Marijuana Legalization Position Statement

Approved by the OPPA Council on Oct. 3, 2015

In November of 2015, Ohioans will decide whether to amend the state constitution to permit both "medical" and recreational use of marijuana. As arguments have largely been motivated by politics and financial interests, the Ohio Psychiatric Physicians Association (OPPA) identified a need for a consensus opinion based upon scientific and medical knowledge. An initial draft was developed by the OPPA's Addiction and Pain Control Committee after extensive review of existing position statements, scientific studies, and discussion amongst its members. Under each statement or position, a brief review of the literature supporting the position was developed. The draft position statement was then presented to the OPPA Council for approval. The position of the OPPA opposing the legalization of marijuana – either for medical or recreational use – are outlined below.

1. **Marijuana, as a plant, is not a medicine. Several compounds contained in marijuana may have therapeutic potential and the government should promote research to identify these and to determine their optimal dosing and toxicity. For these reasons, the OPPA believes that it is not acceptable medical practice to recommend that patients use marijuana.**

Marijuana contains over 400 chemicals, including nearly 70 cannabinoids (chemicals unique to marijuana), all in varying combinations. This precludes standardization of ingredients or dosage. It is almost meaningless to ask, for example, whether "marijuana" is useful for a given condition, when one plant may be high in tetrahydrocannabinol (THC) and another high in cannabidiol and another high in both. Pharmaceuticals, in contrast, contain defined amounts of specified compounds, which have been studied for safety and efficacy.

Prescribing of such substances may also place physicians and patients at legal risk as Federal law still holds such practice illegal regardless of the state's position.

Many of the chemicals contained in marijuana and their synthetic analogues are of pharmaceutical interest and 2 are FDA-approved in the United States as medicines. Dronabinol (Marinol ®) was approved in 1985 for intractable nausea associated with cancer treatment and nabilone (Cesamet®) is approved for nausea and neuropathic pain.

Sativex® contains THC and cannabidiol in equal concentrations and is approved in 27 countries outside the US for muscle spasticity associated with multiple sclerosis. The manufacturer has submitted an application phase-III study for this indication in the US. It is also in phase-III trials in the US for cancer pain.

Epidiolex ® contains pure cannabidiol and is being studied in the US as an anti-epileptic medication. It has also been shown to have antipsychotic activity (Gerra G et al, 2010; Scuderi C et al., 2009).

Rimonabant® is a CB-1 receptor antagonist; i.e., it blocks naturally occurring cannabinoids. It was briefly available in Europe for appetite suppression and smoking cessation. It has also been shown to have antipsychotic efficacy (Roser P et al., 2010). It has not been approved in the US due to its potential to increase depression and suicidality (Bostwick JM, 2012), and it was removed from European markets for the same reason.

The current uncertainty about the benefit and toxicity of marijuana is in part because research has been impeded by its Schedule I designation. (D'Souza DC et al., 2013). It is essential that the government promote research to address the gaps in our knowledge.

2. **The current process for vetting pharmaceuticals through the FDA is the best process we have to ensure purity, sterility, concentration, effectiveness, and safety**. The FDA approval process is well-designed to ensure that drugs are marketed only after demonstrating safety and efficacy. The prospect of individual states making this decision based on the opinions of voters and legislators rather than science is daunting.

3. **Smoking is not an acceptable delivery mechanism for medicines**. Marijuana smoke contains both carcinogens and pulmonary irritants. Additionally, there is little data on what happens to the substances contained in marijuana when they are burned and the danger that combustion products may lead to health concerns.

4. **The public should be made aware of the evidence of medical and psychiatric harms resulting from the use of marijuana**. In the public forum, marijuana is often pitted against alcohol in an attempt to debate which substance is more deleterious to the individual and to society in general. While the public is aware of the harms associated with drinking, those caused by marijuana are less appreciated. These include: cognitive impairment and changes in brain structure and functioning, increased risk of psychosis, accelerating the development of schizophrenic symptoms, exacerbation of anxiety and depression, the dangers of drugged driving, and an increased likelihood of using other illicit substances (the "gateway" phenomenon).

Marijuana has been shown to impair cognition – especially in adolescents (Pope, 2003) (Gruber SA, 2011). A study that followed marijuana smokers over a 25 year period found that chronic use was associated with an eight point decline in IQ that persisted despite sustained abstinence (Meier MH, 2012).

Another revealed that recreational use was associated with a change in size of the amygdala and the nucleus accumbens (Gilman JM, 2014). A third study revealed diminished activity in the prefrontal cortex

and decreased size of the hippocampus in marijuana users (Batalia A, 2013). The implications of these structural and functional changes are unknown but concerning.

There has been increasing evidence of an association between marijuana smoking and chronic psychosis. Marijuana smoking has been shown to increase the risk of developing chronic psychotic disorders including schizophrenia (Kuepper et al, 2011). A review of 83 studies showed that in those predisposed to psychosis, marijuana smokers experienced onset of psychosis earlier than non-smokers (Large M, 2011).

Many users of marijuana report that they use it to self-medicate anxiety and depression. While it may indeed have an acute anti-anxiety effect, studies show that chronic use worsens anxiety and can induce panic (Crippa JA, 2009). With regard to depression, heavy use of marijuana has been shown to be not only ineffective, but to actually worsen depression (Degenhardt L, 2003).

The risks of driving while under the influence of marijuana have been minimized by its advocates; however, it is the illicit drug most commonly associated with impaired driving and fatal accidents (Brady JE, 2014). The risk of an accident nearly doubles when one drives soon after smoking marijuana (Hartman RL, 2013). Studies in driving simulators have shown a correlation between impairment and blood THC level (Lenné MG et al., 2010). A major impediment to reducing driving while impaired is the lack of technology to allow police officers to test THC levels at roadside.

Perhaps the most frequently asked question regarding the issue of marijuana legalization is whether it is a "gateway drug." Most epidemiologic studies have reported that those who smoke marijuana have an increased likelihood of later developing abuse and addiction to other drugs (Agrawal A, 2004) (Hall W, 2007). THC, like alcohol and tobacco, can amplify the way that the brain will respond to other drugs of abuse (Panlilio LV, 2013). More specifically, exposure to THC in utero and in adolescence has been shown to impact the responsiveness and developmental regulation of dopamine-producing neurons in the nucleus accumbens (Pistis M, 2004) (DeNieri JA, 2011). The overall impact of THC on brain responsiveness and the specific changes noted in the reward pathway may explain why THC might sensitize the brain to the addictive potential of other substances.

5. **The public should be made aware of the addictive potential of marijuana**. Although its withdrawal symptoms are less dramatic than those of alcohol and heroin, marijuana has compellingly been shown to be addictive. Of those who have ever smoked marijuana, 9% of adults and 17% of adolescents will eventually meet criteria for addiction (Lopez-Quintero C et al., 2011). Adolescents are at particularly high risk as their brains are still developing and changing into their 20's (Gotgay N, 2004). Of the 5.1 million Americans who are addicted to an illicit drug, over half (2.7 million) are addicted to marijuana (NSDUH, 2012). Though the addictive potential of marijuana is lower than most other illicit substances, more Americans are addicted to it because of its widespread use.

6. **Arguments that legalization of recreational marijuana would mitigate needless incarceration are unjustified, given that Ohio has already decreased legal sanctions for marijuana possession.** Individuals convicted of possessing 100g (enough for nearly 200 marijuana cigarettes or "joints") are subject only to a $150 fine with no incarceration.

7. **Legalization of recreational marijuana will be interpreted by many, especially the young, as an indicator that it is safe**. Studies have compellingly shown that perceived safety correlates with experimentation and use. Therefore illegal but decriminalized is the proper stance for the State of Ohio. It communicates that the drug is unsafe, but that the state won't cause more harm than the drug does.

It is the intent of the OPPA that doctors, citizens, and legislators in the State of Ohio give careful consideration to the positions put forth in this document regarding marijuana legalization. These positions do not represent an exhaustive list, but were meant to represent the most solid positions discussed by this committee with which there was overwhelming consensus opinion. We hope that they will serve as a starting point for ongoing discussion about this critical issue as it enters into the political arena in the State of Ohio.

This position statement was developed by the following members of the OPPA Addiction and Pain Control Issues Committee: Jason Jerry, MD (Chair); Ed Covington, MD; Kettlie Daniels, MD; Jeffrey Goldsmith, MD; Dennis Helmuth, MD; Dan Hosta, MD; Steven Jewell, MD; John Vraciu, DO.

REFERENCES:

Agrawal A, Neale MC, Prescott CA, Kendler KS. A twin study of early cannabis use and subsequent use and abuse/dependence of other illicit drugs. Psychol Med. 2004 Oct;34(7):1227-37. PubMed PMID: 15697049.

Batalla A, Bhattacharyya S, Yücel M, Fusar-Poli P, Crippa JA, Nogué S, Torrens M, Pujol J, Farré M, Martin-Santos R. Structural and functional imaging studies in chronic cannabis users: a systematic review of adolescent and adult findings. PLoS One. 2013;8(2):e55821. doi: 10.1371/journal.pone.0055821. Epub 2013 Feb 4. Review. PubMed PMID: 23390554; PubMed Central PMCID: PMC3563634.

Brady JE, Li G. Trends in alcohol and other drugs detected in fatally injured drivers in the United States, 1999-2010. Am J Epidemiol. 2014 Mar 15;179(6):692-9. doi: 10.1093/aje/kwt327. Epub 2014 Jan 29. PubMed PMID: 24477748; PubMed Central PMCID: PMC3939850.

Bostwick JM. Blurred boundaries: the therapeutics and politics of medical marijuana. Mayo Clin Proc. 2012 Feb;87(2):172-86. doi: 10.1016/j.mayocp.2011.10.003. Review. PubMed PMID: 22305029; PubMed Central PMCID: PMC3538401.

Crippa JA, Zuardi AW, Martín-Santos R, Bhattacharyya S, Atakan Z, McGuire P, Fusar-Poli P. Cannabis and anxiety: a critical review of the evidence. Hum Psychopharmacol. 2009 Oct;24(7):515-23. doi: 10.1002/hup.1048. Review. PubMed PMID: 19693792.

Degenhardt L, Hall W, Lynskey M. Exploring the association between cannabis use and depression. Addiction. 2003 Nov;98(11):1493-504. Review. PubMed PMID: 14616175.

DiNieri JA, Wang X, Szutorisz H, Spano SM, Kaur J, Casaccia P, Dow-Edwards D, Hurd YL. Maternal cannabis use alters ventral striatal dopamine D2 gene regulation in the offspring. Biol Psychiatry. 2011 Oct 15;70(8):763-9. doi: 10.1016/j.biopsych.2011.06.027. Epub 2011 Aug 5. PubMed PMID: 21820648; PubMed Central PMCID: PMC3186868.

D'Souza DC, Ranganathan M. Medical Marijuana: Is the Cart Before the Horse? JAMA. 2015 Jun 23-30;313(24):2431-2. doi: 10.1001/jama.2015.6407. PubMed PMID: 26103026.

Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Drug Alcohol Depend. 2011 May 1;115(1-2):120-30. doi: 10.1016/j.drugalcdep.2010.11.004. Epub 2010 Dec 8. PubMed PMID: 21145178; PubMed Central PMCID: PMC3069146.

Gerra G, Zaimovic A, Gerra ML, Ciccocioppo R, Cippitelli A, Serpelloni G, Somaini L. Pharmacology and toxicology of Cannabis derivatives and endocannabinoid agonists. Recent Pat CNS Drug Discov. 2010 Jan;5(1):46-52. Review. PubMed PMID: 19832688.

Gilman JM, Kuster JK, Lee S, Lee MJ, Kim BW, Makris N, van der Kouwe A, Blood AJ, Breiter HC. Cannabis use is quantitatively associated with nucleus accumbens and amygdala abnormalities in young adult recreational users. J Neurosci. 2014 Apr 16;34(16):5529-38. doi: 10.1523/JNEUROSCI.4745-13.2014. PubMed PMID: 24741043; PubMed Central PMCID: PMC3988409

Global Newswire. http://globenewswire.com/news-release/2015/01/08/695898/10114614/en/GW-Pharmaceuticals-and-Otsuka-Announce-Results-in-First-of-Three-Sativex-R-Phase-3-Cancer-Pain-Trials.html Accessed: 8/26/15

Gogtay N, Giedd JN, Lusk L, Hayashi KM, Greenstein D, Vaituzis AC, Nugent TF 3rd, Herman DH, Clasen LS, Toga AW, Rapoport JL, Thompson PM. Dynamic mapping of human cortical development during childhood through early adulthood. Proc Natl Acad Sci U S A. 2004 May 25;101(21):8174-9. Epub 2004 May 17. PubMed PMID: 15148381; PubMed Central PMCID: PMC419576.

Gruber SA, Sagar KA, Dahlgren MK, Racine M, Lukas SE. Age of onset of marijuana use and executive function. Psychol Addict Behav. 2012 Sep;26(3):496-506. doi: 10.1037/a0026269. Epub 2011 Nov 21. Erratum in: Psychol Addict Behav. 2012 Sep;26(3):506. PubMed PMID: 22103843; PubMed Central PMCID: PMC3345171.

Hall W, Degenhardt L. Prevalence and correlates of cannabis use in developed and developing countries. Curr Opin Psychiatry. 2007 Jul;20(4):393-7. Review. PubMed PMID: 17551355.

Kuepper R, van Os J, Lieb R, Wittchen HU, Höfler M, Henquet C. Continued cannabis use and risk of incidence and persistence of psychotic symptoms: 10 year follow-up cohort study. BMJ. 2011 Mar 1;342:d738. doi: 10.1136/bmj.d738. PubMed PMID: 21363868; PubMed Central PMCID: PMC3047001.

Large M, Sharma S, Compton MT, Slade T, Nielssen O. Cannabis use and earlier onset of psychosis: a systematic meta-analysis. Arch Gen Psychiatry. 2011 Jun;68(6):555-61. doi: 10.1001/archgenpsychiatry.2011.5. Epub 2011 Feb 7. Review. PubMed PMID: 21300939.

Lenné MG, Dietze PM, Triggs TJ, Walmsley S, Murphy B, Redman JR. The effects of cannabis and alcohol on simulated arterial driving: Influences of driving experience and task demand. Accid Anal Prev. 2010 May;42(3):859-66. doi: 10.1016/j.aap.2009.04.021. PubMed PMID: 20380913.

Lopez-Quintero C, Pérez de los Cobos J, Hasin DS, Okuda M, Wang S, Grant BF, Blanco C. Probability and predictors of transition from first use to dependence on nicotine, alcohol, cannabis, and cocaine: results of the National

Meier MH, Caspi A, Ambler A, Harrington H, Houts R, Keefe RS, McDonald K, Ward A, Poulton R, Moffitt TE. Persistent cannabis users show neuropsychological decline from childhood to midlife. Proc Natl Acad Sci U S A. 2012 Oct 2;109(40):E2657-64. doi: 10.1073/pnas.1206820109. Epub 2012 Aug 27. PubMed PMID: 22927402; PubMed Central PMCID: PMC3479587.

National Survey on Drug Use and Health (NSDUH), 2012

Panlilio LV, Zanettini C, Barnes C, Solinas M, Goldberg SR. Prior exposure to THC increases the addictive effects of nicotine in rats. Neuropsychopharmacology. 2013 Jun;38(7):1198-208. doi: 10.1038/npp.2013.16. Epub 2013 Jan 11. PubMed PMID: 23314220; PubMed Central PMCID: PMC3656362.

Pistis M, Perra S, Pillolla G, Melis M, Muntoni AL, Gessa GL. Adolescent exposure to cannabinoids induces long-lasting changes in the response to drugs of abuse of rat midbrain dopamine neurons. Biol Psychiatry. 2004 Jul 15;56(2):86-94. PubMed PMID: 15231440.

Pope HG Jr, Gruber AJ, Hudson JI, Cohane G, Huestis MA, Yurgelun-Todd D. Early-onset cannabis use and cognitive deficits: what is the nature of the association? Drug Alcohol Depend. 2003 Apr 1;69(3):303-10. PubMed PMID: 12633916.

Roser P, Vollenweider FX, Kawohl W. Potential antipsychotic properties of central cannabinoid (CB1) receptor antagonists. World J Biol Psychiatry. 2010 Mar;11(2 Pt 2):208-19. doi: 10.3109/15622970801908047. Review. PubMed PMID: 20218784.

Scuderi C, Filippis DD, Iuvone T, Blasio A, Steardo A, Esposito G. Cannabidiol in medicine: a review of its therapeutic potential in CNS disorders. Phytother Res. 2009 May;23(5):597-602. doi: 10.1002/ptr.2625. Review. PubMed PMID: 18844286.

The Ohio Psychiatric Physicians Association is a statewide medical specialty organization whose more than one thousand physician members specialize in the diagnosis, treatment and prevention of mental illnesses, including substance use disorders. Psychiatric physicians utilize a variety of treatment options including psychotherapy and pharmacotherapy to effectively treat the dynamic, social and physical aspects of mental illnesses (brain disorders). The Ohio Psychiatric Physicians Association is a district branch of the American Psychiatric Association, which was founded in 1844 and represents more than 35,000 psychiatric physicians nationally.

Ohio Psychiatric Physicians Association • A District Branch of the American Psychiatric Association
3510 Snouffer Road, Suite 101 • Columbus, Ohio 43235-4217
(614) 763-0040 • Fax: (614) 481-7559 • E-mail: OPPA@ohiopsychiatry.org • www.ohiopsychiatry.org