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INQUIRY INTO ROAD TRANSPORT AMENDMENT (MEDICINAL CANNABIS-EXEMPTIONS FROM OFFENCES) BILL 2021

Organisation: Lambert Initiative for Cannabinoid Therapeutics

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Medicinal Cannabis and Driving Safety:

A Perspective from the Lambert Initiative at the University of Sydney

A Submission to the NSW Legislative Council

Standing Committees on Law and Justice Inquiry into the

Road Transport Amendment (Medicinal Cannabis-Exemptions from Offences) Bill 2021

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Introduction: The Lambert Initiative

The *Lambert Initiative for Cannabinoid Therapeutics* is a philanthropically funded research program at the University of Sydney. It was established in July 2015 following an unprecedented donation of $33.7M from Barry and Joy Lambert and seeks to explore the therapeutic potential of cannabis and cannabinoids.

Barry and Joy's granddaughter, Katelyn Lambert (aged 10), suffers from Dravet syndrome, a severe treatment-resistant form of epilepsy, and the Lambert family have witnessed a remarkable and sustained improvement in Katelyn's condition as a result of her being treated with cannabis-derived products. This has engendered a strong desire in Barry and Joy to see others suffering from intractable medical conditions having access to cannabinoid-based medicines.

The Lambert Initiative is currently developing novel cannabinoid-based treatments for a range of different diseases and conditions. It is also involved in education, community outreach, science-based advocacy and policy issues relating to medicinal cannabis. At present, the Lambert Initiative supports the research of more than 30 academics, postdoctoral fellows, research assistants and students and has a large number of national and international research collaborators.

The major areas of research in which the Lambert Initiative is currently active are as follows:

Preclinical Research. Our preclinical research program employs cellular and animal models of disease to characterise the therapeutic potential of the more than 140 cannabinoids present in the cannabis plant, and various novel cannabinoid molecules, in treating conditions such as cancer, chronic pain, epilepsy, neurodegenerative conditions, metabolic disorders and mental health conditions. Our medicinal chemistry team synthesises large libraries of cannabinoid molecules as part of this program, and we screen new candidate molecules across a range of disease models.

Clinical Trials. This research stream examines the efficacy and safety of new and existing cannabinoid-based medicines in treating patients with a range of different conditions including insomnia, anxiety, Tourette syndrome, arthritis, chronic pain, and schizophrenia. Our clinical trials frequently involve local and international collaborators.

Driving Research. We have conducted several recent studies characterising the effects of cannabis on driving performance. This includes studies where volunteers have consumed specific doses of cannabis and been assessed for driving impairment either on the actual road (in collaborative studies conducted in the Netherlands) or using a driving simulator. We have also written internationally acclaimed reviews around the magnitude and duration of driving impairment with cannabis and evaluated the accuracy and validity of current roadside drug testing procedures.

Patient Access and Community Use of Medicinal Cannabis. Our final research theme involves surveying patients who are (legally or illegally) self-medicating with cannabis in Australia to determine the types of products they use (e.g., official versus unofficial), their perceptions around efficacy, and their preferred models of access. This has included surveys examining the attitudes and behaviours of medicinal cannabis patients in relation to driving. We have also: (1) conducted surveys of general practitioners and other health professionals to determine their attitudes towards, and knowledge of, medicinal cannabis; (2) used Therapeutic Goods Administration (TGA) data to monitor trends in patient access over time; and (3) conducted cross-country comparisons of cannabis-related policy.

Medicinal Cannabis Access in Australia

Since November 2016, Australian doctors have been permitted to prescribe medicinal cannabis products to their patients under the *Special Access Scheme Category-B* (SAS-B) and *Authorised Prescriber* (A-P) schemes of the TGA. Such pathways reflect the Australian community's overwhelming (>85%) support of patient access to medicinal cannabis products [1].

As of April 2022, the TGA has approved >240,000 SAS-B prescriptions with approvals currently increasing at a rate of around 10,000 per month (Figure 1) [2]. These prescriptions have involved approximately 90,000 individual patients and 4,200 prescribing doctors. Patient numbers are anticipated to continue to rise as the estimated ~500,000 Australians still self-medicating with illicit cannabis gradually transition from these illicit products to quality controlled, reliably-available, legal products [3, 4].

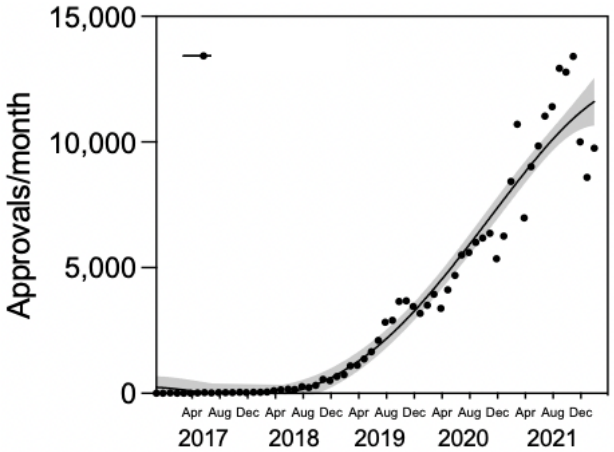

Figure 1. *Total number of SAS-B approvals to access medicinal cannabis each month (2017-2022).*

There are currently around 240 medical cannabis products available for prescription, including oils, cannabis flower, wafers, and capsules. While the most commonly prescribed products have traditionally been 'oils' (i.e., liquid extracts of cannabis) for oral consumption, there has been a steady rise in the prescription of 'flower products' (i.e., cannabis plant material) for vaporisation. Cannabis flower now represents around 40% of all prescriptions [4]. Patients self-medicating with *illicit* cannabis products are more likely to use cannabis smoked in bongs or joints than vaporised cannabis or orally consumed products such as oils [5, 6].

The majority (~75%) of current medicinal cannabis prescriptions are for Schedule 8 (S8) products that contain *Δ^9-tetrahydrocannabinol* (THC), the main intoxicating ingredient of cannabis. The remaining approvals, around 25%, are for Schedule 4 (S4) products where *cannabidiol* (CBD), a non-intoxicating component of the cannabis plant, comprises >98% of the total cannabinoid content [7]. CBD products are almost exclusively oils, capsules, or wafers rather than flower.

THC products have demonstrated efficacy in treating a number of debilitating conditions such as chronic pain, chemotherapy-induced nausea and vomiting, and spasticity in multiple sclerosis [7, 8]. Around 60% of SAS-B approvals are for the treatment of chronic pain conditions such as back pain, neck pain, arthritis, and fibromyalgia [7, 9]. THC-related improvements in quality of life, anxiety, and insomnia have also been observed in randomised controlled trials (RCTs). However, the quality of this evidence is still questionable with more high quality clinical trials required to confirm these effects [9, 10].

CBD has demonstrated efficacy in the treatment of paediatric epilepsy and there is emerging evidence of efficacy in conditions such as anxiety, inflammation, chronic pain, and addictions [4, 7, 9]. The TGA have recently down-scheduled low dose CBD products from *Prescription Only* (S4) to *Pharmacist Only* (S3) medicines. This will allow them to be sold over-the-counter (i.e., without a prescription) in pharmacies in the near future.

Driving Restrictions: A Key Issue for Medicinal Cannabis Patients

The surveys of the Lambert Initiative and our interactions with medicinal cannabis patients in Australia consistently highlight three major concerns:

- Difficulty finding a medical professional willing to prescribe medicinal cannabis products,
- The cost of such products (typically around $300-400 per month, with no PBS subsidy), and
- Restrictions around driving, specifically being warned by their prescribing doctor that they are not allowed to drive while using a THC-containing product.

All Australian jurisdictions currently have "zero-tolerance" laws that prohibit driving with THC present in blood or oral fluid [11]. Having a legitimate medical prescription for a THC-containing product provides no defence against arrest, conviction, and driving disqualification.

Laws are enforced through random *mobile drug testing* (MDT). Random MDT is conducted in all states and territories and typically looks for the presence of THC, methamphetamine, MDMA and (in NSW) cocaine. During 2019, NSW Police conducted 166,351 MDT tests, yielding 9,446 positive results, mostly for THC [12]. THC-positive results tend to be skewed towards younger males living in rural or regional areas and frequently result in criminal conviction [13].

The Australia Federal Department of Infrastructure (*Bureau of Infrastructure and Transport Research Economics*) data for 2020 [14] indicate that, despite an overall drop in testing during 2020 (due to COVID-19), a total of 324,482 tests were performed nationally, with an overall positive rate of 14%. This includes 129,558 tests conducted in NSW (a 22% drop relative to 2019) with a positive rate of around 10%. Incidentally, our recent independent analysis of the devices used for mobile drug testing in NSW [15] shows a worrying degree of insensitivity and inaccuracy (both false positives and false negatives) for THC results in these tests.

The current legal approach to regulating medicinal cannabis and driving is problematic in many regards [16-18]. Most prominently, it applies a different standard for medicinal cannabis products relative to other prescription medications. Under current legislation, patients using many other medications that impair driving to a greater extent than cannabis (e.g., opioids, benzodiazepines, Z drugs, sedating antidepressants) are legally permitted to drive providing they do not '*feel*' impaired or '*under the influence*' of these prescription drugs [11]. In NSW, the definition of '*under the influence*' is not specified. It is also unclear whether anyone is ever charged under such laws.

In contrast, patients prescribed legal MC products are: (1) not permitted to drive even if they are demonstrably unimpaired; (2) subject to random MDT for the presence of THC in oral fluid; and (3) have no exemption from legal sanctions should a positive roadside drug test arise [19].

The disparity inherent in such policy has been subject to recent analysis by the Lambert Initiative and colleagues from the Victorian Department of Health [18]. This unfortunate double standard was also highlighted by the Deputy Speaker of the Federal House of Representatives, The Honourable Llew O'Brien, in a 2021 speech recorded by Hansard [20].

A recent survey by the Lambert Initiative indicates that, despite existing laws, many patients are driving shortly after taking THC-containing products in a manner that puts them at risk of a positive MDT [21]. On the other hand, MDT is a major deterrent for many patients who are not prepared to risk breaking the law and who are therefore forced to avoid therapeutic use of potentially beneficial THC products due to a necessity to continue driving (e.g., for their work or family life) [18].

What Does the Science Tell Us about Cannabis and Driving Impairment?

There have been a substantial number of studies over the past two decades examining the effects of cannabis, and specific THC and CBD products, on driving and other safety-sensitive tasks. Related studies have examined the effects of cannabis on cognitive and psychomotor function, including driving-relevant tasks such as reaction time, divided attention, and tracking [23, 24]. This literature, including several studies undertaken by the Lambert Initiative, is summarised as follows:

CBD and Driving. In agreement with the consensus that CBD is non-intoxicating, our studies of both inhaled and oral CBD has shown no deleterious effects on on-road or simulated driving performance or on overall cognitive function [25, 26]. Another reassuring point for patients is that our recent research shows CBD does not give rise to positive roadside drug tests for THC with the current technologies used by NSW Police (e.g., the Securetec DrugWipe®, Dräger Drug Test® 5000) [27].

THC-induced driving impairment. THC, particularly in higher doses, can produce a state of *intoxication*, which includes sedation, euphoria, sensory changes, and relaxation (i.e., a "high"). These characteristic effects, typically observed at oral or inhaled THC doses >10 mg [28], are associated with psychomotor and cognitive impairment, including driving impairment, particularly in light, occasional users of cannabis [24]. Studies demonstrating THC-impaired driving have been conducted both on-road and using driving simulators. A key measure used in these studies is lateral instability ("weaving"), known technically as *standard deviation of lateral position* (SDLP) [16, 26, 29] (Figure 2A). Drug-induced changes in SDLP have been shown to correlate well with drug-induced changes in crash risk (i.e., r=0.97–0.99).

For example, in an on-road driving study conducted by the Lambert Initiative with researchers in Maastricht (The Netherlands), vaporised cannabis containing around 13.75 mg THC increased SDLP at 30 min but not 240 min after consumption in occasional cannabis users (Figure 2B) [26].

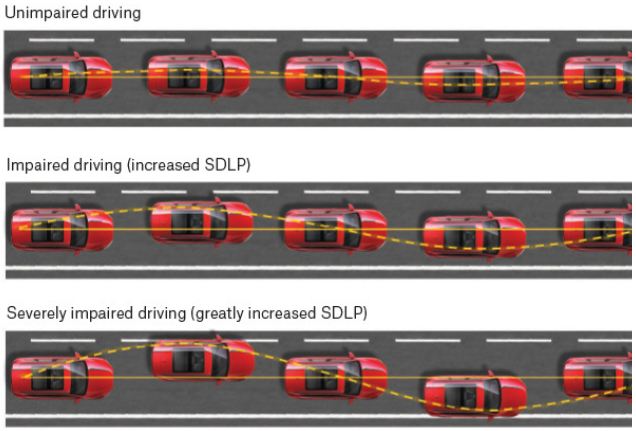

Figure 2A. *Standard deviation of lateral position (SDLP), a key measure of drug-induced impairment, indexes the loss of lateral stability on the road following drug use. From [19].*

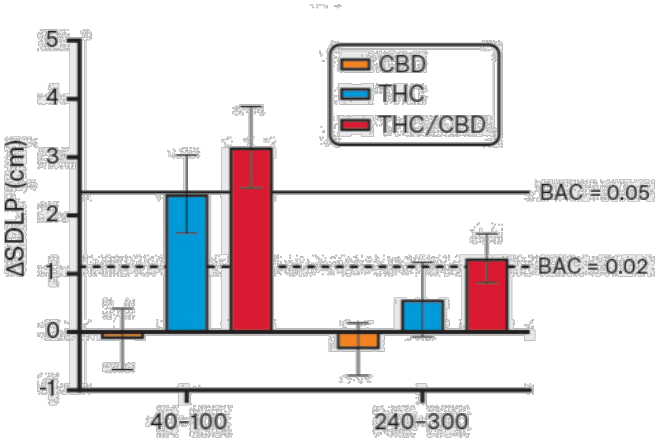

Figure 2B. *Effects of CBD, THC and THC/CBD on SDLP relative to BAC = 0.02 or 0.05. Results are from on-road driving tests conducted 40-100 and 240-300 mins after inhaled drug [26].*

The increase in SDLP observed with acute cannabis intoxication is similar to that seen with a blood alcohol concentration (BAC) of around 0.05 (Figure 2B) but substantially less than that seen with prescription drugs such as opioids, benzodiazepines and sedating antidepressants [16].

Other aspects of THC-induced impairment of driving (in addition to increased SDLP) include deficiencies in the ability to drive safely while performing a competing task (e.g., making a telephone call or completing a memory test) as well as reduced ability to accurately follow another vehicle [30-32].

Cannabis-affected drivers are clearly aware of their own acute impairment and show reduced willingness to drive [26, 30]. If compelled to drive, they will often adapt to their impairment by driving more slowly, taking fewer risks, and leaving a greater distance between their themselves and other vehicles [31, 33]. So, while drivers under the influence of THC show impairment in some measures, they may actually appear somewhat safer in other measures.

Duration of THC Impairment. Our recent review of the literature [24] indicates that impairment with THC or cannabis can last between approximately 3-10 hours depending upon three key factors: (1) *The dose*: higher THC doses produce longer lasting impairment than lower doses; (2) *The route of administration*: inhaled THC is absorbed, metabolised and eliminated more quickly than oral THC meaning that oral products are slower to act but cause longer lasting impairment than inhaled products; and (3) *Regularity of cannabis use:* Occasional cannabis users are become more impaired than regular cannabis users, who develop tolerance to the impairing effects of the drug.

This latter observation is a key point in relation to medicinal cannabis patients, nearly all of whom are regular (i.e., daily) users of cannabis and therefore likely to be far less impaired by THC than occasional users. Our most recent studies have shown little convincing evidence of "next day" or "morning after" impairment in people (including patients) tested for driving or cognitive function the day after consuming THC or cannabis [34, 35]. So, a patient using a THC product to help with sleep at night is unlikely to show driving or cognitive impairment the following morning.

Crash Risk. Epidemiological studies show that the presence of THC in blood is associated with a modest increase in the risk of being involved in any crash (crash risk), and in being responsible for that crash (culpability risk). The elevation in risk is modest (odds ratio [OR]: 1.1–1.4) when a range of potentially confounding factors are controlled for (e.g., the presence of other drugs, the fact that recreational cannabis users are likely to be younger and more prone to risky behaviour). The overall increase in risk in is considerably less than that seen with other prescription drugs for which driving is legal in patients (e.g. opioids (ORs: 1.7–2.3), benzodiazepines (ORs: 1.2–2.3)) and a 0.05% blood alcohol concentration (BAC) (ORs: 1.4–1.8) [19].

Do Blood or Oral Fluid THC Concentrations Predict Impairment? With alcohol, there is a linear relationship between blood alcohol concentrations (BACs) and driving impairment [16, 36-38]. This has given rise to *per se* laws governing alcohol use and driving which stipulate a BAC limit above which drivers are automatically deemed to be impaired (typically 0.02, 0.05 or 0.08% depending upon jurisdiction). Our own analysis, and those of others, shows that there is no such simple relationship between blood or oral fluid THC and driving/cognitive impairment. This reflects the complex non-linear pharmacokinetics of THC and the fact that blood THC concentrations remain very low after oral dosing [17, 23]. Drivers can display moderate THC concentrations in blood or oral fluid while driving normally or low THC concentrations while clearly impaired [17]. This indicates that the key measures currently used in MDT-related prosecutions, are unreliable indicators of impairment [23]. Alternative approaches for detecting and prosecuting THC-related impairment are urgently required.

Is Driving Likely to be Impaired in Medicinal Cannabis Patients?

Most studies showing THC-induced driving impairment have used young, healthy participants who *occasionally* use cannabis for recreational purposes [24]. As noted above, the smaller number of studies involving *regular* cannabis users suggest that these individuals develop tolerance to THC-induced impairment [24, 39].

Importantly, there have been no high-quality studies investigating the effects of THC on driving in *patients*. Patients using THC in oral or inhaled forms, unlike recreational users, simply seek relief from distressing symptoms such as pain, insomnia or anxiety and often wish to *avoid* intoxication. Their regular daily use will likely produce tolerance to the impairing effects of THC [24, 40].

Moreover, THC may alleviate symptoms (e.g., pain, spasticity, insomnia) that in themselves impair driving [41, 42] raising the possibility that driving performance may actually improve in some patients initiating use of THC-based medicines.

The Lambert Initiative has proposed an evidence-based solution to this issue in the form of a clinical trial called the **AMBER** trial. This would be world-first randomised, double-blind, placebo-controlled, multi-site clinical trial investigating the effects of treatment with a prescribed THC-containing product on driving performance in chronic-pain patients.

The trial proposed would track the effects of acute, oral THC versus placebo treatment on simulated driving in 150 chronic-pain patients during the first 12 weeks of using a prescribed cannabis product. This research would inform the development of evidence-based drug driving legislation that improves quality of life among medicinal cannabis patients without compromising road safety to the broader community.

We have sought funding support for the AMBER trial from the Federal government through the NHMRC and via a direct approach to the Health Minister, so far without success. We would be pleased to discuss funding opportunities with the NSW government and relevant local agencies.

Conclusions and Suggestions

As the number of patients using THC increases dramatically, it is essential that policy around medicinal cannabis and driving keeps pace. Overall, patients using cannabis-based medicines require more practical, nuanced, evidence-based advice and legislation in relation to driving, other than simple prohibition. Current laws are a major deterrent for patients who would otherwise wish to use medicinal cannabis products and this needs to be urgently addressed. A typical example of such an impact is provided by this 62-year-old female patient who has battled ovarian cancer for 10 years [18]:

> *'After exhausting all conventional treatments, I received medicinal cannabis as part of a clinical trial and found the results to be favourable. I wanted to continue via a prescription from my GP, however, the police informed me that even though it was medically prescribed, I would be fined and have to go to court should I ever take a roadside drug test. I decided not to continue as I didn't want to give up driving, which is crucial for me to be able to live an independent life. Because of this I am continuing to use MS Contin [opioid] and Lyrica [pregabalin], which I don't like, and would much rather be taking medicinal cannabis to deal with the discomfort.'*

In addition to the many patients who are not prepared to initiate medicinal cannabis due to fears of prosecution, it is clear there are also many patients who continue to drive when using THC-based products placing them at risk of a positive MDT and entanglement within the criminal justice system.

We respectfully suggest, on the basis of our careful consideration of the scientific literature, including our own detailed research, that ***patients with legal access to THC-containing products should be exempted from such prosecution unless there is evidence of impairment.***

This would simply put the legislative approach with medicinal cannabis on an even footing with other prescription drugs that have the capacity to impair driving.

Other jurisdictions, including UK, Norway, Germany, Ireland, and New Zealand apply these exemptions for patients, without any apparent problems (see Table below from [18]).

Table 3
International drug-driving (THC) enforcement approaches.

Country	THC presence offence?	THC detection method	Situation for medicinal cannabis patients	Additional information
United Kingdom	Yes	Oral fluid taken at roadside. Blood at police station or hospital and sent to laboratory.	Medical defence - if not impaired, and using a prescribed product as directed	Prescription medicines also tested for, but 'Zero tolerance' towards the presence of illicit substances. (Norwegian Ministry of Transport and Communications, 2020)
Norway	Yes	Oral fluid taken at roadside. Blood at police station or hospital and sent to laboratory.	Medical defence - if not impaired and using a prescribed, registered product as directed	20 drugs both licit and illicit are tested for against per se limits correlating with impairment. Gjerde et al., 2015)
Germany	Yes	Oral fluid taken at roadside. Blood at police station or hospital and sent to laboratory.	Medical defence - if not impaired, and using a prescribed product as directed	'Zero tolerance' towards the presence of illicit substances, some licit substances also tested for (Bundesregierung, 2020).
Ireland	Yes	Oral fluid taken at roadside. Blood at police station or hospital and sent to laboratory.	Statutory medical exemption certificate – does not apply if the person is found to be impaired (Road Safety Authority, 2020).	'Zero tolerance' towards the presence of illicit substances. (Irish Government, 2017)
New Zealand**	No	Field impairment assessment at roadside. Blood at police station or hospital and sent to laboratory.	Medical defence - if using a prescribed product as directed.	Presence of a licit or illicit drug (in blood) alone is not an offence, there must be additional evidence of impairment. (Ministry of Transport, 2019)

*A bill was introduced into the NZ Parliament in July 2020 which, if passed, will introduce a presence offence for THC detected in oral fluid. A medical defence will be available to patients prescribed medicinal cannabis (Ministry of Transport, 2020). Note, a recent report of the New Zealand Attorney General has concluded that provisions of the proposed Bill are inconsistent with the New Zealand Bill of Rights and recommends changing the focus from general deterrence to impaired driving (Attorney General, 2020).

A nuanced approach might also require patients to not drive during the first few days of using a THC-based product (i.e. when they are most at risk of impairment, prior to tolerance developing with repeated use). The AMBER trial could help inform policy in that regard.

A mandatory time limit (e.g. no driving for 3 hours) after consumption of a THC-containing product might provide an additional layer of safety and would be worth considering in a revised policy approach.

It is acknowledged that the combination of cannabis with other drugs, and particularly alcohol, requires additional caution and prohibition around such combined use might be maintained.

We thank the Senate Inquiry members for the opportunity to provide this submission and would be pleased to provide evidence in person if requested to do so.

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