told himself after repeated "failure" things like "You can do this" and he just tried over and over. He also accepted corrections, which he typically never would without high defensiveness and anger. That was just a start. He was also having real back-and-forth conversations with us as well as peers and other adults. His eye contact greatly increased, and he even began asking other people their thoughts and about how they were doing. He never before would ask someone "How are you" even. His thoughts began to be outside of his inner focus and inner world. Something simple, but noticeable is that he never looked into a camera and he could not smile on command. It took someone else to point

out to me that he was not only looking at the camera, but he was smiling....as in a real and genuine smile! We continue to see him blossom socially. He has found an awareness of his emotions and identifying them to himself, and sharing them with people around him. He is open to listening to ideas to improve outcomes where defensiveness would have blocked him before. He is having fun again and interacting with other children much better. His awareness is reaching out of his own world that he had been trapped in prior to treatment involving Cannabis. We are parents who are successful in our careers and social lives. We have been law-abiding citizens up to the point of desperately seeking medication that has not been available in our state for our child. Please consider making Medicinal use of Cannabis available to our son so that we can legally treat his Autism Spectrum Disorder under medical guidance within our own state of Minnesota.

Thank you for considering adding Autism Spectrum Disorder a qualifying condition under Minnesota's Medical Cannabis program.

With Great Hope,
*A loving Mother

*For obvious reasons, I wish to remain anonymous.