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. This was confirmed by the Constitutional Court, which extended the concept of the use in a ‘private dwelling’ to the use ‘in private’.

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 (Δ9-THC) and its metabolites in body fluids, which are also related to ‘safe’ concentration levels of Δ9-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. The legalisation in effect confirmed that cannabis use in a private dwelling were legalised in 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 (Δ9-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.

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

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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 Δ⁹-THC into the bloodstream and hepatic elimination.\[30\] Absorption is slower when cannabis is taken orally, with the peak concentration delayed depending on the bioavailability and rate of release from the foodstuff.\[31\]

Metabolism is the primary route of elimination of Δ⁹-THC from the body by the hepatic cytochrome P450 liver enzyme system,\[32\] and the elimination half-life of Δ⁹-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 Δ⁹-THC.\[11,13\] The peak psychoactive effects of Δ⁹-THC lag behind the peak blood concentration by 20 - 30 minutes.\[14⁹] Δ⁹-THC is metabolised to the 11-hydroxy-Δ⁹-THC (11-OH-Δ⁹-THC) metabolite, which is also biologically active and which in turn is metabolised to the biologically inactive metabolite 11-nor-carboxy-Δ⁹-THC (THC-COOH).

Urine. Of the Δ⁹-THC, 80 - 90% is excreted within 5 days, with approximately 20% in the urine, with THC-COOH glucuronide conjugates the most abundant metabolites.\[21\] 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 Δ⁹-THC content equal to 1.75% and 88.6 (SD 23.2) hours for a 3.55% Δ⁹-THC cannabis cigarette.\[21,22\]

Oral fluid (OF). A dose of 500 mg Δ⁹-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 Δ⁹-THC level increased to 918 ng/mL within 15 minutes, with a corresponding serum Δ⁹-THC concentration of 27.7 ng/mL.\[23\] OF Δ⁹-THC concentration correlated reasonably well with the serum Δ⁹-THC concentration (r=0.84), suggesting the possible use of OF Δ⁹-THC as a valid biomarker for recent cannabis exposure in qualitative roadside drug tests.\[23,24\]

An initial high concentration of Δ⁹-THC directly after the smoking of cannabis occurs due to the Δ⁹-THC from smoke, which is deposited in the oral cavity and acts as a depot for the oral Δ⁹-THC. The Δ⁹-THC in the oral cavity then dissipates back into the bloodstream within 0.3 to 4 hours to assume a Δ⁹-THC concentration approximately equal to the plasma Δ⁹-THC concentration. The OF-to-plasma Δ⁹-THC ratio varied between 0.5 and 2.2 in six subjects.\[25\]

It is important to note that the biphasic pattern of decline for Δ⁹-THC in OF applies to cannabis smokers. The Δ⁹-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 Δ⁹-THC values above 2 ng/mL serum.\[26-28\] (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.\[24,26-31\] We found no reliable scientific data and information to the same extent regarding cannabis-containing foodstuff.

Performance-behavioural effects of cannabis and threshold levels

The effects of Δ⁹-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.\[12-15\]

The Δ⁹-THC blood concentration is the best indicator of recent cannabis exposure and correlates with odds ratios of crash risk.\[29\] Individuals with blood Δ⁹-THC concentrations >5 ng/mL were 2.1 - 6.6 times more likely to be responsible for the accident.\[30\] Epidemiological data also confirmed that individuals showed no signs of impairment at Δ⁹-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 Δ⁹-THC concentration levels between 2 and 5 ng/mL.\[30\] Impairment became prominent at serum Δ⁹-THC concentrations between 5 and 10 ng/mL and total impairment evident at serum concentrations higher than 30 ng/mL serum.\[21\]

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’.\[30\] The authors of this article consider that a positivist 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 Δ⁹-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. Δ⁹-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 Δ⁹-THC in blood\[31\] is in line with SAs ‘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.\[41\] 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.24 Inconsistent sampling of OF related to stimulated v. non-stimulated collection is a complicating factor for both OF $\Delta^9$-THC screening and confirmation.24,41 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 urine 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.41

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 venepuncture.
- **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 Δ⁹-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 Δ⁹-THC for risk and safety as the only criterion when conducting pre-employment and other fit-for-service diagnostic investigations. Cannabis-use employing administrative cut-off concentrations for Δ⁹-THC should be looked at 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 Δ⁹-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.

Conflict of interest: None.

Declaration. None.

Acknowledgements. None.

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

Funding. None.