## Medicinal Cannabis and Workplace Drug Testing:

## A Perspective from the Lambert Initiative at the University of Sydney

# A Submission to the Legislative Council Legal and Social Issues Committee Inquiry into Workplace Drug Testing in Victoria

Presented by: **Professor Iain S. McGregor** (Academic Director) **Dr Danielle McCartney** (Research Fellow)

On behalf of the: Lambert Initiative for Cannabinoid Therapeutics University of Sydney

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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 clinicians, 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.

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, their perceptions around efficacy, and their preferred models of access. 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.

Driving Research, Drug Testing, and Workplace Safety. We have conducted several recent studies characterising the effects of cannabis on driving, cognitive and psychomotor performance and implications for policy in safety sensitive workplaces. This includes studies where volunteers have consumed specific doses of cannabis and been assessed for driving and cognitive 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 impairment with cannabis and the relation between biomarkers (e.g. saliva, blood and urinary THC) and impairment. Experts from the Lambert Initiative have provided evidence in several national and international legal cases involving contentious issues around workplace drug testing and termination of employment in the mining and transportation industries.

#### THC and CBD: background information on current products and patient use

Cannabis refers to the dried flowering heads of the plant *Cannabis sativa*. Historically, cannabis has been smoked in 'joints' or 'bongs', often in conjunction with tobacco. More recently, cannabis is often inhaled by users through vaporisers (vapes, vape-pens); or ingested via orally administered products (e.g. oils, capsules, wafers, tinctures, sprays) or edible products (e.g. brownies, gummy bears, chocolate); or applied to the skin using transdermal patches, topical gels or balms.

There are more than 140 different bioactive compounds present in the cannabis plant that are classified as *cannabinoids*. It is generally accepted that only one of these compounds –  $\Delta^9$  *tetrahydrocannabinol* (THC) – intoxicates and is primarily responsible for the distinctive psychoactive effects of cannabis [1]. Another non-intoxicating component known as CBD (*cannabidiol*) is also of interest due to its therapeutic properties.

THC has a number of well-recognised therapeutic actions and is widely prescribed and consumed for medicinal purposes. A number of recent clinical trials, systematic reviews and meta-analyses demonstrate beneficial effects of THC in treating conditions such as chronic pain, chemotherapyinduced nausea and vomiting, spasticity in multiple sclerosis and Tourette syndrome [2-5]. CBD is prescribed for treatment-resistant epilepsy in children and has therapeutic properties in treating anxiety, psychosis and addictions [6, 7].

Since becoming legally available in Australia in November 2016, medicinal cannabis products have become a common medical intervention for a range of different medical conditions, particularly chronic pain, anxiety and insomnia [8]. Information available from the website of the Therapeutic Goods Administration (TGA) [9] indicates that there are many hundreds of thousands of Australian patients currently being treated with medicinal cannabis products by more than 5000 prescribers, with more than 500 THC- and/or CBD-containing medicinal cannabis products legally available for prescription to Australian patients.

TGA data indicate that both inhaled and orally- delivered medicinal cannabis products are in widespread use by Australian patients. CBD-only products represent around 20% of current prescriptions [9]. Patients often use inhaled THC-containing plant material products, together with an orally delivered CBD-only oils. The inhaled THC product provides rapid and relatively short duration pain relief and sleep-promoting properties while the oral CBD has longer-lasting, slower onset, anti-inflammatory and anti-anxiety effects [10, 11]. Use of THC products by night can reduce pain and promote sleep without causing next day impairment. CBD-only products, generally, do not cause any impairment, and are safe in the workplace.

#### THC-induced impairment: Background information

When consumed above a certain dose, cannabis products containing THC, can produce a distinctive intoxication (often called the cannabis 'high') which typically involves euphoria, relaxation, feelings of well-being, joviality, appetite stimulation, and enhanced sensory and hedonic experiences.

The side effects of using THC can include dizziness, sedation, and psychomotor and cognitive impairment in some patients [1, 12-16]. A proportion of users may also experience anxiety with cannabis use, although THC-containing products are also often used to *treat* anxiety [8, 17, 18].

When THC is used by patients for medical purposes, under appropriate clinical supervision, side effects tend to be minimised and are overcome in the initial stages of dosing in patients by slowly

increasing the dose of THC over time (so-called 'upwards titration') [10, 11]. It is important to note that the vast majority of medical cannabis users are not seeking to get 'high', but only to treat their symptoms such as chronic pain or insomnia.

The intoxicating effects of THC are more prominent in *occasional* recreational users of cannabis compared to *regular* users of cannabis. This reflects a general lack of tolerance to such effects in occasional users. Intoxication in occasional users is seen with inhaled and oral doses above 10 mg THC [12, 14, 19]. Higher doses of THC generally causing a larger magnitude and longer duration of impairment [20].

This short-term impairment is seen in a range of cognitive (e.g. memory, decision making and attention) and psychomotor tasks (the term *psychomotor* denotes tasks where mental activity directs a particular type of skilled or co-ordinated physical movement such as driving) [20]. The impairment caused by cannabis is known to be primarily due to THC, the main intoxicating component of cannabis, because THC administered alone causes equivalent impairment to cannabis itself [1, 20]. *Impairment* is defined as a deleterious effect of cannabis or THC, relative to placebo or no treatment, on the performance of such tasks.

The tasks showing THC-induced impairment are typically undertaken in academic research laboratories and involve healthy volunteers who are infrequent recreational cannabis users. Tasks shown to be sensitive to impairment include divided attention, tracking performance, information processing, conflict control, fluid intelligence, reaction time, fine motor function, sustained attention and working memory tasks [20].

THC-induced impairment of driving has been described in studies involving on-road driving and laboratory-based driving simulators. Driving studies generally show that acute intoxication with THC causes an array of subtle changes in driving performance. One prominent effect seen in occasional recreational users of cannabis is a tendency for THC to modestly increase lateral instability in drivers ("weaving"), known technically as an increase in the *standard deviation of lateral position* (SDLP) [21].

Notably, however, cannabis-affected drivers appear to adapt to their subjective feelings of impairment by driving more slowly, taking fewer risks, and leaving a greater distance between their own vehicle and the car in front [22, 23]. This contrasts with alcohol, where intoxication generally increases risk-taking.

It is generally accepted that CBD, when used alone, and even at very high doses, does not impair cognitive function, psychomotor function, or driving [24, 25]. Our own group recently published a study in which we gave oral doses of 1500 mg CBD (15 times a typical prescribed dose) to healthy volunteers and undertook detailed assessment of their driving and cognitive function. No impairment was observed even with this very high dose of CBD [26].

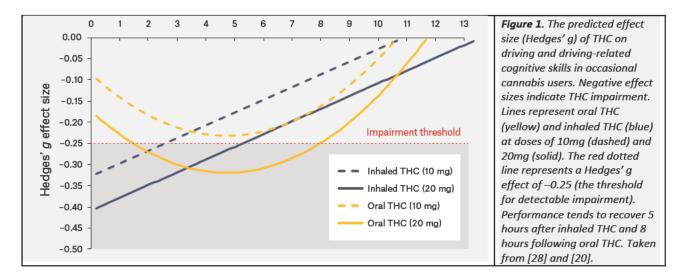
#### How long do impairing effects of medicinal cannabis last?

The duration of cognitive and psychomotor impairment following use of THC is a key issue in safety-sensitive workplaces. Accordingly, our research group has published a systematic review and meta-regression analysis that synthesises all the available data around the duration of cognitive and psychomotor impairment following different doses of oral and inhaled THC [27]. Meta-regression analysis is a formal, quantitative, statistical approach to deriving conclusions from multiple studies that address the same research question.

Our review summarised evidence from 80 published studies that met quality requirements for inclusion. These 80 studies involved 155 experiments and 1534 outcomes [27] probing cognitive, psychomotor and driving impairment after cannabis or THC administration. The evidence was synthesised to produce a model that predicts duration and magnitude of impairment in occasional cannabis users given a particular dose of inhaled or oral THC (Figure 1). The model is expressed in terms of Hedges' g effect size, which is a standardised way of expressing the difference between two treatments (e.g. THC v placebo) where a g value of 0.25 is generally accepted as a small or threshold effect.

The model encompasses an Excel-based calculator which enables individuals to input a particular dose of THC, a specific duration after use of that dose, and to calculate the likelihood of impairment across a range of different cognitive and psychomotor tasks at that dose and time (see Appendix A, Excel spreadsheet, in [20]).

Our key conclusions were that: (a) with inhaled (i.e. vaporised or smoked) THC, occasional cannabis users show impairment for up to five hours following higher doses (e.g. 20 mg) of THC, and impairment of shorter duration (around three hours) and magnitude following lower inhaled doses (e.g. 10 mg). An inhaled dose of 10 mg THC appears to be a threshold, borderline, dose for producing impairment (Figure 1); and (b) with use of oral THC products, occasional cannabis users show a slower onset, but longer duration, of impairment compared to inhaled THC, and this is also dose-dependent. Duration of impairment may be up to eight hours following higher doses (e.g. 20 mg) of oral THC. Lower oral THC doses (e.g. 10 mg) produce a lower magnitude of impairment, again borderline, and for a shorter duration of impairment (around five hours).



In this analysis, a reliable model describing magnitude and duration of impairment could *not* be developed for regular or heavy cannabis users as there was insufficient evidence around THC impairment in these populations. As noted above, the extent of THC-induced impairment varies according to the frequency of cannabis use, with regular cannabis users typically showing less impairment at a given dose of THC than occasional users [29-32]. This is an example of *drug tolerance*.

Tolerance to THC has been characterised in a small number of studies where participants have been housed in research facilities and administered THC daily for a treatment period of up to nine weeks [33-35]. In each instance, the same dose of THC elicited stronger feelings of intoxication at the *start* compared to the *end* of treatment. The longest treatment period (nine weeks) saw an 89% reduction in subjective intoxication (i.e., 1.9 vs 0.2 on a 0–5 scale after 20mg THC [33]). These findings suggest that THC-induced impairment, in as much as it corresponds to subjective intoxication, greatly subsides over time with daily THC treatment.

In one often-cited study, occasional cannabis users were much more impaired than heavy users in their on-road driving, as indexed by SDLP, with a 10 and 20mg THC dose [29]. Other relevant studies have shown differential impairment in occasional versus regular users in laboratory psychomotor tasks following smoked cannabis, with heavy users showing less impairment [30, 31].

Unlike recreational cannabis users, *medical* cannabis users typically use THC: (1) on a regular (daily) basis, meaning that they are likely to develop 'tolerance' to its impairing effects [36, 37]; (2) at lower doses to avoid intoxication; and (3) to alleviate distressing symptoms (e.g., pain, spasticity, insomnia) that may themselves impair driving and cognitive function [38, 39].

A recent driving simulator study conducted by our colleagues at Swinburne University in Melbourne is one of the very few studies examining potential impairment in *medicinal* cannabis users. They assessed driving performance in 40 adults aged between 23 and 80 years in the hours following consumption of their own prescribed medical cannabis product. The doses of THC in the products consumed ranged from 1 mg to 40 mg and both inhaled and oral products were used by the patients in this study. Results showed a negligible impact of THC on driving and cognitive performance in these patients when their products were used as prescribed [40].

Our recent systematic review [20] identified only six low quality studies investigating the effects of THC (1.5–28 mg) on cognitive function in patients suffering from such conditions as diabetic neuropathy, Tourette's syndrome, and dementia. Only one of these studies detected a significant detrimental effect of THC, a study that measured gross motor function in individuals with dementia [41]. The experimenters described a benign adverse profile with modest changes in gait and body sway in these patients within two hours of THC administration.

Other relevant data come from a European registry of patients prescribed nabiximols (THC/CBD oral spray) to treat spasticity in multiple sclerosis [42, 43]. The prescribing clinicians provided data to the registry on patient response to the drug, including adverse events. Of the 387 registered patients for whom data on driving were provided, 303 reported no change in their driving ability, 63 reported an improvement, two reported mixed effects, and only 19 reported a deterioration [43].

#### The possibility of 'next day' impairment with THC

As shown above (Figure 1), our published meta-regression analysis found little evidence that the impairing effects of either oral or inhaled THC persist beyond eight hours in occasional cannabis users [20]. However, studies examining the possibility of longer durations of impairment were not included in the analysis which only included studies examining impairment up to, and including, 12 hours after THC use. There have been some claims in the scientific literature that THC use may cause a 'hangover' the following day [44, 45].

To address this issue, our group has conducted another systematic review that synthesised results from all relevant studies that have examined THC or cannabis-induced impairment at durations between 12 and 48 hours following use (referred to as 'next day' effects for convenience as the vast majority of studies probed performance at 12–24-hours post-treatment) [46]. Our paper reported whether such studies had found 'next day' impairing effects of cannabis, or not, and also closely examined the quality of the studies by applying standard 'Risk of Bias (RoB)' criteria.

Our review identified 20 relevant published studies that involved a total of 345 performance tests (i.e. most individual studies had multiple performance measures tested across the same participants). With a few exceptions, studies administered a single dose of THC and probed cognitive, psychomotor or driving/flight simulator performance at various time points afterwards. Results showed that:

• A total of 209/345 tests conducted across 16 published studies showed no 'next day' impairing effects of THC. Nine of these 16 studies involved good quality experimental designs.

• A total of 12/345 tests conducted across five published studies provided evidence of negative (i.e., impairing) 'next day' effects of THC. None of these five studies used good quality designs and all were published >18 years ago (4/5 were published >30 years ago).

• A total of 121/345 tests conducted across seven published studies had unclear 'next day' effects of THC. Here, there was insufficient information provided in the publications to allow outcomes to be properly assessed.

• The remaining 3/345 tests indicated positive (i.e., performance enhancing) 'next day' effects of THC.

In summary, only a few lower-quality studies report 'next day' effects of THC on cognitive function and safety-sensitive tasks. However, most studies, including those of higher quality, have found no such effects.

A recent placebo-controlled clinical trial from our research group further underlines the low likelihood of impaired 'next day' performance with cannabis use. Our study involved 20 cannabisinexperienced patients suffering from primary insomnia who attended a secure medical facility on two occasions. On one occasion they were given an oral dose of 10mg THC and 200mg CBD and on the other occasion a matched placebo. On both occasions they were kept overnight in the facility where various sleep and EEG parameters were recorded. The following morning, around 10-16 hours after receiving the THC/CBD (or placebo), they were evaluated in an extensive battery of cognitive, vigilance-related and driving simulator tasks. Results showed no notable 'next day' impairments in cognitive or driving performance for THC/CBD treatment relative to placebo. The results of this study are currently submitted for publication [47].

Overall, we believe that the above evidence indicates that it is very unlikely that workers would show any significant impairment in cognitive and psychomotor function in the workplace resulting from medical use of vaporised or oral cannabis in the evening before work. This is because (1) the window of impairment is unlikely to be longer than 8 hours under most conditions; (2) regular, medicinal use of THC appears to cause little impairment at any duration following use; and (3) use of medicinal cannabis products to alleviate symptoms (e.g. pain, muscular spasms) that by themselves might impair performance can be highly beneficial.

#### Does the presence of THC in urine and oral tests indicate impairment?

There has been much recent scientific discussion around the relationship between blood, urinary and oral fluid THC concentrations and impairment. The general consensus is that while higher THC concentrations tend to indicate a greater likelihood of impairment, there is no simple threshold concentration of THC in any biological matrix (blood, urine or saliva) that can be specified that is a reliable proxy for impairment [48, 49]. This reflects the complex pharmacokinetics of THC, and contrasts with alcohol, where we know that blood alcohol concentrations such as 0.05% (50 mg/dl) or 0.08% (80 mg/dl) are reliable correlates of impairment.

Despite this, legal prohibitions in some countries specify a blood, urinary or oral fluid THC concentration (often called a *per se* limit) above which a user is deemed to be impaired (e.g. 1, 2 or 5 ng/ml THC in blood). This approach, analogous to legal prohibitions with blood alcohol concentrations above 0.05%, is controversial given the poor correlation between blood THC concentrations and actual impairment [48, 50]. However, in Australia, with the exception of Tasmania, the *mere presence* of THC in blood or oral fluid in drivers is illegal with no legal cutoff specified. Tasmania allows an exemption for drivers who have a legal prescription for medicinal cannabis.

The complex pharmacokinetics of THC reflect the fact that THC readily lodges in fat stores in the body. As such regular cannabis users develop a substantial 'depot' of THC in their fat tissue that can be slowly released back into blood. This causes long-term persistence of THC and THC metabolites in blood and other biological matrices, particularly urine, even following long-term abstinence from cannabis, and in the absence of impairment. For example, THC, and the metabolites 11-OH-THC and THC-COOH can be readily detected in the urine of frequent cannabis users after more than three weeks of verified abstinence from cannabis [51].

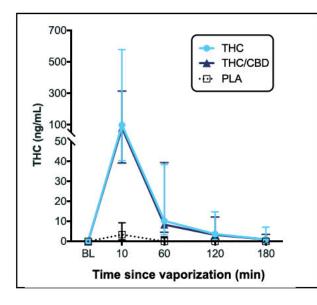
Given that THC-induced cognitive and psychomotor impairment is unlikely to persist for more than eight hours after use (see sections above), urinary THC is a very unreliable proxy measure for impairment. We note that many employers assert that urine testing is an accurate way of determining whether employees are under the influence of alcohol or drugs. We would dispute these assertions, given that urinary THC markers do not in any way predict impairment. It is grossly unfair when employees fail employer-mandated standard urinary workplace drug screens for THC metabolites and suffer termination of his employment. This appears unjustified and unfair given that the presence of THC (or THC metabolites) in urine would have little if any bearing on whether an employee is impaired or not in his workplace.

Given the failure of urinary drug screens to correlate with impairment, it is of interest to determine whether assessment of blood or oral fluid THC concentrations provides a better approach. Blood can almost immediately be ruled out: as well as being a poor correlate of impairment, blood collection is a relatively invasive intervention for employees and it is not practical to organise sampling and analysis routinely in the workplace.

This leaves oral fluid as the main alternative approach. Accordingly, we note that 'point of collection' devices (e.g. DrugWipe 5S, Dräger DrugTest® 5000 [52, 53]) are now in widespread use by Australian police for roadside detection of THC in the oral fluid of drivers under the assumption that the presence of THC in oral fluid is associated with driving impairment. These devices are also sometimes used in the workplace. These devices are sold with a specified cutoff (e.g. The *Securetec DrugWipe® 5S (DW5S)* - the device has a manufacturer-specified detection limit of 10 ng/mL; while the *Dräger DrugTest® 5000 (DT5000)* has the capacity to set the threshold to 5, 10 or 25 ng/ml THC). This means that while the law may specify 'mere presence' of THC as prohibited, the testing conducted by police using these devices actually involves a *de facto* threshold imposed by the detection limits of these devices. Our own research has highlighted the relatively poor sensitivity and accuracy of these devices with significant numbers of false positive and false negative test results for THC [52].

Our research group has published a comprehensive meta-analytic review around whether blood and oral fluid THC concentrations predict cognitive, psychomotor and driving impairment. Our analysis involved a total of 26 published studies and 822 relevant outcomes that met inclusion criteria and where both impairment and blood and/or oral fluid THC concentrations (or THC metabolites) had been measured. Overall, our review found that the relationship between oral fluid THC concentrations and impairment in occasional cannabis users was *weak* [48]. That is, oral fluid can partly predict THC-impairment in cannabis users, but not with any great certainty.

THC concentrations in oral fluid peak quickly after cannabis inhalation and then rapidly decrease over time (Figure 2) and this provides the fundamental reason for their correlation with impairment. That is, impairment tends to decrease in the hours following cannabis or THC use (Figure 1) and so do oral fluid THC concentrations (Figure 2). A cutoff of 25 ng/ml THC in oral fluid will provide a point that captures the peak window of impairment in most occasional users occurring within the first 60 minutes following cannabis use. A cutoff of 10 ng/ml THC in oral fluid was identified in a recent study as being a reasonable marker for recent (< three hours) cannabis use in a large cohort (n=191) of both regular and occasional cannabis users [54]. However, this does not mean that these cutoffs necessarily predict impairment in regular or medical cannabis users.



**Figure 2.** The study by Arkell et al [52] illustrates median oral fluid concentrations of THC over time following vaporisation of cannabis by occasional cannabis users. The cannabis contained either 13.75 mg THC (**THC** condition), or 13.75 mg THC with 13.75 CBD (**THC/CBD** condition), or placebo cannabis containing <1% THC (**PLA** condition). The THC and THC/CBD cannabis treatments caused subjective feelings of intoxication, some cognitive impairment, and increased 'weaving' in a driving simulator task. Note that median oral fluid THC concentrations peak very quickly and then rapidly decrease to below 10ng/ml by two hours. Note also high variability between individuals as shown by error bars signifying the interquartile range. BL = baseline.

Despite the parallel time course of oral fluid THC and impairment, the correlation is weak. One reason for this is a profound variability in oral fluid concentrations across individuals consuming the same amount of cannabis. For example, one study [55] reported peak oral fluid THC concentrations ranging from 387-71,147ng/mL in chronic cannabis users five minutes after smoking the same 500 µg/kg dose of THC. Similarly, a study by our group showed peak THC concentrations ranging from 19-1318ng/mL following vaporisation of the same dose of cannabis [52]. This presumably reflects individual differences in oral physiology: some users have oral fluid and/or an oral cavity that predisposes to THC retention. These users will be particularly vulnerable to retaining THC in oral fluid and will give positive oral fluid tests at much longer durations after use.

Another reason for the poor correlation between oral fluid THC concentrations and impairment is that regular and heavy users of cannabis generally show more persistent and higher concentrations of THC in the oral cavity than occasional users, following consumption of the same dose [56-58]. This appears to reflect a certain accumulation of THC in the oral cavity over time in regular users. This means that they may give a positive oral fluid test at durations such as 24 or 48 hours after use when impairment would not be seen. Also, as noted above, heavy cannabis users, are far *less* likely to show impairment than occasional users at any time interval. Another important variable is the type of cannabis product being used. It is generally found that inhaled cannabis products lead to high oral fluid THC concentrations than orally ingested products (e.g. oils) [56]. Importantly, when THC is taken in capsule form, THC does not come into contact with the oral cavity during consumption and therefore there will be no THC present in oral fluid [59, 60]. While THC delivered in a capsule will enter the bloodstream there is no evidence that it can then pass from the blood into oral fluid. This means that users can be heavily impaired with use of high doses of THC in capsule form but have zero THC concentrations in their oral fluid. Similarly, THC can be delivered via transdermal patches or suppositories (each of which bypass the oral cavity), and can cause impairment, yet no THC will be found in their oral fluid.

Overall, our opinion is that the use of an oral fluid point of collection device such as a Dräger DrugTest<sup>®</sup> 5000 would be something of an improvement in managing workplace impairment over the use of urinary drug testing. Regular users of inhaled THC will always have some THC present in their oral fluid but this will peak immediately following use of his inhaled THC product and then return quickly to a low value within hours. Of course, it remains possible that some employees will have oral physiology that predisposes them to retaining high concentrations of THC in oral fluid, but this could be readily ascertained by determining whether they give a positive result on a device such as the *Dräger DrugTest<sup>®</sup>* 5000 above 10 or 25 ng/ml the morning after use of THC-containing medication.

# Are there any other tests available (besides urine and oral tests) that can confirm impairment after taking prescription cannabis?

There is no generally accepted objective test that reliably shows THC-induced impairment in populations of cannabis users. As shown above, the use of urinary, blood and oral fluid measures of THC and THC metabolites are problematic although oral fluid testing of THC at a specified cutoff has some utility as a marker of recent cannabis use. The use of 'field sobriety tests' has also been investigated, but traditional tests used to determine alcohol intoxication (e.g. walk in a straight line and turn, horizontal gaze nystagmus test) do not reliably predict people intoxicated with THC [21, 29, 61]. A recent large study involving USA highway patrol officers who were trained drug recognition experts (DREs) showed that they were relatively poor in discriminating people who had recently used cannabis from those using placebo through the use of field sobriety tests [61]. The ability to stand on one leg, particularly with eyes closed, has some utility as a predictor of recent cannabis use [21, 61] but the fact that individuals vary greatly in their ability to perform this task renders this measure impractical as a roadside field sobriety test. The DRUID test, a smartphone app sometimes used in the neurocognitive testing of employees, incorporates a one leg stand as part of the overall test battery used to detect cannabis and alcohol impairment [62, 63].

The combination of an oral fluid THC test with a cutoff of 10 ng/ml, together with a short field test of functional impairment such as DRUID, may provide the employer with the best current solution to detect cannabis-induced impairment. The use of the DRUID test would guard against the possibility that employees are, for whatever reason, functionally impaired, and this test could be easily conducted on the employee's phone (taking less than three minutes to complete). The DRUID app stores historical data so employee performance over time can readily be tracked and any anomalous high readings readily identified. The use of an oral fluid THC test would provide an additional means of ensuring that cannabis had not been used recently and add an extra layer of security against possible impairment.

#### Conclusions

Employers currently face significant complexity with increasing numbers of employees using legally-prescribed medicinal cannabis products while occupying safety-sensitive roles in the workplace. There is understandable reticence amongst employers to deviate from strict zero tolerance policies around cannabis, yet current policies are able to manage a wide range of other legally prescribed drugs (e.g. benzodiazepines, opioids, antipsychotics, sedating antidepressants) used by employees that cause significantly greater impairment than cannabis. The key is to use the best available medical and scientific evidence to manage the potential risks.

The current submission outlines the clear evidence that patients using medicinal cannabis products are unlikely to pose a safety risk if they use their products as prescribed and leave a reasonable interval (at least eight hours) between their use of THC-containing products and undertaking safety-sensitive tasks.

The use of point of collection devices to perform random oral fluid tests for THC at a specified cutoff (e.g. 10 ng/ml), while clearly not perfect, can provide an additional layer of security against impairment in employees. This could be coupled to the use of rapid smartphone app-based tests of impairment that can be used to build historical data around psychomotor and cognitive performance in employees.

Overall, it is clear that some employers are using unnecessarily harsh approaches, with termination of employment on the basis of a positive urinary test for THC metabolites. This occurs even with employees who act in a responsible and transparent manner with their employer around their medical condition and his use of cannabis-based medicines to treat that condition. Detailed neurocognitive testing of employees who have THC-based prescriptions has found no cause for concern around next day cognitive and psychomotor performance and indicates that they can safely use medications in the evening and report for work in the morning.

With many hundreds of thousands of Australians currently now using legally-prescribed THCcontaining products, it is imperative that all employers develop nuanced and scientifically justifiable approaches to managing workplace safety in employees who are prescribed cannabis-based medicines.

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