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Department of Public Health public hearings on proposed regulations at 105 CMR 725.000

Testimony of Elizabeth Anne Thiele, MD, PhD

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My name is Dr. Elizabeth Anne Thiele, and I am the Director of the Pediatric Epilepsy Service at Massachusetts General Hospital and a Professor in Neurology at Harvard Medical School. My primary office is located at 175 Cambridge Street, Suite 340, Boston, MA 02114-2796.

I received my medical degree and PhD from Johns Hopkins University School of Medicine in Baltimore, Maryland and completed an internship and residency in pediatrics at the Johns Hopkins Hospital. I also completed a second residency in child neurology and a postdoctoral research fellowship in neurology at Children's Hospital in Boston. A copy of my curriculum vitae is attached hereto.

Based on a review of the literature and first-hand experience treating pediatric epilepsy patients, it is my opinion that medical marijuana—and, particularly, the non-psychoactive ingredient in medical marijuana, cannabidiol (CBD)—may have substantial medical benefit for pediatric epilepsy patients, as well as significantly fewer adverse side effects than many of the other anti-epileptic therapies available today. Accordingly, I believe the proposed regulation's proscription of the use of medical marijuana by children under 18 who do not have a "life-limiting illness"—*i.e.*, an illness for which "reasonable estimates of prognosis suggest death may occur within six months"—would do a significant disservice to the pediatric epilepsy population in Massachusetts.

Epilepsy impacts more than 1% of the population worldwide and is the most common neurologic disorder of childhood. Approximately one-third of all children with epilepsy have seizures that are refractory, or unresponsive, to pharmacologic treatment, or experience intolerable side effects from available antiepileptic medications.[1] As a consequence of repeated seizure activity, many of these children also have significant comorbidities, including cognitive delay or regression, behavioral disturbance, social disabilities or maladjustment, sleep disturbance and injury.[2] Additionally, many of the anti-epileptic drugs available to treat pediatric epilepsy patients have well-documented side effects that can impair cognitive development, behavior, memory, attention and mood.[3]

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1 Kwan P, Brodie MJ. Effectiveness of first antiepileptic drug. Epilepsia. 2001; 42(10): 1255–1260.

2 Duchowney, Michael S. and Blais Bourgeois, Coexisting Disorders in Children with Epilepsy. Advanced Studies in Medicine. July 2003 (3): S680-683.

3 Loring, David W., Cognitive Side Effects of Anti-Epileptic Drugs in Children. Psychiatric Times. Sept. 2005 (22).

Numerous studies performed in the past 40 years have demonstrated the anticonvulsant effects of CBD both in animal models[4] and in human adults.[5] In a double blind, placebo-controlled study showing that CBD reduces seizure activity, the most commonly reported side effect was somnolence, and no patients reported any psychotropic effects.[6] Indeed, studies suggest that CBD has no negative impact on psychomotor or psychological functions.[7] Although the impact of CBD on seizures has not yet been studied in the pediatric population, several of my colleagues and I plan to commence a clinical trial in the near future to demonstrate the safety, efficacy and tolerability of CBD in children with intractable epilepsy.

CBD is not yet pharmacologically available in the United States, although it is currently in clinical trials to treat spasticity related to multiple sclerosis and is currently licensed for this treatment role on over 20 countries (GW Pharma, UK).

In the United States, in those states where marijuana has been legalized for medical use, growers have been able to breed plants that have better than a 30:1 ratio of CBD to THC.[8] In other words, marijuana plants are available that have all of the medical benefits of CBD with virtually no psychoactive ingredient. Moreover, although the American Academy of Pediatrics has expressed concern about certain reported side effects of marijuana use—namely, "negative effects on short-term memory, concentration, attention span, motivation, and problem solving" and "adverse effects on coordination, judgment, reaction time, and tracking ability"[9]—studies suggest that these side effects are caused by THC, and not CBD.[10] Accordingly, these potential side effects are of significantly less concern when patients are treated with marijuana derived from plants with high CBD to THC ratio.

My colleagues and I have witnessed the dramatic effect of CBD on many of our pediatric patients. For example, I have a pediatric patient with severe intractable epilepsy who had been experiencing up to 100 seizures every day, despite trials of 18 antiepileptic drugs. After CBD was introduced into his treatment regimen, his seizures decreased dramatically.[11] He now has between 0 and 5 seizures a day. He is also more alert, and turns out to have a wicked good sense of humor.

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4 Consroe, P., Benedito, M.A., Leite, J.R., Carlini, E.A. & R. Mechoulam. Effects of cannabidiol on behavioral seizures caused by convulsant drugs or current in mice. Eur J Pharmacol. 1982; 83(3-4): 293-8. Izquierdo, I. & M. Tannhauser. The effect of Cannabidiol on maximal electroshock seizures in rats. J Pharm Pharmacol. 1973; 25(11):916-7. Karler, R. & S.A. Turkanis. Subacute cannabinoid treatment: anticonvulsant activity and withdrawal excitability in mice. Br J Pharmacol. 1980; 68(3): 479-84. Turkanis, S.A., Smiley, K.A., Borys, H.K., Olsen, D.M. & R. Karler. An electrophysiological analysis of the anticonvulsant action of Cannabidiol on limbic seizures in conscious rats. Epilepsia. 1979; 20(4):351-63.

5 Cunha, J., Carlini, E.A., Pereira, A.E., Ramos, O., Pimentel, C., Gagliardi, R., Sanvito, W.L., Lander, N. & R. Mechoulam. Chronic administration of Cannabidiol to healthy volunteers and epileptic patients. Pharmacology. 1980; 21:175-85. Mechoulam, R. & F.A. Carlini. Toward drugs derived from cannabis. Naturwissenschaften. 1978; 65:174-9.

6 *See* Cunha et al., *supra* at Note 5.

7 Bergamaschi, M.M., Queiroz, R.H., Zuardi, A.W., & J.A. Crippa. Safety and side effects of cannabidiol, a Cannabis sativa constituent.Curr. Drug Saf. 2011;6(4):237-49.

8 THC refers to Tetrahydrocannabinol, the psychoactive ingredient in the marijuana plant.

9 Legalization of Marijuana: Potential Impact on Youth. Pediatrics. 2004 (113): 1825-26.

10 Turkanis S.A., Smiley K.A., Borys H.K., Olsen D.M., Karler R. An electrophysiological analysis of the anticonvulsant action of cannabidiol on limbic seizures in conscious rats. Epilepsia. 1979;20(4):351-63.

11 This patient currently resides in California, where the use of marijuana for medicinal purposes is legal.

I have heard numerous similar reports from my colleagues practicing in California, Colorado and abroad, where medical marijuana and/or pharmaceutical CBD are available. These anecdotal reports are support by a recently completed survey conducted by researchers at Stanford of parents of children with severe childhood epilepsies who are treating their child's seizures with high CBD to THC ratio marijuana plants. 70% of parents reported a decrease in seizure frequency of >50% after starting this treatment, and only 15% saw no change in their children's seizure frequency. Additionally, these parents reported very few negative side effects from marijuana use. In fact, the most commonly reported side effects were better sleep, increased alertness and better mood. 11 of the 20 parents (55%) also were able to wean their children from an average of two anti-epileptic drugs. Thus, not only does this survey suggest that CBD dramatically reduces seizure activity in pediatric patients with intractable epilepsy, it also demonstrates an improvement in the patients' quality of life.[12]

I recognize that use of medical marijuana to treat pediatric patients is a controversial topic, and that it may not be appropriate in all circumstances. But, unquestionably, there are numerous pediatric patients with intractable epilepsy residing in Massachusetts for whom the use of high CBD to THC ratio marijuana plants may be the best available treatment at this time. Generally, these patients are not likely to die within the next six months; rather, their seizures are a chronic, debilitating problem with significant comorbid conditions that are only exacerbated by many of the available anti-epileptic drugs.

By confining the use of medical marijuana to pediatric patients who have a "life-limiting illness," the proposed regulations eliminate a potentially life-altering treatment for these patients. In my view, this limitation is both unwarranted and unnecessary. The proposed regulations contain numerous procedural safeguards that are more than adequate to ensure that marijuana is only administered to pediatric patients when it is medically beneficial to do so.[13] DPH should trust in these procedural controls, rather than universally and categorically denying children with debilitating medical conditions access to treatment that has the potential to dramatically improve their health and quality of life.

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[12] This survey will be presented in abstract form at the NINDS Curing the Epilepsies Meeting 2013 (Apr. 17-19).

[13] For example, the proposed regulations require that pediatric patients must be "diagnosed by two Massachusetts licensed certifying physicians," and must have a designated "personal care giver" who will be responsible for administrating his or her treatment.