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Email:

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Tim Watling
Committee Secretary
LEGAL AND CONSTITUTIONAL AFFAIRS LEGISLATION COMMITTEE
THE SENATE

The Criminal Code and Other Legislation Amendment
(Removing Commonwealth Restrictions on Cannabis) Bill 2018

Dear Mr Watling
Thank you for the invitation of 16 May 2018 to contribute a submission to the Legal and Constitutional Affairs Legislation Committee regarding the above Bill. I make this submission as a private citizen.

Preamble.
At the outset, I declare that I have no conflicts of interests, pecuniary or otherwise. Heretofore, I have been concerned only with issues relating to the "medicinal" uses of cannabis (also variously referred to as marijuana or marihuana). My understanding of its "recreational" uses is somewhat peripheral; accordingly, I defer to those who have made these issues their specialty.

By way of formalities, I hold the title Emeritus Professor of Anaesthesia of The University of Sydney where my work over the past five decades has been mainly oriented towards the science of anaesthesia and pain medicine. My relevant qualifications include DMedSc, PhD and MSc in the discipline of drug sciences, and BSc in applied chemistry. By way of previous experience regarding medicinal cannabis, I have been a member of the Working Party on Medicinal Cannabis convened by NSW Premier Carr in 2000, published various academic papers on cannabis[1], prepared various scientific advisory papers for the Chief Scientist of NSW, lectured both nationally and internationally and appeared in various lay media and documentary TV productions regarding such issues, and have made submissions to the Australian Senate and various state and territory governments regarding the medicinal uses of cannabis and the introduction of related legislation.

Summary.
The Explanatory Memorandum to this legislation notes that "Cannabis use is less harmful than alcohol use and tobacco use", citing an analysis of the relative harms of 20 drugs (including both socially-accepted alcohol and medically-legally drugs) over 16 separate criteria (pertinent to the user and to others). The results scored "cannabis" at 20, compared to

[1] (i) Cartwright L, Mather LE. Investigation of some samples of Australian grown cannabis. Australian Journal of Pharmaceutical Sciences 1: 49-51, 1972; (ii) Mather LE. Medicinal cannabis – hoax or hope? Regional Anesthesia and Pain Medicine 26: 484-7, 2001; (iii) Mather L. Cannabinoid pharmacotherapy: past, present and future. Minerva Anestesiologica 71: 405-12, 2005; (iv) Mather LE, Rauwendaal E, Moxham-Hall V, Wodak A. (Re-)introducing medicinal cannabis. Medical Journal of Australia 199: 789-791. 2013; (v) Mather LE, Rauwendaal E, Moxham-Hall V, Wodak A. The issue of medicinal cannabis in contemporary Australia. Griffith Journal of Law and Human Dignity 3: 286-313, 2015; (vi) Mather LE. The issue of driving while a relevant drug, Δ9-tetrahydrocannabinol, was present in saliva: Evidence about the evidence. Griffith Journal of Law and Human Dignity 4: 21-52, 2016 [copies of these and other papers cited are available upon request]

the vastly more harmful (by these criteria) alcohol at 72, heroin at 55, methamphetamine at 33, and tobacco at 26, but with ketamine at 15, methadone at 14 and "ecstasy" [3,4-methylenedioxy-methamphetamine (MDMA)] at 9. In an analysis separating harms to "the user" and "to others", alcohol had similar scores for harms "to user" and "to others", as did cannabis, but the scores for "cannabis" remained vastly lower than those for alcohol. [2] The term "cannabis" is used here because, as elaborated below, cannabis is of ambiguous chemical composition and thus ambiguous pharmacological activity.

An independent but strongly supportive commentary on this analysis pointed out that the analysis did not include the issue of multidrug use and this is significant because of "the extreme impairment of driving after the combined use of cannabis and alcohol" [also see footnote 1(vi)]. The authors also pointed out that "the investigators rightly conclude that their findings correlate poorly with present UK drug classification. This conclusion is not surprising, because the UK drug-classification system is subject to national and international drug policies, which are also based on considerations other than the harm of a drug…". They further pointed out that "…the two legal drugs assessed — alcohol and tobacco — score in the upper segment of the ranking scale, indicating that legal drugs cause at least as much harm as do illegal substances." [3] These are all reasonable points.

Others, however, have challenged the analysis, with one commentary stating that "If analysis is to include the capacity to capture the complexity relating to drug using behaviours and environments; specific personal and social risks for particular using populations; and the broader socio-cultural context to contemporary intoxication, there will need to be acceptance that analysis of the various harm vectors must remain separate – the complexity of such analysis is not something that can or should be over generalised to suit political discourse or outdated legal frameworks." [4] These, too, are all reasonable points.

Although I comprehend the above issues, I have not researched them personally. My own research context is chemical-pharmacological-medical, however I have no experience in framing relevant legislation to accommodate any issues arising, of whatever context. It seems clear to me that, although there is no agreed law enforcement-sociological method to approach the issues being raised in the Bill, a common sense and workable approach is essential.

"Cannabis" is a plant from which numerous preparations are made, including those for fibre, food, and pharmacological purposes. Comparisons with alcohol, although inevitable and appealing from a sociological and/or legalistic perspective, are somewhat tenuous from a pharmacological perspective. Alcohol is the same unique chemical (ethyl alcohol, ethanol) regardless of its mode of preparation or ingested form, and is normally used in knowable doses. With cannabis, the chemical composition and doses of its various components, pharmacologically active and otherwise, are normally unknowable, and depend on many factors of plant strain, growth, harvesting, storage, preparation, as well as the chosen mode of administration (whether smoked, or inhaled, or swallowed by mouth). Thus, the issue of "cannabis" variability needs to be considered, somehow, in framing the legislation.

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[2] Nutt DJ, King LA, Phillips LD. Drug harms in the UK: a multicriteria decision analysis. Lancet 376 (9752): 1558-1565, 2010.

[3] van Amsterdam J, van den Brink W. Ranking of drugs: a more balanced risk-assessment. Lancet 376 (9752): 524-1525, 2010.

[4] Rolles S, Measham F. Questioning the method and utility of ranking drug harms in drug policy. International Journal of Drug Policy 22 (4): 243-246, 2011.

From my participation in the NSW Premier's working party in 2000 to examine the case for introducing legislation to permit the medicinal use of cannabis, along with my regular review of the burgeoning academic literature, I have come to the position that cannabis, assuming its reliable supply, should be added to the list of pharmacotherapeutic substances available to patients in need, whilst supporting ongoing research to determine its best uses. And that position has been the basis of the various governmental submissions that I have made. My opinion here is informed by the same considerations.

As stated in the Explanatory Memorandum to the present Bill "Adults should be free to make their own choices as long as they do not harm others." This seems a reasonable proposition, but with provisos.

From my reading of the mainly academic literature, I believe that there is no definitive case to support or reject the sentiment of the Bill. My concurrent awareness (rather than study) of "drug-taking" (including alcohol and tobacco) behaviours in society leads me also to support the growing "harm minimisation" model. I suggest that, as some individuals will always wish to take drugs (of whatever kind, and for whatever reason), then "Legalising cannabis would improve access to cannabis for recreational, medicinal, industrial and other purposes", as stated in the Explanatory Memorandum, and subject to certain provisions as discussed below, would be consistent with the "harm minimisation" model. If it is conceded that there are also direct benefits, then they come from the relative safety of cannabis compared to most other drug choices. Indeed, there is accumulating evidence that cannabis may, to some extent, usefully replace overused or abused opioids in both patients as well as others who take drugs. Again, this would be consistent with the harm minimisation model.

I found the Vox website https://www.vox.com/cards/marijuana-legalization/where-is-marijuana-legal a very sensible resource. Notably, Card 7 is headed **Marijuana is a relatively safe drug — with some risks.** It then goes on "There are no documented deaths from a marijuana overdose, but that doesn't mean pot is harmless." My sentiments, exactly – but clearly, there is still much to learn.

Analysis and discussion.
The following discussion is informed by analysis of the medicinal context for cannabis, and is primarily intended to apply in a generic sense to the safety of users, assuming that any eventual legislation would incorporate such logic.

As presently interpreted, "medicinal" cannabis is an umbrella term used to designate a botanical product harvested from genetically identical cannabis plant clones that meets the reproducibility standards of a product sold for medicinal use, i.e. accurately labelled material of known provenance, having reproducible active principal composition, quality of batch consistency, and being free of harmful contaminants such as microbial growth and agrichemicals. "Medicinal" cannabis thereby contrasts with the cannabis of unknown provenance that is commonly sold on the black market, or obtained by other means including personal growing, and used for both medical and non-medical including "recreational" purposes.

Hardly a week goes by without reports or commentaries about law enforcement raids/seizures/prosecutions and consequent political statements about cannabis – no doubt part of the strategy to "send a message" about the perils of law violation. At the same time,

the academic literature is replete with research on virtually every imaginable aspect of cannabis - from population surveys of use, to human clinical research, to animal laboratory research, to mechanistic research on various cannabis components on various body cells, and on biochemical mechanistic pathways. There are now several academic journals exclusively about cannabis research. However, until recently, in most countries, human medical research on cannabis was hampered by legal and research funding restrictions, whereas research attempting to identify harms from recreational cannabis, especially in adolescents, was being generously funded. This, not surprisingly, has led to "publication bias", so that the "harms" message still remains more prominent, and this tends to polarise society (including various medical societies).

Underlying the proposed change to legislation is the fundamental question: "**is the 'recreational' use of cannabis safe?**", essentially meaning is it safe enough to allow unregulated supply to, and consumption by, adult members of the community. From a pharmacologist's perspective (i.e. my own), this question is problematical. No drug can be deemed to be "safe", but some are "safer" than others; and then further pharmacological questions need to be explored: "for whom?", "under what circumstances?" and "compared to what?".

It is commonplace to commence a discussion about cannabis, for any purpose, with lines such as "Cannabis is an ancient herbaceous plant: its botanical name derives from the Latin for hemp. Various preparations from cannabis foliage and florets have been used for medicinal, dietary, textile fibre-making, religious, spiritual, and recreational purposes, for millennia…" – all true! And it is also commonplace to note that the nearest botanical relative to cannabis/marijuana is hops, the basis of a well-used beverage, and that naming was formerly based on cannabis *indica* and *sativa* varieties but, with cross-breeding over generations, such distinction is no longer useful.[5]

In a medical context it would be commonplace to point out that "Dr WB O'Shaughnessy, Assistant-Surgeon and Professor of Chemistry in the Medical College of Calcutta, described its botanical and physical characteristics and folkloric medicinal use in October 1838. He also described his own observations in human patients that included successful symptomatic treatment in cases of pain arising from acute and chronic rheumatism, of paroxysms from hydrophobia (rabies), diarrhoea from cholera, muscular spasms from tetanus, and infantile convulsions (epilepsy)"[(https://griffithlawjournal.org/index.php/gjlhd/article/view/756 - see footnote 1(v)] – an impressive medicine!

My first research encounter with cannabis in the early 1970s [footnote 1(i)] remains informative. This was the first Australian attempt to analyse the composition of cannabis of unknown provenance that had been seized by the NSW police. The material was analysed for the then-known main constituents Δ^9-tetrahydrocannabinol (THC), the principal psychogenic cannabinoid, cannabidiol (CBD), these days recognised as a non-psychogenic but therapeutically-useful cannabinoid, and cannabinol (CBN), a breakdown product of THC. With present knowledge, it is not surprising that the concentrations of these principal cannabinoids were highly variable, given the way that they had been obtained. Additionally,

[5] Datwyler SL, Weiblen GD. Genetic variation in hemp and marijuana (Cannabis sativa L.) according to amplified fragment length polymorphisms. Journal of Forensic Sciences 51(2): 371-375, 2006; Erkelens JL, Hazekamp A. That which we call Indica, by any other name would smell as sweet. Cannabinoids 9(1): 9-15, 2014; McPartland JM. Cannabis sativa and Cannabis indica versus "Sativa" and "Indica". In, Cannabis sativa L. -Botany and Biotechnology 2017, pp. 101-121; Springer, Cham.

the measured concentrations of those cannabinoids were relatively low compared to more recent findings.[6] This analysis was performed at a time when the medicinal use of cannabis had ceased, for political rather than medical reasons, and long before the pharmacological actions of cannabis were understood, and at a stage when relatively few of its components had been characterised either chemically or pharmacologically. However, within three decades, approximately 100 substances related to THC had been identified, along with hundreds of other substances found in cannabis, many of which contribute to the relevant pharmacological activity attributed to cannabis, both salutary and otherwise. Moreover, during this time, research on the bodies' own array of "chemical messengers" now included the endocannabinoids, substances that are mimicked by various botanical cannabis constituents.[7]

Additionally, those who grow the plants have gained greater expertise, and not only in the context of medicinal cannabis. This is important because, being a plant product, cannabis is comprised of many hundreds of chemical substances, the proportions and amounts of which normally differ depending on the strain of plant, and the conditions of its growth, harvesting, storage, processing, etc. The growing for medicinal use normally standardizes these, so that the end-product is reproducible, and leads to a standardised mixture.[8] While it is generally not known how well individual-grower plants are standardised locally, the legalised growing along with testing in North America indicates that this can be managed.

Cannabis growing for medicinal uses also normally precludes the inclusion of extraneous harmful substances, such as agrichemicals (mainly pesticides and herbicides), microorganisms (mainly bacteria and fungi), as well as heavy metals from the growth media. The issue of intentional contamination of 'street' drugs also has been recognized for many years[9], and anecdotes as well as urban myths abound. Numerous academic publications have reported on the issues of contamination in cannabis of unknown provenance, such as might be encountered in a "recreational cannabis" marketplace.[10] Such 'street' drugs are often diluted or adulterated for profit, and the materials used may themselves be the source of toxicity. In the medicinal cannabis context, such contamination would be expected to have greater impact on unwell patients, particularly the immunocompromised. The chemical composition also depends on the preparation (flowering tops, hot extract, cold extract, etc.) and route (inhaled-transpulmonary smoked, vaporised, oral, sublingual, etc.) used for ingestion. The effects are thus the end-product of very many variables, and these should be construed also as a checklist for potential 'recreational' cannabis use. I am unable to suggest how either issue should be considered in any legislation – but, as it could be a significant issue to consumers, it needs consideration in any legislation proposal.

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[6] Swift W, Wong A, Li KM, Arnold JC, McGregor IS. Analysis of cannabis seizures in NSW, Australia: cannabis potency and cannabinoid profile. PloS One, 8(7), e70052, 2013.

[7] Mechoulam R, Parker LA. The endocannabinoid system and the brain. Annual Reviews of Psychology 64: 21-47, 2013.

[8] Hazekamp A, Fischedick JT. Cannabis-from cultivar to chemovar. Drug Testing and Analalysis 4(7-8): 660-667, 2012; Potter DJ. A review of the cultivation and processing of cannabis (Cannabis sativa L.) for production of prescription medicines in the UK. Drug Testing and Analysis 6(1-2): 31-38, 2014.

[9] McLaren J, Swift W, Dillon P, Allsop S. Cannabis potency and contamination: a review of the literature. Addiction 103(7): 1100-9, 2008.

[10] Mather LE. Reliable supply of medicinal cannabis to patients: analysis and discussion. Report to the Chief Scientist of NSW, 31 July, 2016 [copy available upon request]

What about the relative safety, and for whom? Apart from generally accepted detrimental effects on the developing adolescent brain, and the educational and societal consequences of amotivational effects often attributed to cannabis, it is generally accepted that cannabis/marijuana is (relatively) "safe", and it is often repeated that "no one has died" as a result of ingesting it. Insofar as research in laboratory animals provides a guide, THC is of relatively low acute toxicity, with respective median lethal doses (LD_{50}) after intravenous and intragastric administration of 28.8 and 668 mg/Kg in rats, and 42.5, and 482 mg/Kg in mice.[11] Scaled to humans, these values indicate an acute toxicity of THC on the scale of grams, compared to normally ingested doses on the scale of milligrams. But this is only for THC. And, besides, although the THC in cannabis is unlikely to stop your breathing, as might result from ingestion of opioids, or stop your heart, as might result from ingestion of amphetamines, or injure your gut or kidneys, as might result from some analgesic agents, it says nothing about its causing such disinhibition or lack of judgement that might stop you walking under a bus or refraining from driving a motor vehicle. And it says nothing about the beneficial or otherwise pharmacology of the other many hundreds of chemical compounds ingested concurrently.

If it is conceded that there are also direct benefits, then it comes from the relative safety of cannabis compared to most other drug choices. Indeed, there is accumulating evidence that cannabis may, to some extent, usefully replace overused or abused opioids in both patients as well as others who take drugs.[12] There would be no disagreement that, among drugs, cannabis is safer than most other drugs, especially opioids, that might be used therapeutically or recreationally. Although cannabis use in both circumstances is not without some risks,[13] again, this would still be consistent with the harm minimisation model. [14]

When I was a postgraduate student during the 1960s, we had "learned discussions" in our cohort about putting cannabis availability into a similar class to alcoholic drinks – legal, regulated and taxed. Despite all we didn't know, a common opinion was perhaps there was enough problem with having essentially unrestricted access to alcohol so that we didn't need another legal "social drug", even bearing in mind that cannabis was then a widely used illegal "social drug". But the other common opinion also considered the issue of individual responsibility in consumption, harm minimisation, and the societal and other costs of supressing a drug substance into illegality. And all of this was before the (decidedly flawed) "war on drugs" was declared on society not long afterwards.

It is hoped that this analysis and discussion will assist those charged with the responsibility of considering and/or framing the legislation to permit a wider use of cannabis without the present legal impediments.

End of submission

[11] Forney RB. Toxicology of marihuana. Pharmacological Reviews 23(4):279-284, 1984

[12] Reiman A, Welty M, Solomon P. Cannabis as a substitute for opioid-based pain medication: patient self-report. Cannabis and Cannabinoid Research 2(1): 160-166, 2017; Piomelli1 D, Weiss S, Boyd G, Pacula RL, Cooper Z. Cannabis and the opioid crisis. Cannabis and Cannabinoid Research 3(1): 108-116, 2018.

[13] Hall W. What has research over the past two decades revealed about the adverse health effects of recreational cannabis use? Addiction 110(1): 19-35, 2015

[14] Collen M. Prescribing cannabis for harm reduction. Collen Harm Reduction Journal 9: 1-5, 2012.