AUSTRALIAN MEDICAL ASSOCIATION

WESTERN AUSTRALIA

14 January 2022

Dr Brian Walker
Chair, Select Committee into Cannabis and Hemp
PO Box A11
Parliament House,
WEST PERTH WA 6005

By email: brian.walker@mp.wa.gov.au

Dear Dr Walker,

INQUIRY INTO CANNABIS AND HEMP

The AMA (WA) welcomes the opportunity to make a submission to the Inquiry into Cannabis and Hemp. Please find our response to the Terms of Reference below.

Preliminary comments

Decriminalisation of recreational cannabis use

In the course of carrying out the Inquiry, the Select Committee (**Committee**) should consider that the decriminalisation of recreational cannabis use is a separate issue to whether cannabis and/or cannabis-derived products should be made available for prescription by medical practitioners. Decriminalisation of cannabis for use across society is a decision for the legislature, the judiciary, and society itself. Prescribing cannabis-containing substances for therapeutic benefit is another matter and requires a high standard of scientific evidence to support clinical decision-making.

Historical use of cannabis in society

While it is true to say that cannabis and cannabis-derived products have been 'well-researched' in a general sense, for example in areas such as agriculture and nutrition, it is not accurate to say that medical cannabis has been thoroughly tested as a therapeutic substance for specific conditions, symptoms, and populations in the context of prescription. Public commentary often refers to the historic use of cannabis as proof of its inherent safety, however the notion that daily use at specific concentrations is therefore safe is erroneous. The prescription of medical cannabis products must be based on **high-quality, peer-reviewed scientific research**, which requires large population sizes and long-term studies to be completed, repeated, and reviewed. This degree of quality in the current research is not currently available. A majority of empirically-reviews studies on cannabinoid products in humans are of small scale and should therefore be interpreted and extrapolated with caution.[1]

The *Good medical practice: a code of conduct for doctors in Australia* developed by the Medical Board of the Australian Health Practitioner Registration Authority (AHPRA),[2] provides the following relevant guidelines for medical practitioners:

- 3.2.4 Considering the balance of benefit and harm in all clinical-management decisions
- 3.2.6 Providing treatment options based on the best available information
- 3.2.7 Only recommending treatments when there is an identified therapeutic need and/or a clinically recognised treatment, and a reasonable expectation of clinical efficacy and benefit for the patient

[1] See, for e.g., the majority of studies reviewed in Stevie Britch, Shanna Babalonis and Sharon Walsh, ''Cannabidiol: pharmacology and therapeutic targets' (2021) 238 *Psychopharmacology* 9.
[2] *Good medical practice: a code of conduct for doctors in Australia* developed by the Medical Board of the Australian Health Practitioner Registration Authority (AHPRA)

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- 3.2.12 Making responsible and effective use of the resources available to you
- 3.4.4 Giving priority to investigating and treating patients on the basis of clinical need and the effectiveness of the proposed investigations or treatment
- 8.1 Minimising risk to patients is an important component of medical practice
- 8.1.1 Working in your practice and within systems to reduce error and improve patient safety, and supporting colleagues who raise concerns about patient safety
- 10.7.2 Making only justifiable claims about the quality or outcomes of your services in any information you provide to patients
- 10.12.4 Recognising that pharmaceutical and other medical marketing influences doctors and being aware of ways in which your practice may be being influenced.

With these parameters in mind, the AMA (WA) will draw the Committee's attention to the evidence on medical cannabis below.

ToR 1: Current barriers to pharmaceutical nutraceutical use of cannabinoid products

Pharmaceutical use

The current barriers to pharmaceutical use of cannabis-derived products, particularly THC-containing products, are appropriate given the lack of long-term evidence supporting their safety and efficacy. While this submission is not the appropriate place for a comprehensive literature review, we have included several short summaries of the evidence base on medical cannabis below. **In general, studies are small and short-term, and as such there is not enough high-quality evidence to encourage routine prescription of cannabis and cannabis-derived pharmaceuticals.**

An extensive review published in 2021 of studies conducted over the span of 35 years analysed 10 studies on the pharmacokinetics of CBD.[3] Five studied healthy adults (n total=39), one studied adults with refractory epilepsy (n=8), one studied children with treatment-resistant epilepsy (n=20), one studied patients with Huntington's disease (n=14), one studied children with Dravet syndrome (n=34), one studied adult polydrug users (n=41), and one studied adults with mild to severe hepatic impairment (n total=22). In addition to small sample sizes, there were variations in route and dosage across the studies. This makes extrapolation to the broader population exceptionally difficult. The review highlights the external factors that can also affect individual response to cannabis products. The authors note that consumption of food, particularly high-fat food, increases exposure (area-under-the-curve or **AUC**) by up to 400%.[4] Moreover, CBD is a potent inhibitor of particular enzymes that play a role in drug metabolism.[5] Therefore, drug-drug interactions are a key consideration when prescribing medical cannabis and require extensive trials to confirm safety.[6]

Britch et al reviewed the effects of CBD on neurological disorders, including 11 studies published between 1980 and 2018. Two studies looked at people with Parkinson's disease (n total=27), one studied Huntington's disease (n=15), one studied generalised epilepsy (n=15), one studied patients with severe treatment-resistant childhood-onset seizures (n=137), one

[3] Stevie Britch, Shanna Babalonis and Sharon Walsh, 'Cannabidiol: pharmacology and therapeutic targets' (2021) 238 *Psychopharmacology* 9.
[4] Stevie Britch, Shanna Babalonis and Sharon Walsh, 'Cannabidiol: pharmacology and therapeutic targets' (2021) 238 *Psychopharmacology* 9.
[5] Thomas Arkell, Danielle McCartney and Iain McGregor, 'Medical cannabis and driving' (2021) 50(6) *Australian Journal of General Practice*' 357; Stevie Britch, Shanna Babalonis and Sharon Walsh, 'Cannabidiol: pharmacology and therapeutic targets' (2021) 238 *Psychopharmacology* 9.
[6] Stevie Britch, Shanna Babalonis and Sharon Walsh, 'Cannabidiol: pharmacology and therapeutic targets' (2021) 238 *Psychopharmacology* 9, 15.

studied children with Dravet syndrome (n=120), two studied Lennox-Gastaut patients (n total=383), one studied Febrile infection-related epilepsy (n=7), one studied Tuberous sclerosis complex (n=18), and one studied epilepsy (n=139). The dose, route, and formulation varied across studies, again meaning broad extrapolation is difficult.

Birch et al's review of CBD effects on pain, inflammation and immune function provides a similar level of evidence – 11 studies were reviewed, all with less than 100 participants (ranging from 6-94), looked at different population groups, doses, routes, and outcomes. While their review of studies on CBD effects on psychiatric disorders and substance abuse is more comprehensive, most showed no significant benefit. The International Association for the Study of Pain's (IASP) taskforce on cannabis and cannabinoid analgesia concluded in a 2021 position statement that '[r]eviews of preclinical research and clinical safety and efficacy of cannabis and cannabinoids for pain relief have identified important research gaps. Due to the lack of high-quality clinical evidence, [IASP] does not currently endorse general use of cannabis and cannabinoids for pain relief.'[7] This view is endorsed the Australian and New Zealand College of Anaesthetists Faculty of Pain Medicine.

A 2018 systematic review conducted by Millar et al concluded that there was a general paucity of evidence of the pharmacokinetics of CBD, despite some promising research in the areas of epilepsy, Alzheimer's disease, Parkinson's disease, and multiple sclerosis.[8] The authors provide that bioavailability can vary based on route, and an individual's adiposity, gender, and previous use of cannabis. These factors have not been extensively studied.[9]

Combinations of THC and CBD-based pharmaceuticals offer similar levels of evidence. Recently, one study involving young patients with drug-resistant epilepsy found that a ratio of 3:5 THC:CBD resulted in a 50% reduction in frequency of epileptic seizures in 70% of the patients.[10] However, this pharmaceutical regime was also accompanied by several unwanted side effects including nausea, constipation, and insomnia.[11] Moreover, the small cohort size, variability in drug administration and age, and objectivity of parents reporting seizures over long periods of time suggest this study cannot solely be used to identify the risks or benefits of CBD/THC use in the management of epilepsy. A 2021 review on the efficacy of phytocannabidioids in the treatment of epilepsy found several other studies that highlighted a similar reduction in seizures in young cohorts with Dravet Syndrome, and Lennox-Gastaut syndrome.[12] This review also concluded that on its own, THC did not have sufficient data to conclude it had anticonvulsant properties and thus more studies are needed to justify its use in the treatment of epilepsy.[13] These findings do not highlight that CBD is the only, or most effective, treatment for epilepsy. Merely, they are noting its potential beneficial effects, and its possibility as an alternative therapeutic avenue for the treatment of drug-resistant epilepsy.

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[7] International Association for the Study of Pain, 'International Association for the Study of Pain Presidential Task Force on Cannabis and Cannabinoid Analgesia position statement' (2021) 162, *Pain*, S1-S2.
[8] Sophie Millar et al, 'Pharmacokinetics of Cannabidiol in Humans' (2018) 9(1365) *Frontiers in Pharmacology*.
[9] Sophie Millar et al, 'Pharmacokinetics of Cannabidiol in Humans' (2018) 9(1365) *Frontiers in Pharmacology*.
[10] Gherzi, Marcella et al, 'Safety and Pharmacokinetics of Medical Cannabis Preparation in a Monocentric Series of Young Patients with Drug Resistant Epilepsy', (2020) 51 *Complementary Therapies in Medicine* 102402.
[11] Gherzi, Marcella et al, 'Safety and Pharmacokinetics of Medical Cannabis Preparation in a Monocentric Series of Young Patients with Drug Resistant Epilepsy' (2020) 51 *Complementary Therapies in Medicine* 102402.
[12] Ożarowski, Marcin et al, 'Cannabidiol in Neurological and Neoplastic Diseases: Latest Developments on the Molecular Mechanism of Action' (2021) 22(9) *International Journal of Molecular Sciences* 4294; Devinsky, Orrin et al, 'Randomized, Dose-Ranging Safety Trial of Cannabidiol in Dravet Syndrome' (2018) 90(14) *Neurology* e1204; Devinsky et al, 'Effect of Cannabidiol on Drop Seizures in the Lennox–Gastaut Syndrome' (2018) 378(20) *New England Journal of Medicine* 1888.
[13] Ożarowski, Marcin et al, 'Cannabidiol in Neurological and Neoplastic Diseases: Latest Developments on the Molecular Mechanism of Action' (2021) 22(9) *International Journal of Molecular Sciences* 4294.

Sativex, a combination of THC and CBD, has been found to help in the treatment of resistant MS-related symptoms such as spasticity and neuropathic pain when administered as an add-on therapy.[14] However, this drug is accompanied by several side effects including somnolence, dizziness, fatigue, and nausea. Beyond its effects on MS-related pain, the analgesic effects of THC have been refuted by other studies.

A recent critical review found four studies that suggested that cannabis was an effective treatment option for patients with fibromyalgia as they found a significant reduction in pain intensity/severity,[15] however, like other studies using cannabis, these results were accompanied by a high prevalence of adverse side effects. Furthermore, the authors of the review noted that due to the methodological limitations of this research, no conclusion could be made regarding its efficacy.[16] They also noted that no studies have established enough evidence to denote a relationship between cannabis treatment and symptom improvement in fibromyalgia.[17] As such, there is only a small amount of evidence to indicate that cannabis may have some effect in alleviating neuropathic pain and fibromyalgia-related pain.

Khan et al published a review of studies on schizophrenia and psychosis in Parkinson's disease in 2020.[18] Of seven studies, three showed that CBD alleviated psychotic symptoms and cognitive impairment in patients with Parkinson's disease, and three provided some mixed evidence for the effectiveness of CBD in patients with schizophrenia (n total=27). One study showed improvements in schizophrenia-associated cognitive impairment using 300mg/day CBD, but no improvement with a dose of 600mg/day (n=17). Another showed an improvement in positive psychotic symptoms and general psychopathology associated with schizophrenia at 1000mg/day CBD (n=43). One study reported improvements similar to that of amisulpride (an antiemetic and antipsychotic) at a dose of 800mg/day CBD (n=20). Two minimal quality studies suggested some improvement in patients with schizophrenia, although some negative side-effects were observed, and the total number of participants was very small.

The authors reviewed eight studies on the effects of CBD (some also using THC-containing substances) on cannabis-related disorders.[19] In the CBD-only studies, doses ranged from 200-600mg/day (n total=28). These studies appear to show positive results for cannabis withdrawal, with some negative side-effects. Eight further studies reviewed looked at a range of psychiatric disorders including attention deficit hyperactive disorder (ADHD), autism spectrum disorder (ASD), anxiety disorders, bipolar disorder, post traumatic stress disorder, and Tourette syndrome.[20] Participant size was less than 100 in all cases, producing Grade B recommendations for ASD, anxiety disorders and ADHD, and Grade C recommendations for bipolar disorder, PTSD and Tourette syndrome. Accordingly, the position of the Royal

[14] Markovà, Jolana et al, 'Sativex® as Add-on Therapy Vs. Further Optimized First-Line ANTispastics (SAVANT) in Resistant Multiple Sclerosis Spasticity: a Double-Blind, Placebo-Controlled Randomised Clinical Trial' (2019) 129(2) *International Journal of Neuroscience* 119.
[15] Erinn C. Cameron and Samantha L. Hemingway, 'Cannabinoids for Fibromyalgia Pain: A Critical Review of Recent Studies (2015–2019)' (2020) 2(1) *Journal of Cannabis Research* 1.
[16] Erinn C. Cameron and Samantha L. Hemingway, 'Cannabinoids for Fibromyalgia Pain: A Critical Review of Recent Studies (2015–2019)' (2020) 2(1) *Journal of Cannabis Research* 1.
[17] Erinn C. Cameron and Samantha L. Hemingway, 'Cannabinoids for Fibromyalgia Pain: A Critical Review of Recent Studies (2015–2019)' (2020) 2(1) *Journal of Cannabis Research* 1.
[18] Rabia Khan et al, 'The therapeutic role of Cannabidiol in mental health: a systematic review', (2020) 2(2) *Journal of Cannabis Research*.
[19] Rabia Khan et al, 'The therapeutic role of Cannabidiol in mental health: a systematic review', (2020) 2(2) *Journal of Cannabis Research*.
[20] Rabia Khan et al, 'The therapeutic role of Cannabidiol in mental health: a systematic review', (2020) 2(2) *Journal of Cannabis Research*.

Australian & New Zealand College of Psychiatrists as of January 2021 is that '[e]vidence for the use of medicinal cannabis in the treatment of mental disorders is very limited and there is no substantial evidence to support its use outside of properly approved research trials for these disorders.'[21]

In summary, there is a wide range of conditions on which cannabis products have been tested, but they tend to be short-term, with small sample sizes, and are difficult to extrapolate. At this point in time, there is not enough data for medical practitioners to safely prescribe cannabis products as a standard therapeutic option for the broader population.

Nutraceutical use

Colloquially, a nutraceutical refers to foods, whether naturally occurring or otherwise, that have a benefit over and above what would be considered standard nutritional benefit. When nutrients are isolated and concentrated for consumption, the line between what is a food or drug is blurred. This creates safety and quality issues in the marketplace, given that evidence shows that when substances are isolated, they do not behave in the same way biologically as they would when consumed in the naturally occurring food.

Isolated forms of substances are generally easier to test on humans, as there is more precise control of the dose-response, and it allows for double-blind randomised-controlled trials (DBRCTs) to be undertaken which are difficult to complete with real food items. However, isolated substances are more likely to be consumed in a concentrated form, meaning that a much higher level of intake is possible over a short space of time. Clearly, supplements are convenient for many consumers, and indeed for prescribers, but with increased ease of dosage comes a risk of overdosing. Cannabis may not impact an individual adversely from sporadic recreational use, but it does not follow that a concentrated amount of an isolated substance from cannabis will do the same. In order to practice medicine safely, medical practitioners need to be sure about the safety and efficacy of such products, and it is this evidence that is currently lacking.

If the term 'nutraceutical' is used to categorise cannabinoid products, it needs to be (a) clearly defined and (b) a distinction needs to be made between products with psychoactive constituents and products with non-psychoactive constituents. With the exception of caffeine, commonly-used psychoactive substances are generally regulated, even if they are commercially available. Alternatively, if the Committee's reference to nutraceutical use refers the consumption of cannabis products as food, i.e. hemp seed, hemp seed oil, hemp seed meal, and hemp fibre as foods, we consider that the existing regulations are appropriate.[22] As we understand it, there is currently minimal regulation on the production of hemp products for nutritional benefit. These products are permitted for sale and consumption in Western Australia under the *Industrial Hemp Act 2004* (WA) and the *Misuse of Drugs Act 1981* (WA), so long as the variety of cannabis fits within the definition of industrial hemp (i.e. they are low THC varieties).

[21] Royal Australian and New Zealand College of Psychiatrists, 'Clinical Memorandum: Therapeutic use of medicinal cannabis products January 2021' (Memorandum, January 2021), <https://www.ranzcp.org/files/resources/college_statements/clinical_memoranda/cm-therapeutic-use-cannabis-products.aspx>.
[22] *Industrial Hemp Act 2004* (WA).

ToR 2: Medicinal cannabis, its prescription, availability and affordability

Prescription and affordability

The accessibility of cannabis-derived products is impacted by the lack of quality of evidence. More published research into the use of cannabis-derived products is likely to improve accessibility and affordability.

State driving laws

State driving laws have been cited as a major barrier for patients contemplating or receiving medical cannabis treatment. As of November 2021, Tasmania was the only Australian state or territory to have included a defence for the detection of THC in the oral fluid of a driver where the person has a valid medical prescription. The Committee should consider whether the issue of driving laws can be appropriately categorised as a barrier to the pharmaceutical use of cannabinoid products in the context of the lack of quality evidence for its use. While we understand that the inability to legally drive after using THC-containing products is a barrier for some people, introducing a defence of valid medical prescription is unlikely to remove barriers to prescription, because such a change will not improve the evidence base on the safety, efficacy, or ethics of the prescription of cannabis-derived pharmaceuticals by medical practitioners. Efforts to fund more research into the relevant products would be more likely to have the effect of reducing these barriers.

ToR 3: The potential benefits and risks of permitting industrial hemp for human consumption

The risks associated with permitting industrial hemp for consumption do not appear to be related to the contents of industrial hemp itself, but that it could be used to mask growing, manufacturing, and distribution of other varieties of cannabis. As this relates more directly to law enforcement, regulation of industrial hemp is more likely to be a matter for police and the judiciary rather than for the medical community. We note that hemp seed is a good source of nutrition, including essential fatty acids, iron, magnesium, and fibre. As such, hemp seed and hemp seed oil can form part of a nutritious diet.

Yours sincerely,

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