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Legal and Social Issues Committee
Inquiry into workplace drug testing in Victoria
Parliament House, Spring Street
EAST MELBOURNE VIC 3002

29 January 2024

To whom it may concern,

MEDICINAL CANNABIS AND WORKPLACE DRUG TESTING

The Victorian Legislative Council has deputised the Legislative Council to launch an inquiry into the legislative and regulatory framework for workplace drug testing, with a focus on the treatment of prescription medicinal cannabis as compared to other prescription medications under that workplace drug testing framework, and with the aim of determining whether the framework for occupational health and safety and workplace drug testing may be improved to benefit medicinal cannabis patients and to determine whether the current workplace drug testing laws and procedures are discriminatory in nature.

Safework Health

Safework Health (SWH) is an Australian company founded in 2012. It is the largest provider of workplace drug testing in Australia with a head office in Mount Waverley and employs approximately 150 people. SWH is the only dedicated integrated provider of workplace drug testing in Australia, delivering collection services, laboratory testing and clinical advice to in excess of 2,000 customers, including BHP, Rio Tinto, Boral, Brisbane City Council and Ambulance Victoria.

The function of Workplace Drug Testing

The purpose of workplace drug testing is to reduce the heavy burden of workplace accidents, injuries, lost productivity and equipment damage. A substantial fraction of workplace accidents arise from the impact of drug use – either recreational use, or the inappropriate use of prescribed and non-prescribed medications. Policing recreational drug use that does not impact workplace safety – e.g. weekend cannabis use completed > 24 hrs prior to resumption of work – would be both counter-productive (i.e., being likely to generate opposition by the workforce) and not effective in reducing workplace Lost Time Injury Frequency Rate (LTIFR) levels. Only by focusing on worker impairment – whether arising from drug/medication use or fatigue – can a fair and effective program to reduce workplace harm be implemented. This focus on impairment as opposed to policing prior use was emphasised in the recent Fairwork NSW case Rece Goodsell v Sydney Trains (U2022/9973) which was found in favour of the plaintiff on the basis of negligible impairment at the time of testing.

Impairment is defined by the AACIW (Alberta Advisory Committee on Impairment in the Workplace) as "a disturbance of functions from any cause that results in an unacceptable risk of an individual being unable to safely perform a task at work. The point at which this disturbance in function becomes an unacceptable risk in terms of job performance depends on the job at hand and its hazards." This implies testing for drug-induced impairment must enable the presence of the drug to be detected throughout the period it is exerting a biological effect.

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CANNABIS

The two most abundant bioactive molecules in cannabis are THC (Δ9-tetrahyrocannabinol) and CBD (cannabidiol). THC is the principal psychoactive component of cannabis, responsible for the classical cannabis 'high'. Therapeutic reviews suggest THC may be efficacious in treating chemotherapy-associated nausea and vomiting, chronic pain (including, to a moderate degree non-cancer chronic pain) and multiple sclerosis – associated spasticity. Although use of THC for autoimmune disorders (notably arthritis) anxiety management and insomnia is increasingly popular, there is no conclusive evidence of clinical benefit these conditions. Due to its psychoactive properties, THC use is associated with significant impairment in complex-task performance for some hours following ingestion.

The TGA has categorised Cannabis medications depending on the relevant CBD to THC ratio. With Category 1 Drugs equal or over 98% of the cannabinoids present are CBD and THC constitutes less than 2% of the cannabinoids. These drugs are Schedule 4 drugs 'prescription-only restricted substances' (classed due to a tendency to be abused/or cause dependence) are easily managed at the workplace and have minimal if any associated impairment – in other words, like short-term benzodiazepines (BZO's) when properly used, albeit not like intermediate- or long-duration BZO's which have significant and impairing hang-over effects.

Categories 2 to 5 are Schedule 8 drugs designated as 'drugs of addiction' (like for example morphine) and are subcategorised depending on the increasing THC fraction. The latter 2 categories (4 & 5) are effectively pure or nearly pure THC extracts and as will be noted later – these are the drugs that will need closer supervision.

<u>CBD (Cannabidiol) – associated impairment</u> (Category 1)

Cannabidiol (a.k.a. CBD) is a component of cannabis plants (including both the common C. sativa and the indica variety) that can account for up to 40% of a cannabis extract and was first isolated in 1940. Unlike THC, which modulates the activity of the CB1 receptor in the brain and is the psychogenically active compound in cannabis responsible for the cannabis 'high', multiple meta-analyses have shown that CBD does not exert any intoxicating effects, although it is anxiolytic and has an anti-psychotic effect. A 2011 Meta-analysis reported very few side effects and that CBD was well tolerated even at very high doses, stating "Based on recent advances in cannabinoid administration in humans, controlled CBD may be safe in humans and animals." (Bergamashi et al 2011) Medical studies have found CBD has some general anti-inflammatory and immune-regulatory effects (which has led to its popular use in arthritis) as well as being an effective medication for seizures in Lennox-Gastaut and Dravet Syndrome, especially among children with refractory epilepsy.

Pure low-dose CBD has only minor side-effects, primarily dry mouth and nausea, although diarrhoea may occur. Low blood pressure is a known side-effect, so people with low blood pressure (hypotension) or who take high doses of anti-hypertensive medication, may experience transient light-headedness, and should avoid driving/operating machinery for up to 2 hrs after oral ingestion. Actual sedation is quite rare. CBD may be unsafe to use during pregnancy – the literature is equivocal on that point – and should not be used if the person has Parkinson's disease (even when well controlled). CBD doses should be decreased in the presence of liver disease as it may elevate hepatic transaminase enzyme levels even in healthy individuals. CBD has mixed effects on appetite, with 30% of subadult users reporting a significant increase in appetite, with the remainder experiencing either no change or an actual decrease in food intake.

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In contrast to THC, from a workplace perspective, CBD is benign – because it is not psychotropic it will not cause impairment, so it would be safe to drive or work machinery on a pure CBD-Oil. Note however this is not true for a mixed CBD/THC Oil.

The TGA down-classified some Schedule 4 CBD products to Schedule 3, making them available as over-the-counter products sold at pharmacies, with the proviso of a maximum dose of 150 mg/day (oral or sublingual use).

Despite initial hopes, the addition of CBD to THC preparations does not appear to attenuate THC-associated performance impairment. Current research suggests the addition of CBD to THC preparations, even when given in equal concentration (i.e., a 1:1 THC:CBD ratio) does not decrease THC-associated impairment (Arkell et al 2020; - 2019).

THC: Cannabis-associated impairment (Category 2 to 5)

The issue of the correlation between actual complex task performance impairment and users reporting feeling impaired is a difficult one. Driving is often used as a standard complex task requiring high-level sensorimotor coordination, reasoned judgement memory and rapid reaction times and may stand in as a marker for workplace performance.

- Driving-skill impairment

Cannabis-associated impairment of complex-task performance (primarily driving skills) has been documented in both experimental studies and epidemiological reviews. Experimental reviews commonly involved the administration of fixed THC doses to subjects prior to the of administration of a cognitive performance task (usually involving skillsets central to the task of driving such as tracking performance, lateral control and divided attention) have reported significant post-use impairment (Broyd et al 2018; Hartman and Huestis 2013; Oomen et al 2018). Similarly, epidemiological reviews have shown cannabis use moderately increases the risk of being involved in a motor vehicle accident (Li et al 2012; Rogeberg & Elvik 2016; - 2017; Rogeberg 2019) with the National Academy of Science Engineering and Medicine (2017) review definitively concluding there is substantial evidence of a statistical association between cannabis use and raised MVA risk.

The most-recent epidemiological meta-analyses suggest cannabis-affected drivers are roughly 1.1 to 1.4 times more likely to have a crash than unaffected drivers (Rogeberg & Elvik 2016; - 2018; Drummer et al 2020), although risk may be roughly proportional to blood THC levels (Brubacher et al 2019). At lower range blood THC levels, the crash risk is roughly equivalent to that of low-to-moderately raised BAC – i.e., roughly equivalent to 0.02 to 0.05% BAC.

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The following table from Arkell et al (2021) is instructive:

Table 1. Crash Risk and Culpability Estimates

Drug class	Crash risk estimate	Crash culpability estimate
Alcohol (BAC = 0.02)	1.03–1.19 (Compton & Benning 2015; Blomberg et al 2009)	1.36 (Compton & Benning 2015)
Alcohol (BAC = 0.05)	1.38–1.75	2.19 (Compton & Benning 2015)
Alcohol (BAC = 0.08)	2.69–2.92	3.63 (Compton & Benning 2015)
Cannabis	1.11–1.42 (Rogeberg 2019; Rogeberg et al 2018; Elvik & Risk 2013; Hostiuc et al 2018)	1.20–1.42 (Rogeberg 2019; Rogeberg & Elvik 2016; Rogeberg et al 2018)
Antidepressants	1.35–1.40 (Elvik & Risk 2013; Hill et al 2017))	N/A
Antihistamines	1.12 (Elvik & Risk 2013)	N/A
Benzodiazepines and Z-hypnotics	1.17–2.30 (Elvik & Risk 2013; Dassanayake et al 2011)	1.41 (Dassanayake et al 2011)
Opiates	1.68–2.29 (Elvik & Risk 2013; Chihuri & Li 2017)	1.47 (Chihuri & Li 2017)

On-road driving studies, which more accurately reflect the real-world impact of cannabis on driving than laboratory testing, have shown that cannabis-induced driving impairment – specifically lane weaving (as measured by increased Standard Deviation of Lateral Position) – is roughly equivalent to BAC of ~ 0.05 g/L (Irwin et al 2017), one-night sleep deprivation (Ramakers et al 2012) and a standard 10mg dose of the benzodiazepine Diazepam (Jongen et al 2017). Arnold et al (2020) showed that occasional cannabis users who received a THC dose (13.75mg) roughly equivalent to standard medicinal doses show clinically significant driving impairment up to 240 – 300 minutes post dose (with the majority of impairment occurring from 40-100 minutes post use).

There is a complex relationship between medicinal cannabis use and impairment. Nabiximols (legally marketed as Sativex), is a mixed cannabinoid medication, a 1:1 mix of THC and CBD oral spray extracted from cannabis sativa plant material, prescribed for neuropathic pain and spasticity in multiple sclerosis. When used to combat a physical disorder such as MS-associated spasticity, a majority of patients on long-term Sativex treatment reported either some improvement in their driving ability or no observable change, which is attributed to reduced spasticity (Celius et al 2018). Friedel et al (2015) reported similar findings with a computerised test battery after one to 1 ½ months of treatment.

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- Workplace impact

As noted by Hazle & Hill (2022) studies directly addressing the impact of cannabis use on workplace safety and productivity are relatively uncommon compared with the numerous studies addressing the impact of cannabis use on motor vehicle driving. However, significant numbers of peer reviewed studies have shown potentially serious impairments arising from cannabis use including sensorimotor deficits – such as coordination (Prashad & Filbey 2017), complex task performance (Tefft & Arnold 2020 MVA; Sewell et al 2009 – in both studies focussing mostly on driving deficits) – and cognitive/emotive changes including a significant decrease in overall motivation (Pacheco-Colon et al 2018) and cognitive functioning (Prashad & Filbey 2017 – notably in declarative memory and problem solving). Moreover, as (Bolka et al 2002) noted, the effects of cannabis were found to present in a dose-dependent manner.

Ethical as well as practical limitations in directly testing the impact of cannabis on workplace productivity, performance and safety have led to a reliance on proxy markers (drug test results, injury and near-miss rates)

The comprehensive literature review by the National Academies of Sciences, Engineering, and Medicine (2017) on the health effects of cannabis, searched six major studies for correlation between cannabis use and occupational injury, but concluded it was not definitively possible to 'determine whether general, nonmedical cannabis use is associated with a clearly increased risk of occupational accidents and injuries across a broad range of occupational and industrial settings in the absence of other important risk factors' because the articles various methodologies and definitions of cannabis use rates were incompatible. Despite this Hazle & Hill (2022) noted there is 'suggestive data about a causal connection between cannabis use and workplace accidents'

Zwerling et al 1990 investigated 2537 prospective postal employees with positive pre-employment THC drug screens for THC showing a significant correlation in susceptibility for job turnover (relative risk of 1.56), accidents, injuries (relative risk 1.30-2.64), and workplace discipline, with definite albeit small rises in undesirable outcomes. Absenteeism was also noted to be substantially higher among THC-positive testing employees (7.1% absence rate) compared with a 4.0% absenteeism rate among non-users. Curiously, the effect was similar to that of low-level cocaine use (save that cocaine users appeared less prone to job turnover).

Table 2. Lifetime Use of Cannabis and Risk of Injury (Zwerling et al 1990)

Lifetime use of cannabis	Increased risk of injury	Odds ratio
1–9 Times	1.42	1.12–1.80
10–39 Times	1.46	1.07–1.98
40+ Times	1.94	1.51–2.50

Table 3. Past 30-Day Use of Cannabis and Risk of Injury (Zwerling et al 1990)

Past 30-day use of cannabis	Increased risk of injury	Odds ratio
1–9 Times	1.37	1.06–1.77
10–39 Times	1.51	1.03–2.21
40+ Times	2.47	1.64–3.71

Irrespective of the actual duration of impairment, Arkell et al (2020), reported that 72% of Australian cannabis-users believed their medicinal cannabis use did not impair their ability to drive, which was roughly the same as the 71% of respondents who believed their medicinal cannabis use did not impair their ability to assess their fitness to drive. This contention is clearly false as demonstrated by Arkell et al 2021 who noted more than 1/3rd of respondents (35%) reported 'typically driving within three hours of cannabis use' - well within the substantial impairment period following standard medicinal cannabis use. These findings are supported by surveys from Australia, Canada and the US where between 13 to 50% of respondents admitted to driving within 3-4 hours after recreational cannabis use (Bonnar et al 2019; DiGuiseppi et al 2019; Rotermann 2020).

Carnide et al 2023 investigating Canadian workers in a longitudinal study from 2018 to 2020 concluded that while cannabis use in the past year had no effect on injury rates, workplace cannabis use, or use just prior, was associated with an almost two-fold increased risk of experiencing a workplace injury (RR 1.97, 95% CI 1.32-2.93). Findings were similar for workers in safety-sensitive and non-safety-sensitive work, consistent with other literature reports.

Duration of THC-associated impairment

Regular use of many drugs, cannabis included, may lead to the development of tolerance where a user becomes more adapted to and is better able to compensate for the effects of a drug. Colizzi and Bhattacharya (2018) reported that the acute effects of a single dose of cannabis are somewhat less in regular cannabis users compared to infrequent users – in other words, some level of tolerance was seen with regular use. The effect was most prominent with cognitive functions (intellectual/reasoning skills) but is significantly less with acute intoxication and physical effects. This was confirmed by the meta-analysis of McCartney et al (2021).

McCartney et al 2021 on reviewing the literature concluded that for inhaled cannabis (for which read THC) 'most driving-related cognitive skills recover . . . within ~3- and ~5-hrs of inhaling 10 and 20 mg of Δ9-THC, respectively'; with nearly all users recovering within ~5- and ~7-hs, respectively. They did note that these conclusions may not be absolutely precise as the various studies used different methods to calculate the participants' pre-study cannabis intakes. The picture is a bit different with oral intake – which can be erratic (Ohlsson et al 1980) – with most but not all driving-related cognitive skills not recovering until ~8 hours after a 20mg oral dose of THC.

Eadie et al 2021 reviewed the literature dealing with the duration of neurocognitive impairment with medical cannabis use. It is important to note that only patients taking medicinal cannabis for chronic non-cancer pain or spasticity were included in the study and the findings do not necessarily hold for medicinal cannabis use for anxiety, other psychogenic disorders, insomnia or epilepsy. Cannabis-associated neurocognitive impairment cleared after ~ 4 hours post use. The impairment is dose-dependent and lasts longer the higher the amount taken.

It is important to note that there is no uniform dosing standard for cannabis in Australia, although 10mg is a relatively standard acute dose, with 20mg constituting a relatively high (although by no means atypical) dose under current practice for non-cancer pain and spasticity. THC insomnia relief is dose-dependent being more effective at higher doses which may encourage higher dose use (Vallaincourt et al 2022).

Detection times

Markers of THC-associated impairment

There are currently two specimen types used for the detection of THC in a subject – urine and oral fluid. The former has a long detection window for THC (3-5 days for single low-dose use increasing to a fortnight with regular use) which does not correlate with actual cannabis-associated impairment – the actual situation is worse than that, in that THC is sequestered into body fat, so detection periods for obese people can be extended to 6 weeks or more after cessation of use. Oral fluid has the advantages of convenience and a detection window for THC (unfortunately not for the other drug classes) that crudely match the drug's impairment window. Blood THC testing has been proposed as a potential impairment marker. A plasma THC concentration of 5ng/mL has been proposed as an impairment threshold, being associated with complex task performance impairment roughly equal to a BAC of 0.05%. On the basis of the evidence, the Washington and Colorado states Joint Panel has proposed a serum level of THC plus THC-OH of 5 ng/ml to determine impairment. Canada has proposed a two-tier system with a plasma THC of 2 ng/ml – 5 ng/ml meriting a designation of "Summary Offence", while a plasma THC level > 5ng/ml would be considered a more serious offence similar to drunk driving (Phillips et al 2015). Even should the plasma THC levels prove to be valid impairment markers, venepuncture is neither a practical, fair or ethical route for workplace drug testing, involving as it would potential harm and discomfort to potentially unimpaired workers, not to mention that it would be impractical from a purely logistic perspective.

THC is typically detectable in oral fluid for at least 4–6 hours after inhaling cannabis smoke or vaping (albeit this is affected by frequency of THC use and salivary composition and production level), up to 12 hours post-dose for repeated light use, 16-24 hrs with frequent moderate use or greater (Odell et al 2015; Niedbala et al 2001) – note however, that very heavy dose has been detected up to 3 days post-use but with levels below the reportable threshold used in the Australian oral fluid drug testing standard AS/NZS4760-2019. Thus, oral fluid testing roughly correlates with THC impairment with lower doses, albeit the detection window is somewhat prolonged with sustained high-dose usage. Neither blood, where THC use is detectable for up to seven days on average and substantially longer ($\lesssim$30 days) with very high repeated use (Karschner et al 2009; Bergamaschi et al 2013), or urine where single standard dose use may be detectable up to 48-72 hours since use following cessation of use and up to 3 weeks for repeated use (Lowe et al 2009) are suitable markers of THC-associated impairment. The situation with urine is further complicated by the fact that THC is a sticky, fat-soluble molecule that gets sequestered in the body's adipose tissue – so the more overweight the subject is, the longer the period during which THC will be detected in their urine, even if they have been abstinent since the initial episode of use.

In the interest of ensuring technical completeness, it should be noted that THC is detected in oral fluid for the most part when it is ingested or inhaled through the mouth/oral cavity, and may not be detected in oral fluid if taken rectally via suppositories or dermally through skin patches. Fortunately, from a drug monitoring perspective, THC is overwhelmingly inhaled or ingested orally. Given this, oral fluid testing can legitimately be used as a crude marker of potential impairment, with THC being detectable in most cases during the period the drug will be active, and (barring an increase in non-standard routes of intake) would also function as a rough rule-out marker – i.e., if the drug were not detected in oral fluid, the donor would not be affected by the drug.

In contrast to THC, CBD would not be detected in standard drug tests. Thus, a true pure Cannabidiol (CBD) medication would NOT test positive on a drug screen in any of the common media – urine, oral fluid or hair. Given CBD, by itself, does not cause appreciable impairment, the undetectability of the drug is not a matter of concern. Unfortunately, many preparations sold as 'CBD-Oils' over the internet also contain THC. Any combined THC/CBD medications can result in short-term impairment depending on the THC concentration present and are detectable with workplace and roadside drug tests.

Recommendations

As is evident from the above literature review, cannabis use, whether recreational or medicinal, may certainly have an adverse impact on workplace health, safety and productivity. The crash-risk table (Table 1) demonstrates that cannabis use raises accident risk to a level:

- at least equivalent to low-to intermediate range BAC (i.e., 0.02 to 0.05%),
- roughly equivalent to the effect of incautious use of intermediate-duration benzodiazepines and opiates,
- generally greater than the impact of antihistamines.

Balanced against this is the apparent fact that there are some medicinal benefits to be gained from cannabis usage with certain patients. Thus, the goal should be to monitor and control medicinal cannabis use at the workplace to maximise workers' safety and productivity, whilst permitting those who must use cannabis products to receive treatment. To satisfy these conditions the following recommendations may offer some benefit:

i) CBD

CBD should be considered separately from THC. It is not detectable in standard drug screening assays and is not associated with perceptible complex task impairment. For this reason, it should be viewed as essentially a harmless pharmaceutical, with the caveat that driving or complex task performance not be performed within two hours of ingestion of the medication and that care be taken to factor in potential synergistic interactions with other psychogenic medications most notably antidepressants and sedatives. Category 1 CBD medicinal cannabis products with $\geq$ 98% CBD fraction fall in this class.

ii) Medicinal THC

– Categories 2 to 5 medicinal cannabis products should be considered separately, and their use at the workplace should be monitored and regulated.

– greatest attention should be taken when an individual has:

(a) commenced using a THC containing medication, prior to the expected development of some level of tolerance to the THC associated impairing effects (which would be expected after 6 – 8 weeks of stable use) – this is analogous to the recommendations by Zacharoff 2010 regarding commencing or increasing the dose of a standard opiate medication; and/or

(b) taken Category 4 (THC dominant medicinal cannabis product, 60-90% THC) & Category 5 medicinal cannabis products (THC > 98%).

– where possible medicinal THC use should be confined to periods at least 10 hours prior to driving or complex task performance (i.e., working). This would imply that medicinal cannabis use restricted to the night/rest periods should not pose any significant risk to workplace health and safety, and, where practicable, should therefore be strongly encouraged in preference to multiple daily dosing regardless of the medicinal cannabis drug Category (excluding Category 1 of course). In most such cases THC should not be detectable in oral fluid >12 hours (certainly > 16 hours) post ingestion.

– multiple daily medicinal THC dosing potentially does pose workplace health and safety risk, where practicable should be discouraged (provided this does not adversely impact patient health).

– where high-Category (Category 4 or 5) or multiple daily use occurs, depending on the worker's duties, it may be advisable to obtain an assessment by an experienced OHS physician.

– where concerns have arisen regarding a worker's possible impairment by THC containing medication in the context of restricted daily use (i.e., night-use only) oral fluid testing may be performed. Given that the overwhelming majority of medicinal cannabis prescriptions in Australasia involved either inhaled or orally ingested cannabis products, oral fluid THC detection can be used as a crude rule-out marker of impairment (i.e., if it isn't detected, the worker isn't affected). Note that with multiple daily dosing THC will be detected with oral fluid testing. The confirmed detection of THC doesn't invariably imply the worker is significantly impaired but certainly suggests it is likely some level of cognitive/behavioural effect is present, and should be assessed in conjunction with the worker's current clinical state and work performance (including the use of peer-reviewed impairment assessment checklists like the UCLA Impairment checklist).

– urine testing for THC should not be used to assess a worker's fitness to work as the extensive urinary THC detection window has led to urine THC level not correlating with THC induced impairment and simply functioning as a marker of past THC use. (Note – this does not apply to amphetamine-class stimulants, to cocaine or to benzodiazepines where urine is the superior marker of impairment).

– Post-incident (accident, injury or near-miss) testing and Testing For Cause (worker appearing impaired, confused or drug paraphernalia detection etc) should initially use urine (to exclude non-cannabis drugs) but if THC is detected oral fluid testing should then be performed to exclude possible recent use/impairment (i.e., use as a rule-out THC-associated impairment marker).

Should you require further information about this submission, please contact Dr Phil Tynan, National Chief Toxicologist at Safework Health [redacted]

Yours sincerely

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APPENDIX A - Non-cannabis drugs and Workplace Drug Testing

i) AMPHETAMINE-TYPE STIMULANTS

Amphetamine-type stimulants are a family of popular stimulants, ranging from the mild euphoric MDMA (sold as the party-drug XTC), to amphetamine (often used therapeutically in lower doses as dexamphetamine) and the highly impairing, highly addictive drug methamphetamine (a.k.a. Ice).

The issue of amphetamine-induced impairment is complex. When reviewing the effects of amphetamine on performance and alertness in combatting fatigue, Wesenstein et al 2005 found that amphetamine increases overall alertness and psychomotor vigilance after 64 hours without sleep to a substantially greater effect than caffeine and marginally greater than modafinil but unlike modafinil the general performance scores in tests of executive function are mixed. This was further demonstrated in the study by Ellyahn et al 2007 where it was concluded that amphetamine was useful in managing operational fatigue and maintaining wakefulness (on a par with Modafinil) but it is important to note that it was significantly worse at maintaining appropriate levels of executive function. Additionally, amphetamine-associated side effects were a particular problem, principally the acute excitability, high levels of distraction, agitation and hyperreflexia resulting in poor performance of complex everyday tasks. Thus, while substantial fatigue is a serious impairment factor, and amphetamine-class drugs (in this study amphetamine – a far safer drug than methamphetamine) may blunt the effect of fatigue, they dangerously distort judgement.

Note that, theoretical arguments aside, amphetamine class drug-using subjects have 300% greater accident rate per mile travelled than non- users (Smart et al 1969). The principal factors associated with the high associated accident rate appear to be impaired sleep, distractibility and increased risk-taking (Jones & Holmgren, 2005).

Amphetamine class drug-associated impairment of judgement is a major problem for all commonly abused amphetamine-class drugs, but most markedly so for methamphetamine. There is a marked propensity for risk taking, with a substantially higher willingness to take risks associated with an unrealistically rosy self-appraisal of one's own performance – independent of underlying personality type (Hurst,1962).

Amphetamine class drug withdrawal is also associated with a unique impairment profile (markedly worse with methamphetamine), relatively minor in infrequent low-dose users but marked in long-term, frequent and / or high dose amphetamine users. Dysphoria, commonly associated with varying degrees of depression, irritability and rebound fatigue (often marked by extreme sleepiness and chronic fatigue).

Logan (1996) reviewed the effects of methamphetamine on human performance, actual driving and behaviour including 28 cases in which drivers arrested or killed in traffic accidents had tested positive for methamphetamine. The circumstances surrounding the arrest or accident were examined, together with any observations by the arresting officer regarding behavioural irregularities. Typical driving behaviours included drifting out of the lane of travel, erratic driving, weaving, speeding, drifting off the road, and high speed collisions. Behavioural manifestations of methamphetamine use in arrestees included rapid or confused speech, rapid pulse, agitation, paranoia, dilated pupils, and violent or aggressive attitude. Combined alcohol and methamphetamine use was uncommon and did not affect the analysis, however use of marijuana was evident in about one third of the cases. In addition to impairing judgment and increasing risk taking, the effects of withdrawal from methamphetamine use including fatigue, hypersomnolence, and depression are likely contributors to many of these accidents.

Logan (1996) concluded that 'methamphetamine at any concentration is likely to produce symptoms that are inconsistent with safe driving'.

Most methylamphetamine-associated accidents occur more than 24- hours after use – which may reflect the effect of cumulative sleep deprivation and affect complex judgement-requiring tasks (ASCC 2007, Verstraete et al 2014). Oral fluid drug testing may potentially miss this phase, as the oral fluid detection window for most amphetamine-class stimulants is around 24 hours, whereas the drug effects remain active for at least 36 to 48 hours (with high doses up to 72 hrs for amphetamine and 96 hours for methamphetamine) – which corresponds to the urine drug detection window for those drugs.

ii) COCAINE

Cocaine is a euphoric stimulant that substantially impairs judgement. The US National Highway Traffic Safety Administration (NHTSA) study showed low intake of cocaine can produce performance-related effects that include increased reaction times, improved attention span, higher states of alertness and lower susceptibility to fatigue, in new users but users rapidly habituate to the effect so that even occasional repeat users experience no advantage.

During withdrawal from the cocaine high there is a tendency to exhibit task-related impairment including confusion, lowered ability to shift focus from one task to another, difficulty following spoken or written directions, a distorted sense of time, inappropriately hostile reactions to specific events or general circumstances, loss of normal coordination and a moderate hypersensitivity to light leading to abnormal peripheral vision, poor glare tolerance and a reduced ability to focus on objects within the field of vision (Brookoff et al 1994).

Judgemental impairment is extremely common among cocaine users often marked by decreased risk assessment and a tendency to drive at dangerously high rates of speed and aggressive driving behaviours, often with a loss of vehicular control (Ellinwood et al 1987).

In the US, cocaine or cocaine metabolites (breakdown products) are found in the systems of around 5 to 24% of all people involved in serious traffic violations, vehicular accidents and vehicular fatalities.

Oral fluid detection window is commonly 2 days, but may be as long as 4 days in heavy users. This will cover most of the acute impairment period but not entirely – by contrast the urine detection window for cocaine can be up to 5 to 6 days which will cover the initial and withdrawal phases, the latter being significantly associated with performance impairment.

The problem with oral fluid detection of cocaine use is that cocaine secretion into saliva is affected by the pH of the saliva – so it is relatively easy to ensure cocaine will not be detected by altering the acidity of the oral fluid (lists of the foods to take/chew within an hour of testing are available on the internet).

iii) OPIATES

The standard opiates include medicinal opiates (codeine and morphine), the semisynthetic opiates (fentanyl and oxycodone) and illicit drugs like heroin. The focus of the discussion will be on medicine and will primarily mention codeine, but the same principles apply to the semisynthetic opioids like fentanyl and oxycodone (which are much less frequently prescribed in Australia and whose use for now, although increasing, remains relatively low compared to codeine).

A distinction should be drawn between infrequent opiate users and chronic opiate users as well as opioid-dependent patients on long-term stable doses. Cognitive impairment is most marked with infrequent codeine use or upon the commencement of a long-period of codeine use. A literature review by Fishbain et al (2003) found that the majority of the reviewed studies (69.6%) indicated that opioids do not impair psychomotor abilities in opioid-dependent patients and that cognitive functioning may improve due to better pain control in such cases (Fishbain et al 2003; Sjogren et al 2000). Specifically, there was generally consistent evidence for no impairment of psychomotor abilities and cognitive function in opioid-maintained patients and there is no evidence for an increase in motor vehicle violations / motor vehicle accidents in opioid –controlled patients versus comparable controls and no statistically significant deficit in performance scores on driving simulators (Fishbain et al 2003).

These considerations have led Zacharoff (2010) to issue a formal recommendation that patients commencing codeine use or after increasing codeine intake (generally defined as > 50% rise in dose) should not drive for at least 4–5 days.

The situation with chronic, stable opiate use for pain management contrasts sharply with the impairment noted with infrequent opiate/codeine use or use of opiates for other than legitimate chronic pain management or for the early stages of opiate use. In such cases codeine induced may be marked and includes: Somnolence/Fatigue, Dizziness and impaired coordination, Clouded mentation with a decreased ability to concentrate, and Slowed motor performance including slowed reflexes, significantly increased response time to stimuli.

Codeine-associated impairment will also be markedly enhanced by the ingestion of alcohol and centrally-acting antihistamines (the increase in impairment in both cases being synergistic). In addition, Ersek et al 2004 have demonstrated impairment is substantially greater when administered parenterally (i.e., inject either as codeine per se or as morphine, which acts as a precursor drug).

One advantage of urine opiate testing is that the urinary codeine:morphine ratio can be used to assess opiate-associated cognitive impairment.

Urine codeine levels (considered alone) below 700-500ng/mL are not associated with significant neurocognitive performance impairment at the time of testing. As a rule of thumb, assume the plasma concentration doubles for every 3 to 4 hours in the past that the ingestion is believed to have occurred, and that peak plasma and hence peak neurocognitive effects will have occurred around 1 hour after taking codeine orally.

A morphine to codeine ratio greater than 0.35 is suggestive of impairment (note the caution below) where the codeine level is greater than 250 – 300 ng/mL or the morphine level is above 500 ng/mL (Wayne et al, 2008). Morphine to codeine ratios above 1.5 are indicative of significant impairment. Morphine to codeine ratios greater than 0.5 are rarely consistent with medical (prescribed) codeine use.

Interpretation of possible impairment requires that the context of intake be taken into account. For example: if an infrequent codeine user or illicit user has a urinary codeine concentration of 200 ng/mL (i.e., below 750ng/mL) 30 hours after testing, the plasma post-dose codeine levels will be above the definable impairment threshold six to seven hours earlier and for the period prior to that after ingestion. If the donor however has been taking a stable (i.e. invariant) codeine dose for more than 5 days sequentially for pain- relief there will be negligible (i.e., statistically insignificant) impairment even with urinary codeine levels as high as 800 ng/mL. Codeine levels above 1500 - 2000 ng/mL should prompt review to determine how well the dose is being tolerated.

iv) BENZODIAZEPINES

Benzodiazepine usage in Australia is high with moderately high levels of regular workplace usage reported especially among socially isolated, young male and FIFO workers in manufacturing and mining, as well as isolated professional postings (Ghodse 2005 Hindmarch 2005 Islam et al 2014) – the picture is further complicated in that although the total number of prescriptions of benzodiazepines dispensed through the PBS/RPBS declined from 1992 to 2011, the increase in dispensed quantity per script and the large number of scripts written annually Australia-wide indicates that most prescriptions relate to long-term use (RACP 2013, Islam et al 2014). There is a high incidence of benzodiazepine use by users of illicit drugs, including at the workplace – most notably with benzodiazepines frequently being used to moderate amphetamine withdrawal (ibid 2014) which has been reflected in European and American urine-based studies run concomitantly with oral fluid collections.

Benzodiazepine usage, even within the strictures of prescribed use, is associated with an 81% post-usage impairment with an accident- associated odds ratio between 4.11 – 1.61 over 12 – 16 hours post use (Bramness et al 2002). Drawing an analogy with US and European figures which show statistical agreement in this number, predicted use rates in mining populations under 40 yrs age should be on the order of 2.5 – 2.8% (Olfson et al 2015) which is reflected in urine drug study figures (with expected confirmation figures around 53% - equivalent to what has been found in the current urine figures) but not in matched oral fluid studies.

No oral fluid-based remediation strategy can currently be proposed as the effect is intrinsic to the sample medium chosen – Gjerde et al (2014) has noted that benzodiazepine concentrations in oral fluid are very low being well less than a 1/20th of plasma and there is an extremely wide intra- and inter- individual variation.

Effectively, urine drug test windows for benzodiazepines correspond to the period of activity of the particular benzodiazepine involved and this holds for all major benzodiazepine classes (short-, intermediate- and long- acting benzodiazepines, although in practice intermediate period acting benzodiazepines are the most frequently encountered). Oral fluid will only pick up higher concentrations of benzodiazepines and the oral fluid detection window is shorter than the period of impairment.

REFERENCES

1. Alberta Advisory Committee on Impairment in the Workplace. Addressing Workplace Impairment in Alberta July 2003
2. AIHW 2010 National Drug Strategy Household Survey report. Australian Institute of Health and Welfare.
3. AJM Staff Companies cash in on testing for Kronic problem Australian Journal of Mining June 2011 Jun 09, 2011
4. Andås H.T., Krabseth H-M., Enger A., Marcussen B.N., Haneborg A-Mg, Christophersen A.S., Vindenes V.* Øiestad E.L. Detection Time for THC in Oral Fluid after Frequent Cannabis Smoking. Therap. Drug Monit. Dec 2014; 36(6): 808-14
5. Arkell TR, Lintzeris N, Kevin RC, et al. Cannabidiol (CBD) content in vaporized cannabis does not prevent tetrahydrocannabinol (THC)-induced impairment of driving and cognition. Psychopharmacology (Berl) 2019;236(9):2713–24. doi: 10.1007/s00213-019-05246-8. Search PubMed
6. Arkell TR, Lintzeris N, Mills L, Suraev A, Arnold JC, McGregor IS. Driving-related behaviours, attitudes and perceptions among Australian medical cannabis users: Results from the CAMS 18-19 survey. Accid Anal Prev 2020;148:105784. doi: 10.1016/j.aap.2020.105784.
7. Arkell TR, McCartney D, Mc Gregor IS. Medical cannabis and driving Aust J Gen Pract Jun 2021; 50(6): 357-362
8. Arkell TR, Vinckenbosch F, Kevin RC, Theunissen EL, McGregor IS, Ramaekers JG. Effect of cannabidiol and Δ9-tetrahydrocannabinol on driving performance: A randomized clinical trial. JAMA 2020;324(21):2177–86. doi: 10.1001/jama.2020.21218.
9. Arnold JC, Nation T, McGregor IS. Prescribing medicinal cannabis. Aust Prescr 2020;43(5):152–59. doi: 10.18773/austprescr.2020.052. Search PubMed
10. Ashurst Australia 28 October 2013 Employment Alert
11. Australian Safety and Compensation Council report: Work-related Alcohol and Drug Use – A fit for work issue. ASCC March 2007
12. Bathum L, Johansson I, Ingelman-Sundberg M, Hørder M, Brosen K. Ultrarapid metabolism of sparteine: frequency of alleles with duplicated CYP2D6 genes in a Danish population as determined by restriction fragment length polymorphism and long polymerase chain reaction. Pharmacogenetics1998;8(2):119-123
13. Barceloux, D, G . Medical Toxicology of Drug Abuse: Synthesized Chemicals and Psychoactive Plants. John Wiley & Sons. (March 2012) 910–12
14. Bergamaschi MM, Karschner EL, Goodwin RS, et al. Impact of prolonged cannabinoid excretion in chronic daily cannabis smokers' blood on per se drugged driving laws. Clin Chem 2013;59(3):519–26. doi: 10.1373/clinchem.2012.195503.
15. Blomberg RD, Peck RC, Moskowitz H, Burns M, Fiorentino D. The Long Beach/Fort Lauderdale relative risk study. J Safety Res 2009;40(4):285–92. doi: 10.1016/j.jsr.2009.07.002.
16. Bywood, P., Pidd K. & Roche, A (2006) Workplace Drug & Alcohol Use Information and Data Sheet 5. NCETA, Adelaide.
17. Bolla KI, Brown K, Eldreth D. Dose-related neurocognitive effects of marijuana use. *Neurology*. 2002;59:1337–1343
18. Bonar EE, J.A. Cranford JA, Arterberry BJ, Walton MA, Bohnert KM, Ilgen MA Driving under the influence of cannabis among medical cannabis patients with chronic pain Drug Alcohol Depend., 2019; 195: 193-197
19. Bosker WM, Kuypers KP, Theunissen EL, et al. Medicinal Δ9-tetrahydrocannabinol (dronabinol) impairs on-the-road driving performance of occasional and heavy cannabis users but is not detected in standard field sobriety tests. Addiction 2012;107(10):1837–44. doi: 10.1111/j.1360-0443.2012.03928.x.
20. Bosker WM, Theunissen EL, Conen S, et al. A placebo-controlled study to assess Standardized Field Sobriety Tests performance during alcohol and cannabis intoxication in heavy cannabis users and accuracy of point of collection testing devices for detecting THC in oral fluid. Psychopharmacology (Berl) 2012;223(4):439–46. doi: 10.1007/s00213-012-2732-y.

21. Brookoff D, Cook CS, Williams C, Mann CS. *New Engl J Med* 1994;331:518-22.

22. Brubacher JR, Chan H, Erdelyi S, et al. Cannabis use as a risk factor for causing motor vehicle crashes: A prospective study. Addiction 2019;114(9):1616–26. doi: 10.1111/add.14663.

23. Caraco Y N. Engl. J. Med. (December 2004); 351 (27): 2867–9.

24. Carmide N, Landsman V, Lee H, Fronee MR, Furlan AD, Smith PM Workplace and non-workplace cannabis use and thee risk of workplace injury: Findings from a longitudinal study of Canadian workers Can J Pub Health Dec 2023; 114(6): 947-955

25. Celius EG, Vila C. The influence of THC:CBD oromucosal spray on driving ability in patients with multiple sclerosis-related spasticity. Brain Behav 2018;8(5):e00962. doi: 10.1002/brb3.962.

26. Chihuri S, Li G. Use of prescription opioids and motor vehicle crashes: A meta analysis. Accid Anal Prev 2017;109:123–31. doi: 10.1016/j.aap.2017.10.004.

27. Chou R, Fanciullo GJ, Fine PG et al.

28. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. The Journal of Pain: Official Journal Of The American Pain Society 2009;10(2):113-130

29. Chu, M; Gerostamoulos, D, Beyer, J, Rodda, L, Boorman, M, Drummer, OH. (1 June 2011). Forensic Science International.doi:10.1016/j.forsciint.2011.05.012

30. Colizzi, M., Bhattacharyya, S., 2018. Cannabis use and the development of tolerance: a systematic review of human evidence. Neurosci. Biobehav. Rev. 2018; 93: 1–25.

31. Compton RP, Berning A. Drug and alcohol crash risk. Traffic Safety Facts Research Note. Washington, DC: National Highway Traffic Safety Administration, 2015.

32. Construction, Forestry, Mining and Energy Union v. HWE Mining Pty 2011 FWA8288; 30 November 2011.

33. Crews, KR; Gaedigk, A; Dunnenberger, HM; Leeder, JS; Klein, TE; Caudle, KE; Haidar, CE; Shen, DD; Callaghan, JT; Sadhasivam, S; Prows, CA; Kharasch, ED; Skaar, TC April 2014; Nature 95 (4): 376– 382.

34. Cuba LF, Salum FG, Cherubini K, Figueiredo MAZ. Cannabidiol: An alternative therapeutic agent for oral mucositis? J Clin Pharm Ther 2017;42(3):245–50. doi: 10.1111/jcpt.12504.

35. Dassanayake T, Michie P, Carter G, Jones A. Effects of benzodiazepines, antidepressants and opioids on driving: A systematic review and meta-analysis of epidemiological and experimental evidence. Drug Saf 2011;34(2):125–56. doi: 10.2165/11539050-000000000-00000.

36. Department of Health and Ageing (DHA) 2010. National drugs campaign. http://www.drugs.health.gov.au/internet/drugs/ publishing.nsf/content/home-1

37. Desjardins, J., & Duska, R. (n.d.). Drug testing in employment. In T. L. Beaucamp & N. E. Bowie (Authors), Ethical theory and business Upper Saddle River, NJ: Prentice Hall 6th ed., 2001: pp. 283-294.

38. DiGuiseppi, A.A. Smith, M.E. Betz, L. Hill, H.D. Lum, H. Andrews, C.-S. Leu, H.A. Hyde, D.W. Eby, G. Li Cannabis use in older drivers in Colorado: the LongROAD Study Accid. Anal. Prev., 132 (2019), Article 105273

39. Drummer OH, Gerostamoulos D, Di Rago M, et al. Odds of culpability associated with use of impairing drugs in injured drivers in Victoria, Australia. Accid Anal Prev 2020;135:105389. doi: 10.1016/j.aap.2019.105389.

40. el-Sohly H.N., el-lSohly M.A. and Stanford D.F. J Anal Toxicol 1990 Sep-Oct; 14(5) :308-10.

41. EDRS Bulletin December 2010: Mephedrone use among regular ecstasy consumers in Australia

42. Ellinwood EH, Nikaido AM. *Alcohol Drugs & Driving* 1987;3(1):19-24.

43. Ellyahn et al J Mil Med 2007; 172: 383 – 387

44. Elvik R. Risk of road accident associated with the use of drugs: A systematic review and meta-analysis of evidence from epidemiological studies. Accid Anal Prev 2013;60:2545–67. doi: 10.1016/j.aap.2012.06.017.

45. Elvik, R. , Accident Analysis and Prevention (July 26, 2012).

46. Ersek M., Cherrier M.M., Overman S.S. and Irving G.A. Pain Manag Nurs. 2004 Jun;5(2):75-93.

47. Fairwork NSW case Rece Goodsell v Sydney Trains (U2022/9973)

48. Fattore, L. & Fratta, W. (2011). Beyond THC: the new generation of cannabinoid designer drugs. Frontiers in Behavioral Neuroscience 5, 1-12.

49. Fishbain DA, Cutler RB, Rosomoff HL, Rosomoff RS: J Pain Symptom Manage 25:559-577, 2003

50. Freeman AM, Petrilli K, Lees R, et al. How does cannabidiol (CBD) influence the acute effects of delta-9-tetrahydrocannabinol (THC) in humans? A systematic review. Neurosci Biobehav Rev 2019;107:696–712. doi: 10.1016/j.neubiorev.2019.09.036.

51. Freidel M, Tiel-Wilck K, Schreiber H, Prechtl A, Essner U, Lang M. Drug-resistant MS spasticity treatment with Sativex(®) add-on and driving ability. Acta Neurol Scand 2015;131(1):9–16. doi: 10.1111/ane.12287.

52. Gadsby J Benzodiazepine Awareness Network International 2000.

53. Gardiner, S. J.; Begg, E. J. (2006). "Pharmacogenetics, Drug-Metabolizing Enzymes, and Clinical Practice". Pharmacological Reviews 58 (3): 521–590.

54. Ghodse H. Addiction at Work: Tackling Drug Use and Misuse in the Workplace. London Gower (publ) 2005 pp 61 et seq & Hindmarch I The effect of prescribed and over-the-counter drugs on workplace performance Chapter 7

55. Gjerde H, Langel K, Favretto D, Verstraete AG. Ther Drug Monit. 2014 Apr; 36(2): 252 – 6

56. Guideline for Oral Fluid. European Workplace Drug Testing Society (EWDTS). Ver 01, Mar 2011

57. Hartman RL, Brown TL, Milavetz G, et al. Cannabis effects on driving lateral control with and without alcohol. Drug Alcohol Depend 2015;154:25–37. doi: 10.1016/j.drugalcdep.2015.06.015.

58. Hartman RL, Brown TL, Milavetz G, et al. Cannabis effects on driving longitudinal control with and without alcohol. J Appl Toxicol 2016;36(11):1418–29. doi: 10.1002/jat.3295.

59. Hazle MC, Hill KP, Westreich LM. Workplace Cannabis Policies: a Moving Target Cannabis Cannabinoid Res Feb 2022; 7(1): 16-23

60. Hels T, Bernhoft IM, Lychegaard A, et al. Risk of injury by driving with alcohol and other drugs. Project No. TREN-05-FP6TR-S07.61320-518404-DRUID. European Comission; 2011.

61. Hill LL, Lauzon VL, Winbrock EL, Li G, Chihuri S, Lee KC. Depression, antidepressants and driving safety. Inj Epidemiol 2017;4(1):10. doi: 10.1186/s40621-017-0107-x.

62. Hostiuc S, Moldoveanu A, Negoi I, Drima E. The association of unfavorable traffic events and cannabis usage: A meta-analysis. Front Pharmacol 2018;9:99. doi: 10.3389/fphar.2018.00099.

63. Huestis MA. Cannabis-impaired driving: A public health and safety concern. Clin Chem 2015;61(10):1223–35. doi: 10.1373/clinchem.2015.245001.

64. Huestis M, Mitchell J and Cone E, Journal of Analytical Toxicology, Vol 20:441-52 (Oct 1996)

65. Hurst Psychopharmacologia 1962; 3(2): 5

66. Irwin C, Iudakhina E, Desbrow B, McCartney D. Effects of acute alcohol consumption on measures of simulated driving: A systematic review and meta-analysis. Accid Anal Prev 2017;102:248–66. doi: 10.1016/j.aap.2017.03.001.

67. Islam MM, Conigrave KM, Day CA, Nguyen Y, Haber PS. Intern Med J 2014;44:57-64.

68. Jamison RN, Schein JR, Vallow S, Ascher S, Vorsanger GJ, Katz NP: J Pain Symptom Manage 26:913- 921, 2003

69. Jones, Holmgren & Kugelberg J Stud Alc. Mar 2008; 69(2): 202 – 8

70. Jones & Holmgren JFS 2005; 50(5): 1 – 5

71. Jones KA, Nielsen S, Bruno R, Matthew F, & Lubman D. Australian Family Physician 40(11); November 2011: 862-865

72. Jongen S, Vermeeren A, van der Sluiszen NN, et al. A pooled analysis of on-the-road highway driving studies in actual traffic measuring standard deviation of lateral position (i.e.,'weaving') while driving at a blood alcohol concentration of 0.5 g/L. Psychopharmacology (Berl) 2017;234(5):837–44. doi: 10.1007/s00213-016-4519-z.

73. Jongen S, Vuurman EEPM, Ramaekers JG, Vermeeren A. Comparing the effects of oxazepam and diazepam in actual highway driving and neurocognitive test performance: A validation study. Psychopharmacology (Berl) 2018;235(4):1283–94. doi: 10.1007/s00213-018-4844-5.

74. Joshua L., Fenderson JL, Stratton AN, Domingo JS, Matthews GO, and Tan CD. Case Reports in Psychiatry Volume 2013 (2013), Article ID 381261

75. Karschner EL, Schwilke EW, Lowe RH, et al. Do Delta9-tetrahydrocannabinol concentrations indicate recent use in chronic cannabis users? Addiction 2009;104(12):2041–48. doi: 10.1111/j.1360-0443.2009.02705.x.

76. Karschner EL, Schwilke EW, Lowe RH, et al. Implications of plasma Delta9-tetrahydrocannabinol, 11-hydroxy-THC, and 11-nor-9-carboxy-THC concentrations in chronic cannabis smokers. J Anal Toxicol 2009;33(8):469–77. doi: 10.1093/jat/33.8.469.

77. Key Work Health & Safety Statistics, Australia. Safework Australia 2013

78. Konstantinova SV, Normann PT, Arnestad M, Karinen R, Christopher AS & Mørland J Forensic Sci Int. 2012 Apr 10; 217(1-3):216-21.

79. Kronstrand R & Jones AW. Journal of Analytical Toxicology, Vol. 25; September 2001: 486-7

80. Lafolie P, Beck O, Blennow G, et al. Importance of creatinine analyses of urine when screening for abused drugs. Clin Chem 1991;37(11):1927–31.

81. Lankenau SE & Sanders B 2007. Journal of Psychoactive Drugs 39: 21–29

82. Law B. et al, J. Pharm. Pharmacol. 36: 289-94 (1984).

83. Lachenmeier D.W., Sproll C and Musshoff F. Ther Drug Monit. 2010 Feb;32(1):11-8.

84. Leenders M.E.C., J. Meulenbelt Rijksinstituut voor Volksgezondheid en Milieu RIVM report 267002002/2006

85. Logan BK. Methamphetamine and Driving Impairment. J. Forensic Sci June 1996; 41(3): 457 – 64

86. Løvlie R, Daly AK, Molven A, Idle JR, Steen VM. FEBS Lett.1996;392(1):30-34

87. Lowe RH, Abraham TT, Darwin WD, Herning R, Cadet JL, Huestis MA. Extended urinary Delta9-tetrahydrocannabinol excretion in chronic cannabis users precludes use as a biomarker of new drug exposure. Drug Alcohol Depend 2009;105(1–2):24–32. doi: 10.1016/j.drugalcdep.2009.05.027.

88. Mannucci C, Navarra M, Calapai F, et al. Neurological aspects of medical use of cannabidiol. CNS Neurol Disord Drug Targets 2017;16(5):541–53. doi: 10.2174/1871527316666170413114210.

89. McCartney D, Arkell TR, Irwin C, McGregor IS. Determining the magnitude and duration of acute Δ9-tetrahydrocannabinol (Δ9-THC)-induced driving and cognitive impairment: A systematic and meta-analytic review. Neurosci Biobehav Rev 2021;126:175–93. doi: 10.1016/j.neubiorev.2021.01.003.

90. McCartney D, Benson MJ, Suraev AS, et al. The effect of cannabidiol on simulated car driving performance: A randomised, double-blind, placebo-controlled, crossover, dose-ranging clinical trial protocol. Hum Psychopharmacol 2020;35(5):e2749. doi: 10.1002/hup.2749.

91. McGregor IS, Cairns EA, Abelev S, et al. Access to cannabidiol without a prescription: A cross-country comparison and analysis. Int J Drug Policy 2020;85:102935. doi: 10.1016/j.drugpo.2020.102935.

92. Mensinga Tj.T., de Vries I., Kruidenier M., Hunault C.C., van den Hengel-Koot I.S., Fijen, J.W. Meadway C, George S & Braithwaite R. Forensic Sci Int 1998; 96: 29 – 38.

93. Moeller KE, Lee KC, and Kissack JC, Mayo Clinic Proceedings, 2008; 83(1): 66–76.

94. Moore RA, McQuay HJ: Arthritis Res Ther 7: R1046-R1051, 2005.

95. National Academies of Sciences, Engineering, and Medicine. The health effects of cannabis and cannabinoids: the current state of evidence and recommendations for research. The National Academies Press: Washington, DC, 2017.

96. National Occupational Health and Safety Commission. (1998) Work-Related Traumatic Fatalities in Australia, 1989 to 1992. Summary Report. Commonwealth of Australia, Canberra.

97. Niedbala RS, Kardos KW, Fritch DF, et al. Detection of marijuana use by oral fluid and urine analysis following single-dose administration of smoked and oral marijuana. J Anal Toxicol 2001;25(5):289–303. doi: 10.1093/jat/25.5.289.

98. Odell MS, Frei MY, Gerostamoulos D, Chu M, Lubman DI. Residual cannabis levels in blood, urine and oral fluid following heavy cannabis use. Forensic Sci Int 2015;249:173–80. doi: 10.1016/j.forsciint.2015.01.026.

99. Ohlsson A, Lindgren J, WahlenA, Agurell S, Hollister L, Gillespie H. Plasma delta-9 -tetrahydrocannabinol concentrations and clinical effects after oral and intravenous administration and smoking. Clin Pharmacol Ther 1980; 28: 409-16

100. Pacheco-Colon P, Limia JM, Gonzalez R. Non-acute effects of cannabis use on motivation and reward sensitivity in humans: a systematic review. *Psychol Addict Behav*. 2018;32:497–507.

101. Pidd K. & Roche, A (2006) Workplace Drug & Alcohol Use Information and Data Sheet 3. NCETA, Adelaide.

102. Prashad S, Filbey FM. Cognitive motor deficits in cannabis users. *Curr Opin Behav*. 2017;13:1–7.

103. Ramaekers JG. Drugs and dfriving research in medicinal drug development. Trends Pharmacol Sci 2017;38(4):319–21. doi: 10.1016/j.tips.2017.01.006.

104. Ramaekers JG, Kuypers KP, Bosker WM, et al. Effects of stimulant drugs on actual and simulated driving: Perspectives from four experimental studies conducted as part of the DRUID research consortium. Psychopharmacology (Berl) 2012;222(3):413–18. doi: 10.1007/s00213-012-2766-1.

105. Rogeberg O. A meta-analysis of the crash risk of cannabis-positive drivers in culpability studies-Avoiding interpretational bias. Accid Anal Prev 2019;123:69–78. doi: 10.1016/j.aap.2018.11.011.

106. Rogeberg O, Elvik R. The effects of cannabis intoxication on motor vehicle collision revisited and revised. Addiction 2016;111(8):1348–59. doi: 10.1111/add.13347.

107. Rogeberg O, Elvik R, White M. Correction to: 'The effects of cannabis intoxication on motor vehicle collision revisited and revised' (2016). Addiction 2018;113(5):967–69. doi: 10.1111/add.14140.

108. Rotermann CGM What has changed since cannabis was legalized? Health Rep., 31 (2020), pp. 11-20

109. Russo EB. Current therapeutic cannabis controversies and clinical trial design issues. Front Pharmacol 2016;7:309. doi: 10.3389/fphar.2016.00309.

110. Sewell RA, Poling J, Sofuoglu M. The effect of cannabis compared with alcohol on driving. *Am J Addict*. 2009;18:185–193.

111. Shipp EM, Tortolero SR, Cooper SR, et al.. Substance use and occupational injuries among high school students in south Texas. *Am J Drug Alcohol Abuse*. 2005;31:253–265.

112. Sindicich, N. & Burns, L. (2011) Australian Drug Trend Series No. 82. Sydney, National Drug and Alcohol Research Centre, University of New South Wales.

113. Sjogren P, Thomsen AB, Olsen AK: J Pain Symptom Manage19:100-108, 2000

114. Skopp G and Potsch L, Journal of Analytical Toxicology 32: 160-4 (2008).

115. Smart et al J Safety Res 1969; 1(2): 67 – 73

116. Smith, A., Wadsworth, E., Moss, S. & Simpson, S. (2004) Centre for Occupational and Health Psychology, Cardiff University, Cardiff.

117. Solowij N, Stephens RS, Roffman RA, et al.. Cognitive functioning of long-term heavy cannabis users seeking treatment. *JAMA*. 2002;287:1123–1131.

118. Srinivasan V, Wielbo D, Tebbett IR; Wielbo; Tebbett (1997).European Journal of Pain 1 (3): 185– 90

119. Substance Abuse and Mental Health Services Administration (2002) The NHSDA Report. Sept 6 2002. Office of Applied Studies Substance Abuse and Mental Health Services Administration (SAMHSA) http://www.oas.samhsa.gov/2k2/workers/workers.pdf.

120. Tassain V, Attal N, Fletcher D, Brasseur L, Degieux P, Chauvin M, Bouhassira D: Pain 104:389-400, 2003

121. Therapeutic Goods Administration. Medicinal cannabis – Guidance documents. Woden, ACT: TGA, 2020. Available at www.tga.gov.au/medicinal-cannabis-guidance-documents. [Accessed 9 April 2021]. Search PubMed

122. Tefft BC, Arnold L. Cannabis use among drivers in fatal crashes in washington state before and after legalization. AAA Foundation for Traffic Safety, 2020. https://aaafoundation.org/wp-content/uploads/2020/01/19-0637_AAAFTS-WA-State-Cannabis-Use-Among-Drivers-in-Fatal-Crashes_r4.pdf

123. Vaillancourt R, Gallagher S, Cameron J, Dhalla R. Cannabis use in patients with insomnia and sleep disorders: Retrospective Chart Review. Can Pharm J (Ott) May-Jun 2022; 155(3): 175-180

124. Vandevenne M, Vandenbussche H, Verstraete A (2000). Acta Clin Belg 55 (6): 323–33

125. Vandrey, R., Dunn, K.E., Fry, J.A., & Girling, E.R. (2011). A survey study to characterize use of Spice products (synthetic cannabinoids). Drug and Alcohol Dependence 120, 238-241

126. Verstraete A.G, Legrand S.A., Vandam L. & Hughes B. Drug use, impaired driving and traffic accidents. 2nd edition. ENCDDA-Europa. 2014

127. Wayne Jones A., Holmgren A. and Kugelberg F.C. Journal of Analytical Toxicology, May 2008; Vol. 32: 265 - 272

128. Weitz C.J., Lowney L., Faull K.F., Feistner G. and Goldstein A. Proc. Natl. Acad. Sci. U.S.A. 85 (14): 5335–8. July 1988.

129. Wesenstein et al J Sleep Res 2005; 14: 255 – 266

130. Work-related Alcohol and Drug use: a Fit for Work Issue. Australian Safety and Compensation Council March 2007

131. Zacharoff K.L. Chronic Opioid Therapy: Driving and Work Safety February 2010

132. Zhornitsky S, Potvin S. Cannabidiol in humans – The quest for therapeutic targets. Pharmaceuticals (Basel) 2012;5(5):529–52. doi: 10.3390/ph5050529.

133. Zwerling C, Ryan J, Orav J. The efficacy of preemployment drug screening for marijuana and cocaine in predicting employment outcome. *JAMA*. 1990;264:2639–2643