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Developing limits for driving under cannabis

Franjo Grotenhermen[1], Gero Leson[2], Günter Berghaus[3], Olaf H. Drummer[4], Hans-Peter Krüger[5], Marie Longo[6], Herbert Moskowitz[7], Bud Perrine[8], Johannes G. Ramaekers[9], Alison Smiley[10] & Rob Tunbridge[11]

Nova-Institut, Hürth, Germany,[1] Leson and Associates, Berkeley, USA,[2] University of Cologne, Germany,[3] Victorian Institute of Forensic Medicine and Department of Forensic Medicine, Monash University, Melbourne, Australia,[4] University of Würzburg, Germany,[5] Drug and Alcohol Services South Australia, Parkside, Australia,[6] University of California, Los Angeles, USA,[7] Vermont Alcohol Research Centre, USA,[8] Maastricht University, the Netherlands,[9] Human Factors North Inc., Toronto, Canada[10] and Transport Research Laboratory, Crowthorne, UK[11]

ABSTRACT

Objective Development of a rational and enforceable basis for controlling the impact of cannabis use on traffic safety. **Methods** An international working group of experts on issues related to drug use and traffic safety evaluated evidence from experimental and epidemiological research and discussed potential approaches to developing *per se* limits for cannabis. **Results** In analogy to alcohol, finite (non-zero) *per se* limits for delta-9-tetrahydrocannabinol (THC) in blood appear to be the most effective approach to separating drivers who are impaired by cannabis use from those who are no longer under the influence. Limited epidemiological studies indicate that serum concentrations of THC below 10 ng/ml are not associated with an elevated accident risk. A comparison of meta-analyses of experimental studies on the impairment of driving-relevant skills by alcohol or cannabis suggests that a THC concentration in the serum of 7–10 ng/ml is correlated with an impairment comparable to that caused by a blood alcohol concentration (BAC) of 0.05%. Thus, a suitable numerical limit for THC in serum may fall in that range. **Conclusions** This analysis offers an empirical basis for a per se limit for THC that allows identification of drivers impaired by cannabis. The limited epidemiological data render this limit preliminary.

Keywords Accident risk, adverse effect, cannabis, driving, drug, DUIC, DUID, limit, marijuana, Psychomotor impairment.

Correspondence to: Franjo Grotenhermen, Nova-Institut, Goldenbergstrasse 2, 50354 Huerth, Germany. E-mail: franjo.grotenhermen@nova-institut.de
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INTRODUCTION

The rising prevalence of driving under the influence of illegal and medicinal drugs (DUID) and its potential impact on traffic safety have raised awareness among media, scientists and policy makers in many countries and prompted calls for more effective control. Driving under the influence of cannabis (DUIC) is of particular concern, because the recreational use of cannabis products, i.e. marijuana and hashish, is often second only to alcohol. This highlights the need for effective legal control of the potential risks posed by DUIC.

Current approaches to assessment and control of DUIC

Current DUID laws use one of three basic approaches to determine whether a driver involved in an accident or stopped at a roadside checkpoint, is impaired or under the influence of a particular drug. One is the traditional impairment or effect-based approach; the others are two versions of the '*per se*' approach. The *per se* approach uses, as in the case of alcohol, a science-based finite limit or employs a zero limit for the tolerable concentration of a drug or its metabolites in a driver's blood or other body fluids. In either case, exceedance of this limit is deemed automatically to prove (legal) impairment.

In theory, the impairment approach best meets the objectives of DUID laws. It observes and assesses the fitness of drivers and potentially penalizes those who are actually impaired. Impairment may arise from several, often-synergistic factors, including fatigue and the consumption of multiple drugs. The main limitation of the impairment approach is the lack of standardized methods for measuring and judging the impairment caused by drug consumption. Standardized sobriety tests are sensitive and reliable when used by trained officers to detect blood alcohol contents of more than 0.1%. These tests

also detect drug-induced impairment reliably, particularly with drugs that depress the central nervous system. However, sobriety tests for drugs are less sensitive to modest impairment [1,2]. Procedures for handling drivers suspected of drug use are often not standardized. This renders the assessment of their impairment somewhat arbitrary. Legal disputes are thus common with DUID cases and make the enforcement of impairment-based laws costly.

Because of these shortcomings of the impairment-based approach, many jurisdictions have adopted *per se* limits for DUID. Many of them have been set at the limit of detection and are *de facto* zero limits. This avoids the need for a reliable science-based correlation between drug concentration and level of impairment and facilitates enforcement. However, zero limits by design penalize the presence in body fluids of an active drug ingredient or its metabolites, which does not necessarily correspond to actual impairment. This is a particular concern with cannabis. Its main psychoactive constituent, delta-9-tetrahydrocannabinol (THC), is detectable in blood for up to 2 days. Depending on the frequency of use, its metabolites are detectable in blood and urine for days or weeks after cannabis use. In contrast, even a high dose of smoked THC typically causes acute impairment of driving skills for only 3–4 hours. The slow disappearance of THC from serum is particularly pronounced with heavy users, who consume more than one marijuana cigarette (joint) per day, or even with moderate users of cannabis. Their blood may contain THC concentrations of between 1.0 and 6.4 ng/ml serum even 24–48 hours after smoking the last joint [3]. Thus, blood samples taken from moderate users may still test positive for THC even when they observe a sufficiently long waiting period between cannabis use and driving and impairment has dissipated. Heavy passive exposure to cannabis smoke may also result in measurable THC concentrations in blood serum without causing concurrent impairment [4–6].

There are several potential indicators of cannabis use and its potential impact on driving skills. Because of its good correlation with measured impairment during the later phase of a cannabis high, i.e. more than 2 hours after cannabis consumption, the concentration of THC in blood is still the most meaningful indicator of impairment during that period [7]. Note that during the first hour of a cannabis 'high' no unimodal relationship between impairment and THC concentration exists. However, during this phase, THC concentrations in blood clearly exceed the range considered by the authors for a legal limit. Thus, drivers under the acute impact of cannabis and presenting with THC concentrations in the serum of 20 ng/ml or more would invariably be found in violation.

Commercially available less invasive alternatives to measuring THC concentration in blood, such as testing urine for THC metabolites or analysing hair and sweat samples, suffer from long detection windows and/or poor reproducibility and do not qualify as the sole method for determining cannabis-induced impairment. THC concentrations in saliva appear to correlate reasonably well with THC concentrations in blood, and saliva testing may emerge as a non-invasive screening test for the use of cannabis and other drugs in road checks, to be confirmed by blood analysis.

As is commonly conducted with alcohol, *per se* laws for DUIC may adopt a set of two legal limits for the concentration of THC in blood. These limits will reflect varying degrees of impairment and corresponding risk and translate into varying levels of punishment and the intended educational effect. Violation of the lower limit would result in a fine and a temporary suspension of driving privileges, intended to warn the driver to separate drug use and driving. For example, several European countries have set a lower blood alcohol concentration (BAC) limit at 0.05%. Exceeding the higher limit above which most people will be unfit to drive would result in a higher fine, extended revocation of the driver's licence and, depending on the circumstances, criminal prosecution. Several European countries have adopted such a higher BAC of 0.11%.

Approach and objectives of study

This paper summarizes the findings and recommendations by an interdisciplinary working group of international scientists, convened in 2004/05. Its objectives were to conduct a comprehensive review and discussion of scientific evidence on DUIC from experimental and epidemiological studies and to propose a numerical range for a *per se* limit for THC concentrations in blood, which may serve as indicator of cannabis-induced impairment. Selection of the limit was also to consider physiological, toxicological and analytical factors that may modify the correlation between blood THC concentration and the impairment of a driver.

SCIENTIFIC BASIS FOR A LEGAL THC LIMIT

Epidemiological and experimental studies are the two main sources of evidence on the potential impact of cannabis use on driving skills and accident risk.

Epidemiological studies

Findings from epidemiological studies have historically been the basis for *per se* limits for alcohol and driving. These studies examine the statistical association between rare events (traffic crashes, injury or death) and a risk factor, such as the consumption of alcohol or a drug, and the corresponding indicators, such as the BAC. Using a

case–control or culpability approach, epidemiology assesses the actual risk of a drugged driver causing an accident, relative to that of a sober person driving under similar road conditions. That relative risk is expressed as odds ratio (OR). An OR greater than 1 corresponds to a higher accident risk for the 'case group', i.e. drivers under the influence of a drug, compared to the 'control group'.

Epidemiological studies measure the effect of drug use on driving performance and accident risk under 'real life' conditions and are thus suited to correlate the concentrations of a drug use indicator to an actual risk. For alcohol, scientists have developed, based on the results of numerous epidemiological studies, hazard curves that assign each alcohol concentration to a certain accident risk. As with all epidemiological findings, the validity of each study depends critically on the number of cases included. Driving under the influence of alcohol is a widespread phenomenon and screening of drivers for alcohol using breath analysers is non-invasive. This allowed researchers to collect, for a given time of day, region, road condition and for each BAC class enough cases to yield statistically significant ORs.

Fortunately for traffic safety but unfortunately for epidemiological research DUIC is far less common. Furthermore, meaningful testing for cannabis use requires the collection of blood samples, a procedure that in most countries cannot be used unless a driver is suspected of DUI. Thus, epidemiological studies on DUIC do not usually have sufficient THC positive cases to calculate reliably concentration-dependent ORs.

Detailed overviews of epidemiological studies on DUIC have been provided by Bates & Blakely [8], Chesher & Longo [9], Ogden & Moskowitz [10] and Ramaekers *et al.* [11]. Drummer *et al.* conducted one of only few epidemiological studies that correlated THC concentrations in blood and accident risk and met quality criteria not met by other such studies [12]. The study used accident data from drivers fatally injured in accidents in Australia and found that THC concentrations in whole blood in the range of 0–5 ng/ml were associated with an OR of 0.7 and concentrations between 5 and 100 ng/ml with an OR of 6.6 (95% CI: 1.5–28). Note that both ORs represent an average for the entire respective range of THC concentrations, so the average OR for a driver with a THC concentration in blood of anywhere between 5 and 100 ng/ml is 6.6. Because OR and blood THC concentration are probably correlated by a linear or even exponential function, the point risk at 5 ng/ml THC in whole blood is considerably much lower than 6.6.

To differentiate more clearly the correlation between OR and THC concentration in the 0–20 ng/ml range G. Berghaus and G. Sticht (personal communication) developed the data by Drummer *et al.* into a polynomial function. The results in Fig. 1 show that THC concentrations

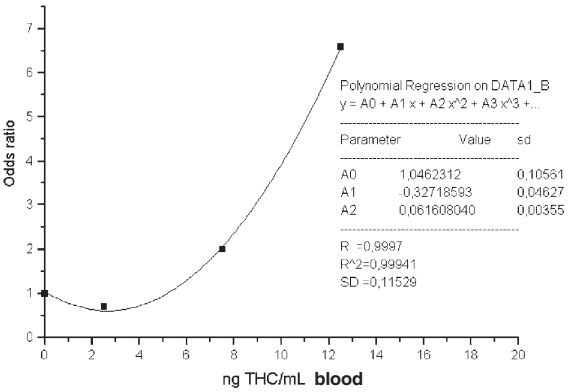

Figure 1 Correlation between delta-9-tetrahydrocannabinol (THC) concentration in whole blood and accident risk (odds ratio) calculated with the data of the study by Drummer *et al.* [12]

in blood are not associated with an elevated risk (OR > 1) until they exceed about 6 ng/ml.

Comparison of these cannabis-induced risks to those associated with driving under the influence of alcohol yields a first approximation to a numerical *per se* limit for DUIC. A BAC of 0.05% alcohol is associated with an OR of about 1.5–2 [13–15]. According to Fig. 1, that range corresponds to a THC concentration in whole blood of about 6–8 ng/ml, equivalent to a THC concentration in serum of about 12–16 ng/ml. The latter assumes a typical conversion factor of 2 between THC concentrations measured in blood versus serum.

As the study by Drummer *et al.* was based on only 58 cases whose blood samples contained only THC and no other indicators of drugs, the above considerations do not yield a statistically acceptable basis for an enforceable *per se* limit. The latter would require epidemiological data from a far larger number of cases.

A more recent epidemiological study, conducted in France by Laumon *et al.* [15], evaluated a much larger sample of THC-positive drivers ($n = 681$) who were involved in fatal accidents. Of them, 285 also tested positive for alcohol with a BAC > 0.05%. The adjusted OR (adjustment for alcohol, driver's age, type of vehicle and time of crash) for all THC positive cases was 1.78 (95% CI: 1.40–2.25), with the OR of cases with THC concentrations in blood of less than 1 ng/ml being 1.57 (95% CI: 0.84–2.95) and the OR of the subgroup with the highest THC concentrations (≥ 5 ng/ml whole blood) being only slightly higher (OR = 2.12, 95% CI: 1.32–3.38). The overall OR of 1.78 reported by Laumon *et al.* [15] is similar to that found by Drummer *et al.* [12] (OR = 2.7, 95% CI: 1.02–7.0), and in line with other studies that found only a small overall increase of accident risk in THC positive drivers, e.g. Terhune [16] (OR = 2.1), or even no increase, e.g. Longo *et al.* [17] (OR = 0.9). However, the findings by Laumon *et al.* [15] contradict those from all

other experimental and epidemiological studies in that they suggest an increased risk for THC blood concentrations below 1 ng/ml and only a slightly higher risk for blood concentrations above 5 ng/ml. A possible explanation for the weak dose–effect relationship is that many of the blood samples were collected 3 or 4 hours after the accident. Delayed sample collection causes a decrease in THC concentration, artificially inflates the calculated accident risk for a given THC concentration and blurs the differences between THC concentration classes. The study also suffered from other flaws, such as the classification of concurrent low concentrations of alcohol as 'null BAC', all of which reduces the value of the obtained data and the study's conclusions.

Overall, current epidemiological evidence on the effects of cannabis on accident risk is much less conclusive than for alcohol and must be considered insufficient for deriving a science-based legal limit for THC in blood. However, it suggests that the presence of THC as the sole drug in whole blood at concentrations above some 5 ng/ml correlates with a gradually increasing accident risk.

Experimental studies on impairment by cannabis

With inadequate epidemiological evidence, the extensive body of experimental research on cannabis use and driving skills may offer a second line of evidence and an alternate approach to deriving *per se* limits for THC. To date, some 150 experimental studies have tested the impact of cannabis use on skills that are essential to driving performance under laboratory conditions, in driving simulators and under road conditions. Most of these studies tested participants who had smoked or ingested a known dose of THC for significant impairment of one or several relevant skills. A typical result of such a test would read: a group of drivers who consumed a specific dose of a drug performed 'significantly worse' on a specific test compared to the performance of a control group who had not taken the drug.

Smiley reviewed driving simulator and on-road studies, which had examined the impact of THC on driving, and compared the latter to the effects by alcohol [18]. In summary, simulator and on-road studies showed that cannabis may impair some driving skills at smoked THC doses of as low as 6.25 mg. However, results varied considerably between the skills tested and among studies, and some of the skills tested were not impaired at doses as high as 18 mg. The impairment caused by cannabis appeared to be partially mitigated because subjects were aware of their impairment and, where possible, tended to compensate by not overtaking, by slowing down and by focusing attention in anticipation of a required response. Such compensation is not always possible in response to an unexpected event. In blind ratings, police officers rated drivers with a BAC of 0.08% as more impaired than those who had taken moderate to high doses of cannabis, and driving instructors rated subjects with a BAC of 0.04% as impaired, while those who had consumed a dose equivalent to 7 mg THC were rated as unimpaired.

Meta-analysis and comparison with alcohol

Findings from experimental studies may vary considerably because the outcome of a particular study is largely a function of study design and the choice of critical parameters, such as drug dose, smoking versus eating, time lapsed between drug use and testing and type and severity of tests during on-road driving. The apparent variability is best addressed through a meta-analysis of experimental studies. Scientists commonly perform meta-analyses of published research on a particular subject to evaluate and compare the results from a multitude of studies that meet a set of minimum quality criteria. Key results from the analysed studies are coded, compiled and analysed statistically. If a sufficiently large number of studies meet these entrance criteria, the meta-analytical approach strengthens the significance of findings from individual experimental studies.

A meta-analysis of a sufficiently large number of compliant experimental studies on cannabis and driving skills balances the variability in key design parameters. It also allows for a comparison with results from a meta-analysis of experimental studies on the impact of alcohol on driving skills, for which risk-based *per se* limits for BAC are well established. Such comparison will suggest a range of THC concentrations in blood from which a *per se* limit for DUIC may be selected.

The following factors support further the rationale for this approach. First, experimental studies on the effects of cannabis and other drugs on driving skills use the same methods, equipment and procedures as those for alcohol, i.e. laboratory tests of isolated skills, driving in simulators and on-road driving. They also use the same statistical methods to process data and report results. Secondly, most studies report information on cannabis dose, mode of application (smoked versus oral) and the time lapsed between consumption and test [19,20]. Using a pharmacokinetic model one can then estimate the THC concentration in blood at the time of testing. THC concentrations in blood show a considerable intra- and interindividual variation after consumption of the same dose [7,21] and the modelling results use mean concentrations. Thirdly, the large number of epidemiological studies on alcohol and driving has produced a strong correlation between BAC and accident risk and jurisdictions world-wide now typically use BAC concentrations of between 0.05 and 0.11% as indicators of various degrees of impairment by

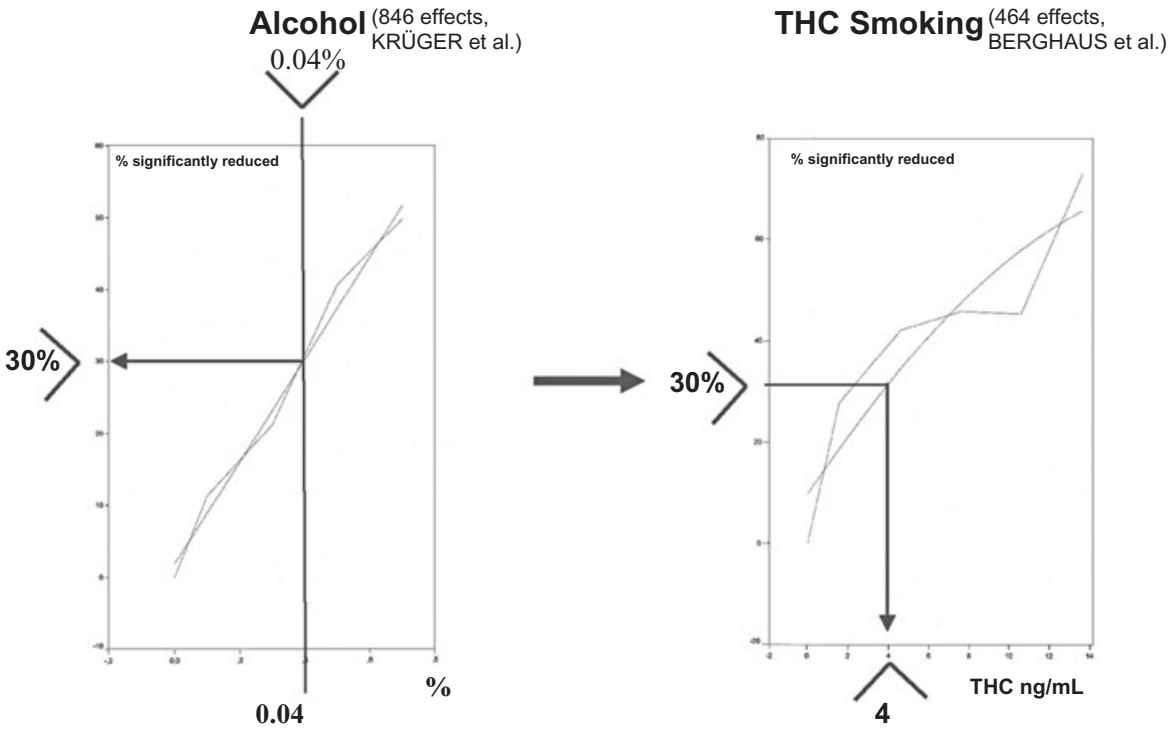

Figure 2 Comparison of survival functions for delta-9-tetrahydrocannabinol (THC) (in serum) and alcohol (in whole blood) and establishment of points of equal impairment. One curve represents the data really measured (unequal curve), the other curve represents the linear (blood alcohol concentration) or exponential (THC) smoothing

alcohol. A major shortcoming of this approach is its failure to consider whether the influence of alcohol and cannabis, respectively, promote different adaptive behaviors that may modify accident risk under actual road conditions [18]. Another limitation of this meta-analysis, as described below, is that it included test results for indicators with no clear link to driving performance, such as flicker fusion.

Within these limitations, a comparison of results from meta-analyses for alcohol and THC, respectively, then generates, for a given THC blood concentration, the corresponding BAC that causes the same level of impairment in test skills and for which accident risk is well established. For example, one may regard the THC concentration in blood at which the same percentage of all test results shows impairment as with a BAC of 0.05% as the THC concentration equivalent to that BAC.

The working groups of Krüger and of Berghaus conducted, in the 1990s, meta-analyses of suitable experimental studies on the effects of low doses of alcohol and cannabis [19,22,23]. Their work allowed a first systematic and quantitative comparison of the results of experimental research on the effects of THC and alcohol, respectively. For their meta-analysis of experimental studies on cannabis, Berghaus *et al*. first selected, out of more than 120 studies, those published in English or German and meeting the following minimum criteria: testing of at least one driving-relevant skill, a minimum of five human participants per study, information given on THC dose and mode of administration; number, age and gender of subjects; time delay between consumption and testing; type of test performed (e.g. tracking, visual function), and the specific tasks (e.g. two-hand-coordination, flicker fusion). Test results had to be coded as 'significant improvement or impairment', at least at the 5% level or as 'no significant change' [19].

Studies in which THC had been taken together with other drugs or alcohol were excluded. Overall, 66 studies in which cannabis had been smoked and 21 with oral intake of cannabis were selected, including laboratory tests, driving simulator and on-road studies. Blood THC concentrations at the time of testing were estimated from the information on THC dose and other factors using the pharmacokinetic model by Sticht & Käferstein [21].

Figure 2 summarizes the key results from the two meta-analyses. For alcohol and smoked cannabis, respectively, each graph shows a set of two 'survival functions'. The respective curves give the percentage of results from all tests that showed significant impairment at a given BAC or THC concentration in serum. One curve represents the original data; the other curve shows the results of linear (BAC) or exponential (THC) smoothing. Comparison of the two graphs thus suggests that a BAC of 0.04% and a serum THC concentration of 4–5 ng/ml

both impair driving related skills by about 30%. Thus, a lower legal limit for the concentration of THC in serum that produces the same level of impairment and possibly accident risk as a BAC of 0.05% would be somewhere above 4–5 ng/ml of serum. Note that the correlation between THC serum concentrations and impairment did not depend on the route of administration of cannabis (inhalation, oral ingestion).

The above comparison lumps together the results from tests for a range of driving-related skills, including automatic and controlled functions. A closer analysis of the respective impact of alcohol and THC on these functions suggests that across the BAC range of 0.05–0.11% an increase in BAC further impairs automatic and controlled functions equally (data not shown). In contrast, an increase in serum THC concentrations beyond 5 ng/ml further impairs automatic functions while performance of tasks requiring cognitive control remains stable up to concentrations of 10 ng/ml [20]. This supports the above-mentioned observations from driving studies that drivers under the influence of cannabis may compensate consciously for some of the impairment of their automatic performance, for example by reducing speed or keeping more distance.

These meta-analytical data are in good agreement with the results of a recent experimental study on the relationship between THC concentrations in serum after smoking cannabis and impairment [24]. First signs of impairment were found at THC serum concentrations in the range of between 2 and 5 ng/ml. This degree of impairment may correspond to the impairment at a BAC of 0.03%, where the impairment by alcohol becomes significant. Because the observation pertains to the entire THC concentration range of between 2 and 5 ng/ml, impairment may have started at a THC concentration between 3 and 4 ng/ml serum.

PROPOSAL FOR A *PER SE* LIMIT FOR DUIC

In summary, current evidence from scientific studies offers the following conclusions on the correlation between THC concentrations in blood and cannabis-induced potential impairment of driving performance. Evidence from the few meaningful epidemiological studies on cannabis use and driving is insufficient for deriving a risk-based *per se* limit for DUIC. While based on too few cases of drivers who had used cannabis and not other drugs, the study by Drummer *et al.* suggests that a serum THC concentration of 12–16 ng/ml may correspond to the same accident risk as a BAC of 0.05% [12]. More culpability studies using a larger number of cases, considering non-fatally injured drivers and conducting accurate and timed measurement of blood THC concentrations are needed for a reliable determination of the accident risks associated with different THC blood concentrations.

Alternatively, experimental studies offer a preliminary basis for *per se* limits for DUIC.

Specifically, the results from a comparison of two meta-analyses on alcohol and cannabis, respectively, suggest that a BAC of 0.04% and a serum THC concentration of 4.2 ng/ml cause comparable impairment of driving-related skills.

When using this equivalency as the basis for a *per se* limit, two areas of uncertainty must be considered. First, for a given time-lapse between smoking and blood testing, the correlation between a smoked THC dose of THC and the resulting THC blood concentration shows considerable inter- and intra-individual variability. According to the pharmacokinetic model of Sticht & Käferstein, which was used in the above meta-analysis to estimate THC blood concentrations, a male weighing 70 kg and smoking a THC dose of 19 mg will, after 3 hours, present with a serum concentration of 4.9 ng/ml with a confidence interval of 3.1–7.7 ng/ml [21]. To minimize false positive test results among drivers with THC concentrations at the upper end of this range without being impaired, a risk-based lower serum limit of 7 ng/ml, rather than 4.2 ng/ml, is thus suggested.

Secondly, enforceable legal limits for DUI must consider the effects of analytical errors made during blood analysis. For example, in Germany, the lower legal BAC limit of 0.05% includes the risk-based limit of 0.04% plus a safety margin for analytical errors of 0.01%. That margin is based on interlaboratory proficiency tests and reflects typical variability. Similar proficiency tests conducted for THC have shown a much larger variation. A recent comparison by the German Society of Toxicological and Forensic Chemistry suggested a suitable safety margin for THC of 3.4 ng/ml [25]. Adding such a safety margin yields a lower THC limit of 7–8 ng/ml in serum (4.2 + 3.4), or 3.5–4 ng/ml THC in whole blood, which corresponds to a lower BAC limit of 0.05%. Other countries, including Australia, ask laboratories to assess accuracy of their measurements and to consider it when comparing results to a legal limit. This allows for differences between laboratories with regard to analytical accuracy. For example, a laboratory with a documented internal accuracy of ±2.5 ng/ml for THC in serum at the measured concentration would report samples exceeding 6.7 ng/ml as in violation of a 4.2 ng/ml *per se* limit. Combining these two correction factors would render serum THC concentrations in the range of between 7 and 10 ng/ml (3.5–5 ng/ml in whole blood) equally impairing as a BAC of 0.05% and suggest that range for the selection of a lower legal limit based on the meta-analysis of experimental studies.

Other modifying factors

Three other potentially modifying factors must be considered when setting legally binding numerical *per se* limits for THC. First, the epidemiological study by Drummer *et al*. suggests that THC concentrations indicate elevated accident risk at levels higher than indicated by experimental studies [12]. This may be due to the more pronounced adaptive behaviours (slowing down, reduced risk-taking) observed with cannabis-affected drivers in driving simulator and on-road studies, both of which represent more closely real-life conductions. In that case, comparison of experimental studies for alcohol and THC, respectively, would result in systematically lower *per se* limits for THC than derived from epidemiological studies.

Secondly, cannabis consumption produces measurable THC residues in blood long after smoking. At 10 hours after smoking residual THC concentrations in the serum of occasional or even frequent users have declined to typically less than 5 ng/ml. The suggested *per se* limit in the range of 7–10 ng/ml safely avoids misclassification of drivers presenting with THC residues from previous cannabis use. It would also spare drivers with low but measurable THC concentrations caused by passive exposure to cannabis smoke or by smoking or oral intake of low THC doses for medicinal purposes [26–31].

Finally, a legal *per se* limit for cannabis must consider that the concurrent use of alcohol and cannabis impairs driving skills more than each drug individually [32]. For drivers presenting with measurable THC concentrations and a BAC exceeding 0.03% or 0.05%, a lower *per se* limit for THC than proposed above may be appropriate.

Using current scientific evidence on cannabis-induced impairment of psychomotor skills and the related accident risk, this paper suggests a range of 7–10 ng/ml THC in the serum for an initial non-zero *per se* limit. It offers reasonably reliable separation of drivers whose driving is in fact impaired by cannabis from those who are not impaired. Inadequate evidence from epidemiological studies renders this limit preliminary and suggests the need for review and possibly revision in the future. Our findings also suggest that using a zero limit for legal determination of impairment by cannabis, which in practice corresponds to the limit of detection for THC in blood, would classify inaccurately many drivers as driving under the influence of, and being impaired by, the use of cannabis.

References

1. Heishman S. J., Singleton E. G., Crouch D. J. Laboratory validation study of drug evaluation and classification program: ethanol, cocaine, and marijuana. *J Anal Toxicol* 1996; **20**: 468–83.
2. Heishman S. J., Singleton E. G., Crouch D. J. Laboratory validation study of drug evaluation and classification program: alprazolam, d-amphetamine, codeine, and marijuana. *J Anal Toxicol* 1998; **22**: 503–14.
3. Skopp G., Richter B., Potsch L. Cannabinoidbefunde im Serum 24 bis 48 Stunden nach Rauchkonsum [Serum cannabinoid levels 24–48 hours after cannabis smoking]. *Arch Kriminol* 2003; **212**: 83–95.
4. Cone E. J., Johnson R. E. Contact highs and urinary cannabinoid excretion after passive exposure to marijuana smoke. *Clin Pharmacol Ther* 1986; **40**: 247–56.
5. Mason A. P., Perez-Reyes M., McBay A. J., Foltz R. L. Cannabinoid concentrations in plasma after passive inhalation of marijuana smoke. *J Anal Toxicol* 1983; **7**: 172–4.
6. Morland J., Bugge A., Skuterud B., Steen A., Wethe G. H., Kjeldsen T. Cannabinoids in blood and urine after passive inhalation of cannabis smoke. *J Forensic Sci* 1985; **30**: 997–1002.
7. Grotenhermen F. Pharmacokinetics and pharmacodynamics of cannabinoids. *Clin Pharmacokin* 2003; **42**: 327–60.
8. Bates M. N., Blakely T. A. Role of cannabis in motor vehicle crashes. *Epidemiol Rev* 1999; **21**: 222–32.
9. Chesher G., Longo M. Cannabis and alcohol in motor vehicle accidents. In: Grotenhermen F., Russo E., editors. *Cannabis and Cannabinoids. Pharmacology, Toxicology, and Therapeutic Potential*. Binghamton, NY: Haworth Press; 2002, p. 313–24.
10. Ogden E. J., Moskowitz H. Effects of alcohol and other drugs on driver performance. *Traffic Injury Prev* 2004; **5**: 185–98.
11. Ramaekers J. G., Berghaus G., van Laar M., Drummer O. H. Dose related risk of motor vehicle crashes after cannabis use. *Drug Alcohol Depend* 2004; **73**: 110–19.
12. Drummer O. H., Gerostamoulos J., Batziris H., Chu M., Caplehorn J., Robertson M. D. *et al.* The involvement of drugs in drivers of motor vehicles killed in Australian road traffic crashes. *Accid Anal Prev* 2004; **36**: 239–48.
13. Borkenstein R., Crowther R. F., Shumate R. P., Zeil W. W., Zylinan R. *The Role of the Drinking Driver in Traffic Accidents*. Bloomington, IL: Department of Police Administration, Indiana University; 1964.
14. Zador P. L. Alcohol-related relative risk of fatal driver injuries in relation to driver age and sex. *J Stud Alcohol* 1991; **52**: 302–10.
15. Laumon B., Gadegbeku B., Martin J. L., Biecheler M. B. Cannabis intoxication and fatal road crashes in France: population based case–control study. *BMJ* 2005; **331**: 1371.
16. Terhune K. W. *The Role of Alcohol, Marijuana and Other Drugs in the Accidents of Injured Drivers*. Technical Report to US Department of Transportation, Calspan Field Services, Inc., 1982.
17. Longo M. C., Hunter C. E., Lokan R. J., White J. M., White M. A. The prevalence of alcohol, cannabinoids, benzodiazepines and stimulants amongst injured drivers and their role in driver culpability. Part II: the relationship between drug prevalence and drug concentration, and driver culpability. *Accid Anal Prev* 2000; **32**: 623–32.
18. Smiley A. M. Marijuana: on road and driving simulator studies. In: Kalant H., Corrigal W., Hall W., Smart R., editors. *The Health Effects of Cannabis*. Toronto: Addiction Research Foundation; 1999, p. 173–91.
19. Berghaus G., Schulz E., Szegedi A. Cannabis und Fahrtüchtigkeit. Ergebnisse der experimentellen Forschung [Cannabis and driving skills: results of experimental research]. In: Berghaus G., Krüger H. P., editors. *Cannabis im Straßenverkehr [Cannabis and Driving]*. Stuttgart: Gustav Fisher Verlag; 1998, p. 73–97.

20. Berghaus G., Krüger H. P., Vollrath M. Beeinträchtigung fahrrelevanter Leistungen nach Rauchen von Cannabis und nach Alkoholkonsum—Eine vergleichende Metaanalyse experimenteller Studien [Impairment of driving-related performance after smoking of cannabis and of alcohol use—a comparative meta-analysis of experimental studies]. In: Berghaus G., Krüger H. P., editors. *Cannabis im Straßenverkehr [Cannabis and Driving].* Stuttgart: Gustav Fisher Verlag; 1998, p. 99–112.
21. Sticht G., Käferstein H. Grundbegriffe, Toxikokinetik und Toxikodynamik [Basic terms, toxicokinetics and toxicodynamics]. In: Berghaus G., Krüger H. P., editors. *Cannabis im Straßenverkehr [Cannabis and Driving].* Stuttgart: Gustav Fisher Verlag; 1998, p. 1–10.
22. Berghaus G. Cannabis und Fahrtüchtigkeit—Relationen zwischen Blutalkohol- und Tetrahydrocannabinol (THC)-Konzentrationen auf der Basis einer Metaanalyse experimenteller Studien [Cannabis and driving skills–Relationship between blood alcohol and THC concentrations based on the meta-analysis of experimental studies]. In: Bundesanstalt für Straßenwesen, editor. *Drogen und Verkehrssicherheit [Drugs and Traffic Safety].* Berichte der Bundesanstalt für Straßenwesen, Mensch und Sicherheit, Heft M 41, Bremerhafen: Wirtschaftsverlag NW; 1995, p. 44–51.
23. Krüger H.-P., Berghaus G., Schulz E., Hein M. *Vergleich fahrrelevanter Leistungseinschränkungen nach Cannabis- und Alkoholaufnahme [Comparison of Impairment in Driving Skills Following Consumption of Cannabis and Alcoho].* Berichte der Bundesanstalt für Straßenwesen, Mensch und Sicherheit, Heft M 41, Bremerhafen: Wirtschaftsverlag NW; 1995, p. 78–82.
24. Ramaekers J. G., Moeller M. R., van Ruitenbeek P., Theunissen E. L., Schneider E., Kauert G. Cognition and motor control as a function of Delta9-THC concentration in serum and oral fluid: limits of impairment. *Drug Alcohol Depend* 2006; **85**: 114–22.
25. Schmitt G., Herbold M., Aderjan R. Wissenschaftliche Bewertung von GTFCh-Ringversuchen für Betäubungsmittel im Blut 2003 [Scientific evaluation of GTFCh- inter-laboratory proficiency tests of narcotic drugs in blood]. *Blutalkohol* 2005; **42**: 20–31.
26. Isbell H., Gorodetzky C. W., Jasinski D., Claussen U., Von-Spulak F., Korte F. Effects of Δ^9-tetrahydrocannabinol in man. *Psychopharmacologia* 1967; **11**: 184–8.
27. Jones R. T. Marijuana-induced 'high': influence of expectation, setting and previous drug experience. *Pharmacol Rev* 1971; **23**: 359–69.
28. Domino E. F., Rennick P., Pearl J. H. Short-term neuropsychopharmacological effects of marihuana smoking in experienced male users. In: Braude M. C., Szara S., editors. *The Pharmacology of Marihuana.* A Monograph of the National Institute of Drug Abuse. New York: Raven Press; 1976, p. 393–412.
29. Lucas V. S. Jr, Laszlo J. Delta 9-tetrahydrocannabinol for refractory vomiting induced by cancer chemotherapy. *JAMA* 1980; **243**: 1241–3.
30. Müller-Vahl K. R., Prevedel H., Theloe K., Kolbe H., Emrich H. M., Schneider U. Treatment of Tourette syndrome with delta-9-tetrahydrocannabinol (delta 9-THC): no influence on neuropsychological performance. *Neuropsychopharmacology* 2003; **28**: 384–8.
31. Chesher G. B., Bird K. D., Jackson D. M., Perrignon A., Starmer G. A. The effects of orally administered delta 9-tetrahydrocannabinol in man on mood and performance measures: a dose–response study. *Pharmacol Biochem Behav* 1990; **35**: 861–4.
32. Sexton B. F., Tunbridge R. J., Board A., Jackson P. G., Wright K., Stark M. M. *et al. The Influence of Cannabis and Alcohol on Driving*. TRL Report 543. Crowthorne: TRL Limited; 2002.

