MEDICINE AND THE LAW

# Cannabis legalisation and testing for cannabis use in safety- and risk-sensitive environments

**J B Laurens,**[1] BSc (Ed), BSc Hons, MSc (Chem), MSc (Appl Tox), MPhil (Med Law), PhD (Chem), PhD (Med Law);
**P A Carstens,**[2] BLC, LLB, LLD

[1] *Forensic Toxicology Laboratory, Department of Chemistry, Faculty of Agriculture and Natural Sciences, University of Pretoria, South Africa*
[2] *Centre for Law and Medicine, Department of Public Law, Faculty of Law, University of Pretoria, South Africa*

***Corresponding author:*** *J B Laurens (tim.laurens@up.ac.za)*

The legalisation of cannabis by the High Court of South Africa, which was confirmed by the Constitutional Court, imposes challenges to occupational medical practitioners acting as medical review officers in compliance testing and fit-for-service medical examinations. The lipophilic character of the psychoactive component of cannabis, delta-9-tetrahydrocannabinol ($\Delta^9$-THC), and its prolonged elimination half-life, create challenges for the ethically and scientifically correct management of the legal use of cannabis in risk-sensitive environments. Important issues to consider in testing for cannabis use are: the stance of 'zero tolerance'; screening and confirmation cut-off concentrations; and the bio-matrices used for testing. Constitutional rights relate to privacy, freedom, autonomy, freedom of religion and the equal enjoyment of rights and privileges, which must be balanced against the health and safety of others.

*S Afr Med J* 2020:110(10):995-998. https://doi.org/10.7196/SAMJ.2020.v110i10.14615

Cannabis use, possession, and cultivation by an adult for private use in a *private dwelling* were legalised in South Africa (SA) in a ground-breaking High Court decision.[1-3] This was confirmed by the Constitutional Court, which extended the concept of the use in a 'private dwelling' to the use 'in private'.[4]

Health practitioners are often required to advise on prohibited substance regulation and testing policies in safety-sensitive environments, and make risk-related decisions during pre-employment and fit-for-service medical examinations of individuals who consume substances that have impairment potential. They may also act as medical review officers (MROs) to validate prohibited substance test results in risk- and safety-sensitive environments.

The legal use of cannabis should now be viewed from the same perspective as legal alcohol use, in terms of prohibited substance regulation and testing practices. Health practitioners are often challenged on issues related to the regulation and testing for cannabis use in safety-sensitive environments, including:

- An understanding of the stance of 'zero tolerance' by the organisations
- Which bio-matrix should be employed to test for cannabis use in prohibited substance testing programmes
- Establishing screening and confirmation cut-off concentrations for delta-9-tetrahydrocannabinol ($\Delta^9$-THC) and its metabolites in body fluids, which are also related to 'safe' concentration levels of $\Delta^9$-THC and its metabolites in biological matrices.

## Relevant legislation

Constitutional rights that apply to the use of cannabis relate to privacy, freedom, autonomy, freedom of religion, and the equal enjoyment of rights and privileges, which must be balanced against the health and safety of others.[5] The legalisation in effect confirmed that cannabis users should enjoy equal protection and benefit of the law, including the enjoyment of rights and freedom.[6] The Constitution also holds that foreign law may be considered when interpreting the Bill of Rights, allowing for the consideration of legislation of other countries to assist with decisions locally.[7] The Canadian Cannabis Act is an example of foreign law where cannabis use has been legalised and where roadside screening for $\Delta^9$-THC is performed on oral fluid (OF) with confirmation blood testing of positive screening tests.[8]

The constitutional judgment, however, had no impact on the statutes regulating health and safety in workplaces and other risk-sensitive environments, mainly the Occupational Health and Safety Act (OHSA)[9] and the General Safety Regulations of the Machinery and Occupational Safety Act (MOSA).[10] The status quo regarding safety and the use of 'intoxicating liquor and drugs' still applies, and organisations must ensure a safe and healthy workplace. The statutes influenced by the judgment are the Drugs Act and the Medicines Act, which apply to the possession of cannabis.[11,12]

The OHSA holds that 'an employer shall not permit any person *who is or appears to be under the influence of intoxicating liquor or drugs,* to enter or remain at a workplace, and that no person at a workplace shall be under the influence of, or have in his possession, or partake of, or offer any other person intoxicating liquor or drugs'. The MOSA requires that 'an employer shall not permit any person *who is, or who appears to be drunk or under the influence of drugs,* to enter or remain at a workplace or on the premises where machinery is used if such person's presence constitutes a threat to the safety of himself or other persons at such workplace or on such premises'.[13]

A legally defensible approach requires consideration of the absorption, distribution, metabolism and excretion of the psychoactive component in cannabis, namely $\Delta^9$-THC. Consideration should also be given to performance-behavioural effects of cannabis and corresponding threshold concentration levels.

## Absorption, distribution, metabolism and excretion of Δ9-THC

Smoking of cannabis, with its psychoactive component ($\Delta^9$-THC), enables rapid absorption with a quick effect on the brain and its

euphoric effects. Plasma concentrations may increase to 160 ng/mL with peak concentrations occurring at approximately 9 minutes.[14] The blood concentration then declines to approximately 10% within 1 - 2 hours, owing to a rapid distribution to the lipophilic tissues in the brain, fat and muscle. This is followed by the second phase of slow redistribution of $\Delta^9$-THC into the bloodstream and hepatic elimination.[15] Absorption is slower when cannabis is taken orally, with the peak concentration delayed depending on the bioavailability and rate of release from the foodstuff.[16]

Metabolism is the primary route of elimination of $\Delta^9$-THC from the body by the hepatic cytochrome P450 liver enzyme system,[15] and the elimination half-life of $\Delta^9$-THC is approximately 1 day in casual smokers and 3 - 5 days in chronic smokers. The relatively long half-life is due to the lipophilic character of $\Delta^9$-THC.[17,18] The peak psychoactive effects of $\Delta^9$-THC lag behind the peak blood concentration by 20 - 30 minutes.[19] $\Delta^9$-THC is metabolised to the 11-hydroxy-$\Delta^9$-THC (11-OH-$\Delta^9$-THC) metabolite, which is also biologically active and which in turn is metabolised to the biologically inactive metabolite 11-nor-carboxy-$\Delta^9$-THC (THC-COOH).

**Urine.** Of the $\Delta^9$-THC, 80 - 90% is excreted within 5 days, with approximately 20% in the urine, with THC-COOH glucuronide conjugates the most abundant metabolites.[20] The THC-COOH concentration has been reported to be above the US Substance Abuse and Mental Health Services Administration (SAMHSA) cut-off level of 15 ng/mL urine for 33.7 (standard deviation (SD) 9.2) hours after smoking a cannabis cigarette with $\Delta^9$-THC content equal to 1.75% and 88.6 (SD 23.2) hours for a 3.55% $\Delta^9$-THC cannabis cigarette.[21,22]

**Oral fluid (OF).** A dose of 500 mg $\Delta^9$-THC in volunteers, who smoked a cannabis cigarette, resulted in a serum concentration equal to 95 ng/mL within 5 minutes of administration, which decreased to 1 - 2 ng/mL serum after 3 - 5 hours. The OF $\Delta^9$-THC level increased to 918 ng/mL within 15 minutes, with a corresponding serum $\Delta^9$-THC concentration of 27.7 ng/mL.[23] OF $\Delta^9$-THC concentration correlated reasonably well with the serum $\Delta^9$-THC concentration ($r$=0.84), suggesting the possible use of OF $\Delta^9$-THC as a valid biomarker for recent cannabis exposure in qualitative roadside drug tests.[23-25]

An initial high concentration of $\Delta^9$-THC directly after the smoking of cannabis occurs due to the $\Delta^9$-THC from smoke, which is deposited in the oral cavity and acts as a *depot* for the oral $\Delta^9$-THC. The $\Delta^9$-THC in the oral cavity then dissipates back into the bloodstream within 0.3 to 4 hours to assume a $\Delta^9$-THC concentration approximately equal to the plasma $\Delta^9$-THC concentration. The OF-to-plasma $\Delta^9$-THC ratio varied between 0.5 and 2.2 in six subjects.[24]

It is important to note that the biphasic pattern of decline for $\Delta^9$-THC in OF applies to cannabis smokers. The $\Delta^9$-THC levels in subjects who inhaled cannabis smoke passively, however, declined linearly and rapidly. A 30-minute waiting period, before sampling of OF, limits the risk of a positive test, which may be due to passive exposure. Reported passive exposure investigations also did not increase $\Delta^9$-THC values above 2 ng/mL serum.[26,27] (Blood concentrations correspond to approximately half of the serum concentration values.)

A serum-to-OF ratio of between 0.5 and 2 was reported after a *stimulated* OF collection, employing citric acid on the collection device. Another study found a serum-to-OF ratio of 12 - 33 with a *non-stimulated* sampling protocol of OF. The significant difference between serum-to-OF ratios of these studies was attributed to the difference in OF collection methods, *i.e. stimulated v. non-stimulated*. The literature also indicates a significant OF-to-blood ratio inter-individual variability ranging from 0.01 to 568.9.[24,25,28-31] We found no reliable scientific data and information to the same extent regarding cannabis-containing foodstuff.

## Performance-behavioural effects of cannabis and threshold concentration levels

The effects of $\Delta^9$-THC start rapidly during smoking, with a peak after 30 - 60 minutes. The dose-dependent acute effects last between 2 and 4 hours. Acute consumption causes impairment of psychometric tasks, memory, sense of time, motor coordination and reaction speed. Most reports on the performance-behavioural effects of cannabis relate to driving impairment.[32-35]

The $\Delta^9$-THC blood concentration is the best indicator of recent cannabis exposure and correlates with odds ratios of crash risk.[36] Individuals with blood $\Delta^9$-THC concentrations >5 ng/mL were 2.1 - 6.6 times more likely to be responsible for the accident.[37] Epidemiological data also confirmed that individuals showed no signs of impairment at $\Delta^9$-THC serum concentrations below 2 ng/mL and that slight selective impairment was present for perceptual-motor control, motor impulse control and cognition at serum $\Delta^9$-THC concentration levels between 2 and 5 ng/mL.[38] Impairment became prominent at serum $\Delta^9$-THC concentrations between 5 and 10 ng/mL and total impairment evident at serum concentrations higher than 30 ng/mL serum.[23]

## Discussion

### Legislation

In SA, a driver is regarded as under the influence of intoxicating liquor if: 'the skill and judgement normally required in the manipulation of a motor car is *obviously* diminished or impaired as a result of the consumption of alcohol'.[39] The authors of this article consider that a *positivistic* legal interpretation of the concept of 'intoxication' is problematic since an individual's faculties and ability to perform a safety-sensitive task may be impaired long before it becomes 'obvious'. The authors of this article also consider that a *natural law* perspective would serve the statute more effectively since the intention is to ensure that an individual is not impaired while taking part in risk- and safety-sensitive activities and that no level of impairment will be tolerated. An individual with a blood $\Delta^9$-THC concentration level below a scientifically and medically validated threshold concentration should not be regarded as *intoxicated* and should be allowed to take part in a risk-sensitive activity. $\Delta^9$-THC and its metabolites should now be considered as prohibited substances at a threshold concentration. The approach of the Canadian legislation with a threshold for drivers of 2 ng/mL $\Delta^9$-THC in blood[8] is in line with SA's 'zero-tolerance' approach for vehicle drivers who have blood alcohol concentrations above the statutory threshold of 0.05 g/100 mL blood, for instance.

Confusing the stance of 'zero tolerance' with 'zero concentration' as a first approximation is not within the ambit of the Constitution and may infringe an individual's right to use cannabis lawfully and responsibly. Secondary reasons such as problematic sampling, for instance, may influence the practicability and veracity of the test and may require the implementation of a threshold of 'zero concentration' for a prohibited substance. The concept of 'zero concentration' should be considered carefully, since the lowest level of detection is related to the analytical technique used for detection. It would, therefore, be scientifically more correct to employ the limit of detection (LOD) for the specific analytical method as the 'zero concentration' threshold.

### Detection of cannabis users

**Observational identification** of an individual who is 'under the influence' includes impairment indicators, which have an inherent risk of non-selectivity due to observational error, possible bias and learned behaviour by the subject.[40] A skilled person is required to

judge the levels of impairment, which lies on a continuum of severity, to an eventual state of 'intoxication'. In a routine testing environment, this approach is not practical owing to time limitations and other reasons. It is also problematic for a lay person to recognise the effects of intoxication.

**Analytical chemical detection,** however, may provide an objective means to identify a drug user at concentration levels well below those that correspond with 'obvious impairment'. A typical protocol involves a preliminary or screening test, which is followed by a confirmation test for all non-negative screening test results.[41]

The most often used screening tests for $\Delta^9$-THC are based on immuno-assay technology and do not show cross-reactivity for ethanol because of the vast difference in the molecular structure. Substances that may interfere with the screening tests for cannabis are usually listed in the package insert of a test kit. These lists can never be exhaustive, and there may be many more exogenous and endogenous compounds in biofluids that may exhibit cross reactivity. It is, therefore, a requirement for all non-negative screening tests to be subjected to confirmation testing by a forensic toxicology laboratory.

## Bio-matrices

### Blood

The use of blood specimens for compliance drug testing in the workplace is invasive because of the intimacy of venepuncture. Ethical concerns may also be raised as less invasive alternative matrices, such as OF and urine, may be used to achieve the same goal of minimising risk.[42] Blood collection requires a registered phlebotomist, unlike the collection of urine and OF. The *voluntary* component of consent may be diminished when blood is employed for prohibited substance testing in the workplace, which is also in the private law domain as opposed to the criminal law domain, where individuals may be arrested before blood collection.

### Oral fluid or urine?

**OF.** The elimination time for $\Delta^9$-THC in OF is more rapid than for urinary elimination, which suggests that OFs are useful to test for recent exposure, i.e. a few hours for OF v. a few days for urine. OF (with stimulated collection) mimics blood $\Delta^9$-THC concentrations closely with a serum-to-OF ratio of between 0.5 and 2.[24]

Residual $\Delta^9$-THC in the oral mucosa after smoking cannabis may give rise to claims of passive exposure; however, a 30-minute observation period is sufficient to allow for the OF $\Delta^9$-THC levels to decrease below 2 ng/ml.[27] Inconsistent sampling of OF related to stimulated v. non-stimulated collection is a complicating factor for both OF $\Delta^9$-THC screening and confirmation.[24,43] The opinion of the authors is that the 'memory effect' may be more prominent in the case of non-stimulated sampling, where the OF is not freshly generated during sampling.

**Urine.** The long elimination half-life of $\Delta^9$-THC in the form of urinary THC–COOH may result in chronic users never having a urinary concentration below an administrative THC-COOH cut-off concentration, which may constitute an infringement on their freedom and autonomy to use cannabis legally. Urine collection, however, does not have the same risk of contamination as OF.

Neither the $\Delta^9$-THC concentration level in OF nor the THC–COOH in urine can be employed as a proxy for impairment, as a result of the vast range of blood-OF and blood-urine ratios. The limitation is compounded by the continuous physiological change of the water content in the urine and OF because of the body's changing hydration status. Therefore, we believe that these two markers for cannabis use will not withstand legal scrutiny as markers for impairment.[44]

## The way forward

A clear and well-written prohibited substance regulation and testing policy is the starting point of the whole process to provide regulatory certainty for both the organisation and the test subjects. Specifying a threshold concentration of 2 ng/mL $\Delta^9$-THC in OF corresponds with the 'zero-tolerance' approach in SA for vehicle drivers who have blood alcohol concentration levels above the statutory threshold of 0.05 g/100 mL blood, for instance. A specific threshold concentration will then counter all possible claims regarding varying metabolic rates, time of consumption, blood-OF and blood-urine ratios. The American Mandatory Guidelines for Federal Workplace Drug Testing Programs, for example, specify a confirmation threshold concentration of 2 ng/mL $\Delta^9$-THC in OF and a 15 ng/mL THC-COOH in urine.[41]

An LOD approach, also referred to as a *zero-concentration* approach, may be seen as an excessive restriction on the freedom and autonomy of an individual, which in effect may prevent him or her from using cannabis legally at all. The motivation for such a severe limitation should be rational and may, in some instances, be to the satisfaction of the law.

The law of contract is invoked when an individual voluntarily joins an organisation. A prohibited substance regulation and testing policy is therefore paramount to serve as an 'agreement' between the employer and employee and to serve as a guideline. Non-compliance with the prohibited substance regulation and testing policy would constitute a breach of contract.

In addition, the matrices, as well as the collection and analytical detection protocols to be employed, must also be specified in the policy. We believe that because a large variation in blood-OF ratios has been reported, which can be attributed to the collection procedure, legal challenges will result because the reliability and accuracy, or the veracity, of the test may be compromised. The organisation should, therefore, standardise on a specific type of OF collection device which must be used consistently throughout the organisation. The specific commercial collection and testing devices should also be specified in the policy, and any changes in the type or configuration of the devices must be cleared with the employees and their representatives. The possible presence of residual $\Delta^9$-THC in the oral mucosa is a definite threat to the reliability of an OF cannabis screening and confirmation test; however, a 30-minute observation period is sufficient to counter claims of passive exposure.

Not adhering to these recommendations may create an 'impossibility' of performance in terms of the contract, that will prevent the creation of legal obligations, resulting in the test subject being absolved from liability.[45]

The following options for cannabis testing in the workplace arise from the discussion:

- **Blood testing** for $\Delta^9$-THC is the best marker to estimate the level of impairment. The availability of a registered phlebotomist is required, and consent may be problematic because of the invasiveness of venipuncture.
- **OF and urine testing** are scientifically accurate and less invasive alternatives for $\Delta^9$-THC testing; however, the concentration levels cannot be used to make conclusions regarding the level of impairment or 'intoxication'. The policy should act as the official guideline in the decision related to breach of contract.
- **Sobriety testing** and other observations regarding the test subject can also act as supportive evidence and are sometimes regarded as sufficient evidence for impairment on the balance-of-probabilities standard of proof. A qualified practitioner should perform sobriety testing since this may be challenged because of the diagnostic nature thereof.

Prohibited substance regulation and testing are primarily intended to act as a deterrent and not to police individuals, especially if only a small proportion of a group is randomly selected to undergo a compliance test. The difference in excretion time between OF and urine can be used to the advantage of risk management since OF $\Delta^9$-THC levels can be employed to detect recent use as opposed to urinary THC-COOH levels, which may be used for longer-term risk management.

Occupational health practitioners should exercise caution when employing administrative cut-off concentrations for $\Delta^9$-THC for risk and safety as the only criterion when conducting pre-employment and other fit-for-service diagnostic investigations. Cannabis-use examinations should be done with an approach similar to alcohol use, which requires additional diagnostic evidence beyond the mere presence of the parent compound or metabolites above a threshold concentration applicable for risk and safety.

**Declaration.** None.

**Acknowledgements.** None.

**Author contributions.** Both authors contributed equally to the initial concept and preparation of the manuscript.

**Funding.** None.

**Conflicts of interest**: None.

1. Prince v Minister of Justice and Constitutional Development 2013 Case No: 8760 (WCC).
2. Rubin v National Director of Public Prosecution 2013 Case No: 7295 (WCC).
3. Acton v National Director of Public Prosecution 2012: 31 March 2017, Case No: 4153 (WCC).
4. Minister of Justice and Constitutional Development v Prince 2018 CCT 108/17 (ZACC)
5. The Constitution of the Republic of South Africa, Chapter 2, section 36.
6. The Constitution of the Republic of South Africa, Chapter 2, section 9(1) and 9(2).
7. The Constitution of the Republic of South Africa, Chapter 2, section 39(c).
8. Canada. Cannabis Act (S.C. 2018, c. 16). Justice Canada. Government of Canada. https://laws-lois.justice.gc.ca/eng/acts/C-24.5/index.html (accessed 9 May 2019).
9. South Africa. Occupational Health and Safety Act No. 85 of 1993 (OHSA), Sections 8, 9, 14, 23; Section 2(A), 2(C) of the regulations in terms of the Health and Safety Act.
10. South Africa. General Administrative Regulations of the Machinery and Occupational Safety Act No. 6 of 1983 (MOSA), Regulations 6 and 12(2).
11. South Africa. Drugs and Drug Trafficking Act No. 140 of 1992, Sections 4(b) and 5(b).
12. South Africa. Medicines and Related Substances Control Act No. 101 of 1965 (Act 101 of 1965), Section 22A(9)(i).
13. South Africa. General Administrative Regulations of the Machinery and Occupational Safety Act No. 6 of 1983 (MOSA), Regulations 6 and 12(2).
14. Heustis MA, Sampson AH, Holicky BJ, et al. Characterisation of the absorption phase of marijuana smoking. Clin Pharmacol Ther 1992;52(1):31-41. https://doi.org/10.1038/clpt.1992.100
15. Matsunga T, Iwawaki Y, Watanabe K, et al. Metabolism of delta-9-tetrahydrocannabinol by cytochrome P450 isozymes purified from hepatic microsomes of monkeys. Life Sci 1995;56(23-24):2089-2095. https://doi.org/10.1016/0024-3205(95)00193-A
16. Ohlsson A, Lindgren JE, Wahlen A, et al. Plasma delta-9-tetrahydrocannabinol concentrations and clinical effects after oral and intravenous administration and smoking. Clin Pharmacol Ther 1980;28:409-416. https://doi.org/10.1038/clpt.1980.181
17. Johansson E, Agurell S, Hollister LE, et al. Prolonged apparent half-life of delta-9-tetrahydrocannabinol in plasma of chronic marijuana users. J Pharm Pharmacol 1988;40:374-375. https://doi.org/10.1111/j.2042-7158.1988.tb05272.x
18. Jones RT. Drug abuse profile: Cannabis. Clin Chem 1987;33:72B-81B.
19. Domino LE, Domino SE, Steven E, et al. Relation of delta-9-THC concentrations to subjective 'high' marijuana users: A review and reanalysis. In: S Agurell, ed. The Cannabinoids: Chemical, Pharmacologic, and Therapeutic Aspects. Orlando, Fla.: Academic Press, 1984:245-261.
20. Harvey DJ. Absorption, distribution, and biotransformation of the cannabinoids. In: Nahas G, Sutin KM, eds. Marijuana and Medicine. Ottowa: Humana Press, 2001:91-103.
21. Johansson EK, Halldin MM. Urinary excretion half-life of delta-9-tetrahydrocannabinol-7-oic acid in heavy marijuana users after smoking. J Anal Toxicol 1989;13(4):218-223. https://doi.org/10.1093/jat/13.4.218
22. Williams PL, Moffat AC. Identification in human urine of delta-9-tetrahydtocannabinol-11-oic glucuronide: A tetrahydrocannabinol metabolite. J Pharm Pharmacol 1980;32(7):445-448. https://doi.org/10.1111/j.2042-7158.1980.tb12966.x
23. Ramaekers JG, Moeller MR, van Ruitenbeek P, et al. Cognition and motor control as a function of delta-9-THC concentration in serum and oral fluid: Limits of impairment. Drug Alcohol Depend 2006;85(2):114-122. https://doi.org/10.1016/j.drugalcdep.2006.03.015
24. Huestes MA, Cone EJ. Relationship of delta-9-tetrahydrocannabinol concentrations in oral fluid and plasma after controlled administration of smoked cannabis. J Anal Toxicol 2004;28(6):394-399. https://doi.org/10.1093/jat/28.6.394
25. Samyn N, Haeren C. On-site testing of saliva and sweat with drug-wipe and determination of concentration of drugs of abuse in saliva, plasma and urine in suspected users. Int J Legal Med 2000;113:150-154. https://doi.org/10.1007/s004140050287
26. Cone EJ, Johnson RE, Darwin WD, et al. Passive inhalation of marijuana smoke: Urinalysis and room air levels of delta-9-tetrahydrocannabinol. J Anal Toxicol 1987;11(3):89-96. https://doi.org/1093/jat/11.3.89
27. Niedbala S, Kardos K, Salamone S, et al. Passive cannabis smoke exposure and oral fluid testing. J Anal Toxicol 2004;28(7):546-552. https://doi.org/1093/jat/28.7.546
28. Gjerde H, Mordal J, Christophersen AS, et al. Comparison of drug concentrations in blood and oral fluid collected with Intercept sampling device. J Anal Toxicol 2010;34(4):204-209. https://doi.org/10.1093/jat/34.4.204
29. Wille SM, Raes E, Lillsunder P, et al. Relationship between oral fluid and blood concentrations of drugs of abuse in drivers suspected of driving under the influence of drugs. Ther Drug Monit 2009;31(4):511-519. https://doi.org/10.1097/FTD.0b013e3181ae46ea
30. Toennes SW, Raemakers JG, Theunissen EL, et al. Pharmacokinetic properties of delta-9-tetrahydrocannabinol in oral fluid of occasional and chronic users. J Anal Toxicol 2010;34(4):216-221. https://doi.org/10.1093/jat/34.4.216
31. Milman G, Schwope DM, Schwilke E, et al. Oral fluid and plasma cannabinoid ratios after around-the-clock controlled oral delta-9-tetrahydrocannabinol administration. Clin Chem 2011;57(11):1597-1606. https://doi.org/10.1373/clinchem.2011.169490
32. Schmitt JAJ, Lamers CTJ, Kuypers KPC, et al. Performance and behavioural effects of illicit drugs. In: Burns M, ed. Medical-Legal Aspects of Drugs. 2nd ed. Tucson, Ariz.: Lawyers and Judges Publishing Company, 2007:74-75.
33. Liguori A, Gatto CP, Jarrett DB. Separate and combined effects of marijuana and alcohol on mood, equilibrium and simulated driving. Psychopharmacology (Berl) 2002;163(3-4):399-405. https://doi.org/10.1007/s00213-002-1124-0
34. Ramaekers JG, Robbe HWJ, O'Hanlon JF, et al. Marijuana, alcohol and actual driving performance. Hum Psychopharm Clin 2000;15(7):551-558. https://doi.org/10.1002/1099-1077(200010)15:7<551::AID-HUP236>3.0.CO;2-P
35. Phillips JA, Holland MG, Baldwin DD, et al. Marijuana in the Workplace: Guidance for Occupational Health Professions and Employers: Joint Guidance Statement of the American Association of Occupational Health Nurses and the American College of Occupational and Environmental Medicine. Workplace Health Saf 2015;63(4):139-164. https://doi.org/10.1177%2F2165079915581983
36. Laumon B, Gadegbeku B, Martin JM, et al. Cannabis intoxication and fatal road crashes in France: Population based case-control study. BMJ 2005;331(7529):1371. http://doi:10.1136/bmj.38648.617986.1F
37. Drummer OH, Gerostamoulos J, Batziris H, et al. The involvement of drugs in drivers of motor vehicles killed in Australian road traffic crashes. Accid Anal Prev 2004;36(2):239-248. https://doi.org/10.1016/S0001-4575(02)00153-7
38. Grotenhermen F, Leson G, Berghaus G, et al. Developing limits for driving under cannabis. Addiction 2007;102(12):1910-1917. https://doi.org/10.1111/j.1360-0443.2007.02009.x
39. Burchell J, ed. Principles of Criminal Law. 4th ed. Cape Town: Juta, 2014:787-788.
40. Lee D, Huestes MA. Current knowledge on cannabinoids in oral fluid. Drug Test Anal 2014;6:88-111. https://doi.org/10.1002/dta.1514
41. Substances and Mental Health Services Administration (SAMHSA). Mandatory Guidelines for Federal Workplace Drug Testing Programs, Federal Register, Vol 82, No 13, 2017. https://www.samhsa.gov/sites/default/files/workplace/frn_vol_82_7920_.pdf (accessed 9 May 2019).
42. World Medical Association. World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. https://www.who.int/bulletin/archives/79(4)373.pdf (accessed 16 January 2019).
43. Crouch DJ. Oral fluid collection: The neglected variable in oral fluid testing. Forensic Sci Int 2005;150:165-173. https://doi.org/10.1016/j.forsciint.2005.02.028
44. Marsot A, Audebert L, Attolini B, et al. Comparison of cannabinoid concentrations in plasma, oral fluid and urine in occasional cannabis smokers after smoking cannabis cigarette. J Pharm Pharm Sci 2016;19(3):411-422. https://doi.org/10.18433/J3F31D
45. Du Plessis J. Possibility and certainty. In: Hutchison D, Pretorius CJ, eds. The Law of Contract in South Africa. 2nd ed. Cape Town: Oxford University Press, 2015:207-208.

*Accepted 1 June 2020.*